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MEETING THE CHALLENGES OF ASSESSING CLINICAL TRAINING IN A DIPLOMA AND BACHELOR OF NURSING PROGRAM

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Abstract

Clinical learning is foundational to the Health Sciences University of Mongolia Nursing program. The Discipline of Nursing in collaboration with academics, clinicians and managers, developed an instrument to evaluate contextual learning, involvement and reflection of nursing students during clinical training. The purpose of this paper is threefold: to illustrate the process by which the evaluative instrument was developed, to report the results of the survey, and to explore the positive learning outcomes that might result with the use of the instrument.

Key words: Clinical training assessment, checking list, clinical case, clinical environment

INTRODUCTION

Clinical learning is a significant component of the Nursing program *l\l.* Students are encouraged to actively learn from their individual experiences while on clinical training. Real-life experience is valuable and each experience may be treated as a unique but interrelated learning episode. Within the program, clinical experiences are assessed by the use of a clinical assessment checking list measures the level of competency in the cognitive, psychomotor and affective domains. In particular, the competencies examined include professional and ethical practice, critical thinking and analysis, management of care and enabling, problem-solving, and performance is assessed against a set of standards. Student performance is rated as being independent, assisted, supported, directed or dependent and the descriptors of performance standard are articulated in the clinical assessment tool. Both of student and supervisor discuss and evaluate performance against each competency; areas of strength and further improvement are identified. Reflective checklist is also kept by students and is another method by which students are prompted to think critically about their clinical experiences. Acknowledging that an encouraging and supportive clinical training is conducive to positive learning outcomes, the Discipline introduced recently a clinical training instrument. Essentially, the instrument was designed to measure student satisfaction with the clinical training. Choi & Hannafin (1995) asserted that 'knowledge is situated' and that the transfer of knowledge is not limited to conventional schooling *121.* Learning advances through collaborative social interaction and social construction of knowledge, occurring during schooling and at work. In these settings, knowledge is transformed from the classroom to real-life situations and students begin to put theory into practice and develop self-monitoring skills. Such theories enable us to understand how knowledge is applied in the practice setting, specifically during clinical placements where the

focus is on work-based learning and problem-solving. Learning is continuous and the socialization with clients, nurses, and other health professionals, will further enrich their capacity to interact, reflect, collaborate and value the roles played by professional nurses.

More recently, authors such as Oliver (2002, 2004) have drawn our attention to the trajectory of experience and the context of clinical learning in becoming competent in practice and have debunked the myth that more clinical hours are necessary to assist students in their clinical learning and gaining experience/3-4/. Students in this study reported an increased sense of independence with patient care and satisfying clinical experience when clinical teaching was shared among heads of nursing departments.

In addition to the current ways of preparing students for practice in modern literature there are some innovative approaches. For instance, students might benefit from attending additional sessions, extra-coaching as heeded by Aviram, et al. (1998), the use of clinical challenge or contract, and use of more clinical laboratory simulation, which has been shown to improve transition of theory to practice (Olesinski, Brickell, & Pray, 1998) /5-6/. Directing students to preceptors or clinical supervisors is another strategy suggested by many scholars (LeGris & Cote, 1997; Nordgren, Richardson & Laurella, 1998; & Teasdale, Brocklehurst and Thom, 2001) /7-9/. Preceptors and supervisors are valuable for professional and personal support and instruction (Hawkins &Shohet, 2000)/10/. These mechanisms have been shown to yield more productive and meaningful experiences and increase self-confidence among students. We have taken these ideas on board and working with students to facilitate clinical learning.

Purposes of study:

To evaluate by learners teaching plan, curriculum content and correlation on clinical and non-clinical program.

To study of opinion learners on clinical teaching methodology and teaching technology.

To conduct of sociological study of learners understandings on nursing teaching tools.

MATERIALS AND METHODS

An eighteen-item structured instrument was developed to gather evaluative data. The clinical training evaluation tool was designed to evaluate the general content, methodology of the clinical training and theirs recommendations for improvement clinical training by nursing college students.

Two hundred thirty eight (238) nursing students (110 of whom where diploma students, 127 - bachelor students) were invited to participate in this evaluation activity.

The students were recruited through course coordinators, who distributed the questionnaires. Coordinators explained the aims of the evaluation, the benefits to be derived from the activity, students' and nurses actual involvement. They were assured that their names were not required on the questionnaire and that their names would not appear at any stage of the project including collecting, analyzing and reporting of data.

Statistical analyses were performed with SPSS 11.5 for Windows. The mean percentage values of the changes calculated using Mann-Whitney U tests.

RESULTS

Our clinical training and health facilities provide our students with the necessary clinical experience to prepare them as nurses. Through the evaluative process, clinical instructors can better facilitate student learning in a variety of areas because there is tangible evidence supporting students' learning. Evaluations provide students with the opportunity to reflect and examine issues of practice, enabling them to focus on particular issues or concerns, e.g. adequate orientation to the workplace, availability of assistance from staff members and so forth. Moreover, training evaluations allow students to express their general satisfaction or dissatisfaction with clinical training. Summary of the results of student responses is shown below.

Table 1. Clinical training evaluation

		Respouse i perceaugc) '238 siudents
1	clinical training was a pleasant learning experience	94 * 1,53
2	clinical training provided good earning opportunities for getting clinical skills	79 8 ± 2.6
3	On a basis of pre-medical training student was well prepared for the clinical training	66 8 ± 3.05
4	Nursing students have enough n-.odern books, handbooks for the clinical training	30 3 ± 2,98
5	Clinical placement, working witi reai patients' most effective assisted student learning	34 ± 3.07
6	Clinical laboratory simulation. rr.odels. dolls, videotapes useful for transition of theory to practice	66 ±3.07
7	Amongthe clinical training menods such as classroom discussions. working with textbooks, interne[1], sources clinical placement more enhanced clinical knowledge ana skills	84 4 ±2.35
3	For the improving quality of clinical training most important to improve training environment	

The responses to the instrument showed that the majority of students' impressions about clinical training were favorable. Most important is that the students believed they learned.

The health facilities were supportive of learning, professional growth, skills development and practice. Having been exposed to a wide range of clinical experiences, many of the students reported that they met their objectives, felt confident about working in the same area in the future.

Results of this survey showed that the majority of students perceived their clinical training as rich in learning experiences but 33.2% of students reported dissatisfaction with a basic premedical training which have to prepare them for the clinical training. They fined that don't have enough basic knowledge to understand some clinical disciplines.

Majority, 74.8% of nursing students reported that for the improving quality ofclinical training important to improve training environment by supplying with Clinical laboratory simulation technology, models, dolls, videotapes. Also there's a shortage of modern books, handbooks for the nursing clinical training. Among the clinical training methods such as classroom discussions, working with textbooks, internet sources clinical nursing placement training was the most enhanced clinical knowledge and skills method reported 84.4% of students.

One of the deficiencies identified by students was the feeling of being inadequately prepared for clinical placement practice. This is an important aspect that was identified by some 22% of students. Student concerns about preparation, confidence and expectations about what they can do or cannot do need to be examining. Hence, in addition to the current ways of preparing students for practice, some innovative approaches of student assessment as method of training may need implementation.In our survey we have done evaluation of today's student's clinical knowledge and skills assessment methodology using in Darkhan, Dornogobi, Ulaanbaatar Nursing schools.

Table2. Students clinical knowledge and skills assessment method evaluation

To assess students clinical knowledge recently more often using multiple choices tests in 22.3 %, Essay in 0.4 %, Oral tests in 2.9 %, Mix method in 74.4%.To assess students' clinical skills more often using Practical nursing activities assessment in 28.2%, Clinical cases in 5.9 %, Essay in 6.7%. Assessment for students' clinical skills using 'special developed checklist' were done only in 33.2 %. Assessment for students' clinical skills using 'special developed Clinical cases' were also only in 32.8%.

DISCUSSION

Clinical training is facilitated by the collaboration of the university, health facilities and student. Lave and Wenger (1991) argue that learning is a function of the 'activity, context and culture' in which it occurs /l 1/. Results of this survey also showed that the 84.4% of students reported that among the clinical training methods such as classroom discussions, working with textbooks, internet sources clinical nursing placement training was the most enhanced clinical knowledge and skills method of students. Majority, 74.8% of our nursing students reported that for the improving quality ofclinical training important to improve training environment

by supplying with Clinical laboratory simulation technology, models, dolls, videotapes. The current studies surrounding clinical teaching and learning in nursing are directed at providing nursing students with positive clinical training experiences and facilitating the meeting of goals and expectations. In order to enable students to experience learning-by-doing, curriculum changes may be required and learning gained in service areas formalized. MacLeod and Farrel (1994) warn us of the need to revise structural and power relationships between education and practice /12/. They talk about a practice-driven approach, which should be the central theme of curriculum change. Powerful economic forces are driving systems of higher education to implement change, according to Myer (1999)/13/. Myer suggests the need to develop an outcomes-based educational delivery system. The most important performance indicator is to determine whether or not students have learned. This is an important aspect that was identified by some 22% of our nursing students. Student concerns about preparation, confidence and expectations about what they can do or cannot do need to be examining. Hence, in addition to the current ways of preparing students for practice, some innovative approaches of student assessment as method of training may need implementation. In conclusions. there is a definite need to develop core curriculum of bachelor degree in Nursing and nursing diploma program. Also it is necessary to develop and improve teaching technology and methodology of nursing according to the demands of students and international requirements. It's the essential to develop of content of diploma and bachelor of nursing program curriculum by depending from different tasks of graduates and nursing processes with enrichment of new health sciences accomplishments.publishing new handbook and textbooks for students, according to current practice requirements and international standards and establishing Nursing Skill Laboratory is demanded by students.

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CLINICAL CORRELATES OF GALLSTONE COMPOSITION

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Abstract

The prevalence of cholelithiasis has been established in population-based surveys employing ultrasonography, and major risk factors have been identified. However, the clinical and epidemiological features that distinguish patients with pigment stones from those with cholesterol stones have received little attention. We respectively surveyed 150 patients undergoing cholecystectomy for gallstone disease at State University Hospital of Ulaanbaater. Clinical and epidemiological data were collected during patients interviews and by chart review. Gallstones were collected at surgery, physical measurements were recorded, and stone composition was determined by visual inspection and X-ray diffractometry. Patients with pigment stones were older than patients with cholesterol stones ($p<0.01$). Almost all patients under age 50 years old had cholesterol stones, but most patient over 61 had pigment stones. Patients with pigment cholilethiasis had stones that were generally smaller in diameter and fewer in number than those with cholesterol stones.

Key words: Gallstone disease, body mass index, X-ray diffractometry

INTRODUCTION

According to epidemiological studies, gallstone disease (GSD) is a very common disease in the United States and Western world. A report on the finding appears in the latest issue of American Journal of Epidemiology about one in 10 men and one in five women will develop gallstones /l -4/. The number of patients with gallstone disease increases during the last 15 years. According to data from the Health Statistical Information (2005), the incidence of gallstone disease and chronic cholecystitis in the Mongolia has increased by 1.73 times in the period of 1991 -2005*151*. The population-based surveys have more precisely determined the principal risk factors for cholelithiasis, among them advancing age, female gender, obesity, childbearing, racial and ethnic heritage and abstinence from alcohol *161*. However, most epidemiological studies have failed to acknowledge that gallstones are heterogeneous in chemical composition. Cholesterol gallstone develops in a setting of bile cholesterol super saturation and crystal nucleation. Pigment gallstone, whose etiology is poorly understood /7-8/. Because, these gallstone types differ in composition, thus possibly in pathogenesis, their risk factors are unlikely to be identical. Cholesterol stones predominate, it is assumed that risk factors identified in epidemiological surveys apply primarily to such stones. Pigment gallstones have been linked to advancing age, chronic hemolytic disease, cirrhosis, biliary tract infection, and possibly alcoholism /9-10/.The pathogenesis of cholesterol and pigment gallstones is not similar. We therefore have used data from a surgical experience to compare the clinical and socio-demographic characteristics of patients undergoing surgery for pigment gallstones with those of patients with cholesterol and mixed patients. In addition, we have compared the physical characteristics of the stone recovered at

surgery in relation to their composition.

MATERIALS AND METHODS

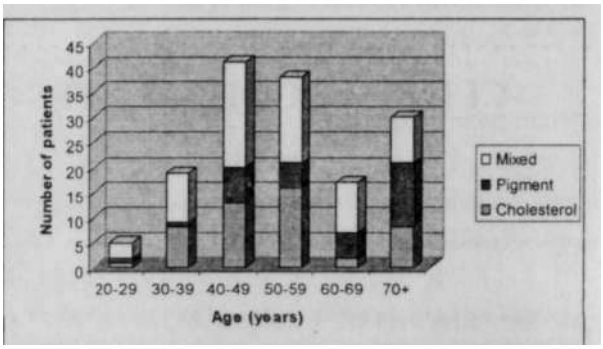
We prospectively surveyed 150 patients undergoing cholecystectomy for gallstones at the State University Hospitals of Ulaanbaatar city between September 2000 and April 2003. Clinical data were collected by inpatient review. After surgery, each subject's gallstones were collected and stored in the room temperature. We later counted the number of stones in each vial, determined their weight, described their shape and color, and measured the diameter of each subject's smallest and largest stone. Stones from 80 subjects, or 53.3% of the total sample were ground to a powder and analyzed for cholesterol and calcium bilirubinate content by X-ray diffractometryll. Most cholesterol stones had cholesterol acetate, cholestanol and cholanic acid and pigment stones had predominated with calcium bilirubinate, phosphate and more ferrum and copper content. Mixed stones were cholesterol cholanic acid and calcium bilirubinate, palmitate and quartz.

For statistical analysis, the SPSS 10.0 version for Windows, we used. For categorical variables, differences between patients with pigment gallstones and those with cholesterol stones were assessed with the corrected *c2* test, Student's / test was used for continuous variables. For variables with highly skewed distributions, nonparametric tests were used. Statistical significance was defined as a two-sided p< 0.05. The values are expressed as mean ± SD.

RESULTS

Total of 150 patients were enrolled in this study and 119 (79%) were women. Their median age was 51. Approximately 59% of the patients underwent surgery for treatment of chronic calculus cholecystitis, and the 26% for the biliary colic, and the other because of acute cholecystitis or common bile duct stones. By visual inspection, 32 (18%) patients had cholesterol gallstones at surgery, and 32 (21.3%) had pigment stones, and 70 (46.2%) patients had mixed type. Patients with pigment gallstones were significantly older than patients with cholesterol and mixed stones (60.8 ± 14.8 years vs. 52.2 ± 13.3 and 51.7± 12.7, (p< 0.005). The age distribution of study patients is displayed in Figure 1. The greatest number of cholecystectomies was performed in patients with 40-49 years old.

Figure 1. Number of patients with cholesterol, pigment and mixed type of gallstones according to 10 year age groups



Most patients over age 60 had pigment stones. The relationship of pigment stones to advancing age was statistically significant for the total sample and for each gender (p<0.001). Obesity is a well established risk factors for gallstones, we compared the mean body mass index [BMI calculated as weight in kilograms divided by height in meters squared] in patients with gallstone types (Table 1).

Table I. Body mass index, parity and alcohol use in relation to gallstone composition (Mean ± SD)

Mean BMI values were moderate for both gallstone types in both sexes, but no significant differences were observed. Increased parity has been found to be a risk factor for gallstone in most studies. However, mean parity did not differ between women with cholesterol, pigment and mixed stone. Results with respect to alcohol use, presented in table 1 indicate a significant relationship of gallstone composition to drinking pattern for men (p< 0.05). We compared the physical characteristics of the gallstones recovered at surgery with respect to their composition. Patients with pigment and mixed

cholelithiasis had fewer stones than those with cholesterol stones. Moreover, we observed a trend between stone number and composition, such that patients with fewer stones more likely to have pigment than cholesterol and mixed stone (p< 0.007) (Table 2).

Table 2. Gallstone size and number, weight an color in relation to stone composition.

Nixnbeiofsfor*-;			
1	23(32 1%)	9(36 1%)	4(5 716)
2-«	-coos*)	ocean)	i3<iso%)
3-19	0(123%)	9(261%)	19(2? 1%)
i20	7(1<0°*)	8(25%)	34(48 0%)
Store SCB (mm)			
<5	BCB7%)	8(250%)	14(200%)
5-9	3(104%)	9(281%)	33(47 1%)
tJ-19	0(31 3%)	12(37 3%)	19(27 1%) 0023
2D-29	-0(313%)	2(0 3%)	4(3 7%)
• 30	3(10 4%)	1(3 1%)	
GjIBla* wo-gMigr	3 9 1 2 3	23*. 13	2 5 : 1 8 0GOOB
color			
whloVgioy	25 (321%)		13 (214%)
t-own	7(140%)	22(0B8%)	38(343%)
bock		*0(313%)	2(29%) 0000
mown	14(29 2%)		15(214%)
gnMn	2(4 2%)		

We compared the physical characteristics of the gallstones recovered at surgery with respect to their composition. Patients with pigment and mixed cholelithiasis had fewer stones than those with cholesterol stones. Moreover, we observed a trend between stone number and composition, such that patients with fewer stones more likely to have pigment than cholesterol and mixed stone (p <0.007) In addition, pigment stones were generally smaller than cholesterol and mixed stones (mean diameter of largest pigment stone 9.3 ± 4.6 mm versus 16.5 ± lO.l mm and 10.4 ± 6.2, p=0.023).Total stone weight was greater in patient harboring cholesterol stones (median 3.9 gr vs 2.3 g and 2.5 gr, p< 0.0006). Finally, pigment stones were significantly more often described as triangle in shape and brown color than cholesterol stones, which were most often characterized as mulberry or oval in shape and white, grey or yellow in color (p= 0.000).

DISCUSSION

The principal findings of this study is that pigment gallstones are more strongly associated with advancing age than cholesterol and mixed type stones. Our results also indicate that patients coming to cholecystectomy for pigment gallstones have both fewer and smaller stones than those with cholesterol and mixed cholelithiasis. Our findings demonstrate that pigment stones are primarily a disease of the elderly and are rare in persons under age 40. Factors underlying the association of pigment stones with advancing age arc poorly understood. Obesity is an important risk factor for cholelithiasis, we found no differences in body mass index between patients with pigment stones and those with cholesterol, mixed types. Van Erpecum et al (1988) similarly found no relationship of the stone composition to body weight. Trotman and Soloway (l 975) found that those with pigment stones were leaner than those with cholesterol stones, but did not account for patient age or sex in their analysis.Parity, another generally accepted risk factor for cholelithiasis, was not significantly related to stone composition in our analysis, although multiparity was associated with cholesterol stones in a report from India/I3/.In contrast, Trotman and Soloway (1975) found alcoholism to be equally common in patients with pigment and cholesterol stones. We found significant relationship between a history of alcoholism and pigment cholelithiasis.Kaufman et al (l 994) found no significant differences in stone number between patients with pigment and cholesterol cholelithiasis, but did not report data on stone diameter. We found significant relationship between number and size of gallbladder stones and their composition. Sarin et al (1986) reported that patients with pigment disease were more likely to have solitary stones.In conclusion, compared to patients with cholesterol and mixed gal Istones, those with pigment stones are older and their stones are smaller in size and fewer in number than those from patients with cholesterol cholelithiasis. Advanced age is associated with pigment stones.

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INTERFERON ALPHA 2 A AND THYMUS FACTOR TREATMENT OF ADULTS WITH CHRONIC HEPATITIS C AND ITS IMPACTION ON LYMPHOCYTES SUBPOPULATION

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Abstract

Chronic HCV infection results in the induction of a strong humoral immune response. We recently described study of impaction on lymphocytes subpopulation during interferon treatment. Aim was to evaluate effect of the interferon alpha 2a and thymus factor combination treatment in adults with chronic hepatitis C and its impact on blood lymphocytes subpopulation. Study period is a one year and involved 36 patients with chronic hepatitis C.

Key words: hepatitis, interferon, thymus factor, subpopulation, lymphocyte

INTRODUCTION

The research intends to evaluate effect of the interferon alpha 2a and thymus factor combination treatment in adults with chronic hepatitis C and its impact on blood lymphocytes subpopulation. Chronic hepatitis caused by hepatitis C virus is the challenge for the modern medicine. Inflammation of the liver caused by this infection leads to cirrhosis and cancer of this organ /l,2,3,4/. Mechanism, by which hepatitis C virus affects the immune system, is still not clear and that attracts high attention of researchers. Currently, effectiveness of the interferon and ribavirin combination treatment is 50-70%. Since this combination has contraindications in some cases, a search for a new, an effective and safe treatment option is continuing.

MATERIALS AND METHODS

Thirty six patients (16 female, 20 male) with age 21-63 years old were involved in the study. Specimens with viral genetic material samples were taken from the each patient through liver biopsy and RT-PCR molecular biological method.

The interferon alpha 2a and thymus factor combination treatment was conducted during 24 and 48 weeks. Clinical examination and detailed blood tests were regularly conducted for monitoring of the results during course of the treatment. Count of lymphocytes was conducted before and on 12.h or 24.h week of the treatment course.

Specimens with viral genetic material samples were taken on 12'", 24lh week of the treatment course and 6 months after, using RT-PCR method. Liver biopsy and serum clearance 99 m Tc Hepidy test were conducted before and after the treatment. CD3+, CD19+, CD 4+, CD8+, CD3+/DR and NK were identified in blood lymphocytes subpopulation. All patients involved in the study were divided into two groups based on the presence or elimination of HCV-RNA in the serum 6 months after the treatment:

- Group 1: HCV-RNA negative;
- Group II: HCV-RNA positive.

120 patients were taken as a control group! Shapiro-Wilk, Fisher, T-Student, U MannaT-Tukey criteria and Kruskall-Wallis methodology' were used for the statistical analysis.

RESULTS

Table 1. Increase of ALT level in whole study group

Study period	ALT level	
	normal	**Increased**
Before treatment n=36	**0 (0%)**	**36 (100%)**
12 week, treatment n=36	**21 (58,3%)**	**15 (41,7%)**
24 week treatment n=36	**15 (41,7%)**	**21 (58,3%)**
6 months after treatment n=36	**12 (33,3%)**	**24 (66,7%)**

Table 2. Normal ALT level in group I and II /patients number/

Study period	Normal ALT level	
	group I n=10	group IE n=26
Before treatment n=36	0	0
12 week treatment n=36	7	14
24 week treatment n=36	7	2
6 months after treatment n=36	10	**2**

Table 3.Results of HCV-RNA identification in whole study group

Study period	Results of HCV-RNA	
	negative	positive
Before treatment n=36	0 (0%)	36 (100%)
12 week treatment n=36	22 (61.1%)	14 (38,9%)
24 week treatment n=36	19 (52,8%)	17 (47,2%)
6 months after treatment n=36	10 (27,8$_v$%)	26 (72,2%)

Table 4.Results of HCV-RNA identification in group I and II

Study period	HCV-RNA negative	
	group I n=10	group n=26
Before treatment n=36	0	0
12 week treatment n=36	10	12
24 week treatment n=36	10	9
6 months after treatment n=36	10	0

Table 5. Results of serum clearance 99 m Tc Hepidy test conducted before and after the treatment course in group I and II

Tc Hepidy test Ml/mm/l 73m^2	Before treatment	Confidence interval	After treatment	Confidence interval
group In=10	161.17i41.29	96.00-243,00	207.00*41,29	160.00-240.00
group **n** n=23	159.90*49.81	88.00-284,00	168.74*38.86	112.00-239.00

Table 6. Results of pathohistological studies conducted before and after the treatment in whole study group

Ittttf**"*	Before treatment	After treatment
Grading/ necrosi£-i^mattion/	2,33±0,68	2.10±0.g4
Staging/ fibrosis/	U H M 2	2.33±0.63

Table 7. Results of pathohistological studies conducted before and after the treatment in group

Histopathologic*) study n=l 0	Before treatment	1 After treatment
Gradffig/ necrosis- in flamaUion	2.10±0,74	1,40*0.70
Staging/ fibrosis/	2,43±0,64	2,38±0,74

The majority of researches concluded that in patients with continuing reaction to virus were observed improvement in histology *15, 61*. But, Shiffman et al (1998) concluded in their studies that

in patients treated with interferon viral infection and histology' are correlated. All researchers noticed that after treatment in HCV-RNA negative patients, necrosis of the liver tissue inhibited, which is same in HCV-RNA positive patients. HCV-RNA didn't disappear during the treatment but Alric et al (2000) observed interesting fact that transaminase levels become normal. In HCV infection, the involvement of immunological reactions against HCV has been implicated in the pathogenesis and progression of liver diseases. Many researchers concluded that CD3+, CD19+, CD 4+, CD8+, CD3+/DR and NK are at normal level during hepatitis C virus infection .'9,10,11,12/. But according to some researchers CD3+, CD19+, CD 4+ and CD8+ levels are decreased /13/. It has been reported that cytotoxic lymphocyte might be involved in liver inflammation or the reduction of viral load in infected patients. Some researchers have reported that patients who showed strong HCV-specific helperTcell responses eradicate HCV after initial exposure. In contrast, patients who display only a weak T cell response show a tendency to develop to the chronically infected state. Some plausible explanations exist for such poor T-cell response against HCV. First, the amount and immunogenic potential of HCV antigens may not be enough to induce adequate immune responses. Second, the functions of T cells may be altered in hepatitis C patients /14/.

In conclusion, the interferon alpha 2a and Thymus Factor viral combination treatment resulted in elimination of the virus reaction in 10 (27.8%) of the 36 patients with chronic hepatitis C. Improvement of biochemical tests indicators, inhibition of liver necrosis and invasion of the sclerotic tissue processes were observed as a result of the interferon alpha 2a and Thymus Factor combination treatment. Levels of CD3+, CD 19+, CD 4+ subpopulations of lymphocytes were decreased during the course of treatment, and CD4+, CD8+, CD3+/DR and NK levels were fallen. Number of NK cells with virus elimination was increasing after 24 weeks compare with levels before the treatment and with NK levels were higher compare with group with no virus elimination, which are important indicators for further prognosis.

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DETERMINATION OF THE EFFECTIVE WAY OF FIXATION OF MANDIBULAR FRACTURE WITH DISSPLACEMENT

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Abstract

In this study we tried to find the best solution of fixation of concrete type of fracture. Due the purpose we selected three methods of osteosynthesis; two wire types and one type of miniplate. Pre and postoperative conditions were examined, xray films were used for the comparison of the treatment results. According to results we suggesting that in case of horizontal or vertical fracture miniplate is the more efficient method of fixation of fragments.

Key **words:** Osteosynthesis, miniplate, mandibular fracture

INTRODUCTION

The one of the most often occurring traumas in maxillofacial region is the mandibular fracture. By investigation of Plechoki (1983) the number of patients with mandibular fracture at the hospital and outpatient clinic increases annually 10-15 percents. Last years (Ellis 1991, Jurjen 1999) the broad applications of miniplate l,0-2,0mm wide with screws were used to adjoin the osseous tissues in the mandibular fracture osteosynthesis /3-6/.

The finding the appropriate and efficient way of mandible fracture treatment was unsettled in our country and it was the clue to perform this investigation.

MATERIALS AND METHODS

In 1999-2003, at the Maxillofacial surgery clinic of the National Central Clinical Hospital from 154 patients with mandible angle fracture diagnose 52 cases were treated by miniplate osteosynthesis.

Surgical method

1. The surgical area under general anesthesia will be sterilized by the way of rubbing thrice with spirit-iodine then the surgical area will be separated with sterile matter.
2. 1.5-2 cm off from mandible comer will be shape of 4.5cm long that borders with corner of mandible. Further by the blunt way with assistance of mosquite will be separated each strata of muscle and fascia timely stopping the wound. Upon reaching periosteum it will be cut by scalpel and by assistance of a straight raspator exfoliated from related bone. Upon releasing the clutched muscle and fascia the fracture line will be uncovered.
3. After the fracture reposition by placing miniplate and forming outlets with the same diameter at-the external plate of bone it will be fixed with 2mm screw on 4 places.
4. The wound will be bathe with 0.02 percent furacillin, fascia and muscle covered at each strata with Vecril 3.0 and the skin with plane 5.06. Drainage and aseptical bandage.

Figure 1. Mandible fracture with displacement: condition by which the small body of fracture is displaced above and outside

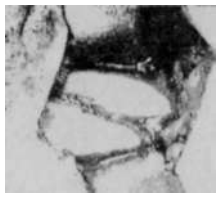


Figure2. Condition of mandible condition by which the small body of fracture is osteosynthesis by miniplate displaced above and outside

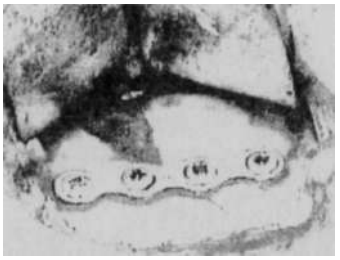
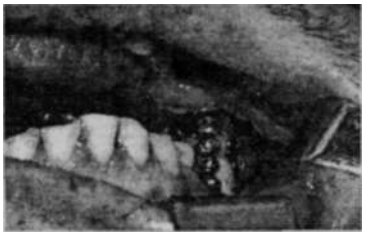


Figure 3. Minor fragment of mandibular fracture lufte up

Figure 4. Intraoral osteosynthesis by miniplate method



RESULTS

We carried the investigation by comparing results of osteosynthesis with miniplate of 52 patients treated during 1999-2003 at the Maxillo-facial surgery clinic of the National Central Clinical Hospital.

Table 1. Indices of results comparison of operations by way of osteosynthesis with wire and by miniplate

1999	29	2	£4	0	0	25	672	5	20	2	64						
200C	28	14	50 0	3	2!	7	25 0		0		25 0						
2001	30		466		14	6	20 0		0		33 4						02
2002	35	8	22 8	1	01	5	14 4	1	28	22	628						04
2003	32	13	40 6	1	07	3	25 0	0	0	11	344						0
1	154	51	332	7	13	51	33 2	6	11	52	33 6	3	0!				

According to the results of investigation, the complication occurrence in patients with mandibular fracture as osteomyelitis in combined wire method was 1.3%, in "X"wire method 1.1%, in miniplate 0.5%.

DISCUSSION

From 52 patients that were operated and treatad by miniplate the 99.5% were recovered initially in 7-8 days. The results of our investigation quite similar to the results of other researchers including Gerhard Undt, Christtian Kermer and Edward Ellis III /4-6/.13 subjects have had osteomielitis complication from 102 patients treated by wire osteosynthesis. By clinical study (1978-1979) done at Emergency Ambulance of Stomatology of Moscow, 4 subjects had osteomielitis from 85 patients treated by wire osteosynthesis, therefore in compare our data is negative different.In the group treated by miniplate, from 52 patients 3 subjects complicated by osteomielitis, which is similar to the results of clinical study (1988-1991) done at Health Center of Texas, USA, where from 52 patients 4 subjects complicated.Ellis at al (2000) reported that the complication percentage ofminiplate osteosynthesis was 7.5, which is higher in compare to our results. This high level of complication was the consequence of severe fracture and already contaminated soft tissues. Due to miniplate technique these complication was not more severe, then it could be.

In conclusion, the miniplate treatment is effective for the fixation of the mandibular fracture, particularly in horizontal and vertical types (99.5%). The complication of mandibular fracture osteosynthesis in wire type was 2.4 %, in miniplate type 0.5 % , therefore the treatment by using miniplate osteosynthesis is the most effective treatment.

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CORONARY ARTERY DISEASE RISK FACTORS AND THEIR RELATIONSHIP WITH THE ENDOTHELIAL DYSFUNCTION AMONG MONGOLS

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Abstract

The inflammatory process plays a key role in coronary artery disease initiation, progression, and complication. The inflammatory response in large vessels involves the up-regulation of vascular adhesion molecules such as vascular cell adhesion molecule (VCAM)-l and E-selectinand inflammatory cytokines such as TNF, IL-1, or IL-6. A healthy endothelium plays a core role in cardiovascular control. Besides its regulatory functions on vasomotor tone and blood flow, endothelial NO is known to inhibit the platelet activation and modulate migration and growth of the vascular smooth muscle. Unfortunately, none of related studies has been done in Mongolia at the molecular level. Thus, the main goal of this study was to determine the prevalence and means of risk factors for CAD in Mongolia. 60 patients with macroangiopathy and 60 healthy controls were enrolled in the study. Serum mean NO values were (17.2±9.8) uM in the CAD patients and (19.6± 12) |.iM in the healthy controls without any statistical significance. In addition, serum NOx levels was not associated with presence of plaques (r=^-0.111), but significantly correlated with soluble VCAM-1 (r=-0.384) and triglyceride level (r=0.544). Levels of sVCAM-1 showed a strong correlation with IL-1. In summary, among Mongols, pathogenesis of atherosclerosis is might be mostly explained by inflammation mechanisms in addition to traditional risk factors such as age, family history of CAD, gender and dyslipidemia.

Key words: atherosclerosis, inflammation, endothelial dysfunction, sVCAM-1, **IL-1** and NO.

INTRODUCTION

In 2005, about 35 million people died due to non-communicable diseases and this contributes to 60 percent of the world mortality rate. From all the non-communicable diseases, cardiovascular disease, diabetes and cancer contribute currently about 60% of deaths and 43% of the global burden of disease *111*. Major change in vessel, atherosclerosis which causes the most cardiovascular diseases, is the one of the leading cause of death and disability in the world itself. For example, atherosclerosis of the coronary artery commonly causes myocardial infarction and angina pectoris, which kills 7 million people annually where as atherosclerosis of the arteries supplying the central nervous system frequently provokes strokes and transient cerebral ischemia. which kills nearly 6 million people every year *131*.

Since the beginning of 1990s the mortality pattern shows a rapid epidemiological transition in Mongolia. In recent years the incidence of cardiovascular diseases and injuries is increasing steadily, and they remain as leading causes of population mortality. Cardiovascular diseases - from country average of 86.2 per 10'OOO in 1980 to 479.39 per 10'OOO in 2003 and from capital city average of 54.5 per lO'OOO in 1980 to 409.84 per lO'OOO in 2003/4/. Thus, the death from heart infarction and stroke is increasing year by year and atherosclerosis is becoming as one of the most frequent causes of

death and disabling symptoms worldwide, including Mongolia.

The exact pathogenesis of coronary atherosclerotic disease is not clear, and no single theory adequately explains the atherosclerotic process. Two main explanations have been proposed: the lipid hypothesis and the chronic endothelial injury hypothesis. Immunologic, inflammatory, viral, chemical, mechanical, and behavioral factors including lack of physical activity play important role in the development of atherosclerosis. Thus, atherosclerosis is the multifactorial process and some researchers have notified that genetic influences play major role in the development of atherosclerosis *151.* The inflammatory process plays a key role in coronary artery disease initiation, progression, and complication. One of the best studied of the inflammatory stimuli is oxidized low-density lipoprotein (LDL) which can damage endothelial cells and induce plaque formation *161.* However, it is likely that other mediators are also involved, some of which may be of infectious origin. This point is strongly reinforced by findings that markers of systemic inflammation such as serum levels of C-reactive protein, IL-1 and TNF represent significant risk factors for atherosclerosis 6-7/. The inflammatory response in large vessels involves the up-regulation of vascular adhesion molecules such as vascular cell adhesion molecule (VCAM)-l and E-selectin and inflammatory cytokines such as TNF, IL-l,orIL-6/7-8/.

VCAM-1, Selectins, eNOS and NO represent an important group of genes implicated in the pathogenesis of atherosclerosis, for which regulation is associated with oxidative stress through redox-sensitive signals and transcriptional factors /8-9/. A healthy endothelium plays a core role in cardiovascular control. In the endothelial cell, nitric oxide (NO) is synthesized by the endothelial nitric oxide synthase (eNOS) encoded by a 26-exon gene (NOS 3) located on chromosome /10/. Besides its regulatory functions on vasomotor tone and blood flow, endothelial NO is known to inhibit the platelet activation and modulate migration and growth of the vascular smooth muscle. Indirect evidence suggests that alterations of the NO pathway might lead to endothelial dysfunction and atherosclerosis *l\\l.* Expression of VCAM-1 occurs particularly in the neovascular endothelium and is strongly associated with increased intimal leukocyte accumulation /12/. Therefore multiple pathways contribute to accelerated coronary atherosclerosis in diabetics and nondiabetics, including increased oxidative stress and inflammatory burden /5-13/.

Unfortunately, none of related studies has been done in Mongolia at the molecular level. Therefore, the clarification of precise multifactoral pathways and their relationship with the endothelial dysfunction represent an important paradigm for understanding the pathogenesis of atherosclerosis and the development of future therapeutic treatments and it is essential to determine which pathway play significant role in the development of the atherosclerotic changes in Mongolian population. Thus, the main goal of this study was to determine the prevalence and means of risk factors for CAD in Mongolia. Also we aimed to evaluate possible leading mechanism of the atherosclerosis development among Mongols.

MATERIALS AND METHODS

Subject population

60 patients with macroangiopathy (43 males and 17 females; 45.47 ±9.10 years old) and 60 healthy controls (15 males and 15 females; 44.71 ±9.14 years old) were enrolled in the study. Information regarding the clinical background and the angiography reports were obtained from the Cardiology Department of Shastin Memorial Hospital. Cardiomyopathy, serious organ disease, systemic illness, chronic alcohol abuse and/or serious psychiatric disorder in all of the subjects and pathological electrocardiographic Q waves, hypertension (blood pressure> 140/90 mmHg); diabetes mellitus (type 2), fasting glucose level>7.77 mM, and family history of vascular disease specifically in the control group were the applied exclusion criteria. Controls were selected at the same hospital during ultrasonic dopplerography study and health examination. Patients were also evaluated according to the atherosclerotic risk factors, including hypertension, diabetes mellitus (type 2), hypercholesterolemia and smoking. All participants confirmed the use of data for research

purposes via written informed consent. Ethical approval was received by the Human Study Committee, Ministry of Health. The detailed characteristics of patients and controls were listed in Table 1.

Blood samples

Blood was drawn from all study subjects under standardized conditions before coronary angiography was performed. All samples were placed into vacutainer tubes with or without 2 mg/ml disodium ethylenediaminetetraacetic acid (EDTA). Serum samples without disodium EDTA were centrifuged within 30 min, at 1200 *g* for 5 min, and divided into two aliquots. One aliquot was stored at -20 °C for the NO measurement. Another aliquot was immediately used for routine biochemical assays. Blood samples with disodium EDTA were used for the analysis of VCAM and **IL-1.**

Laboratory analysis

Venous blood were collected by standard venipuncture using vacutainer tubes (EDTA) after a 12-hour fast from all subjects. Serums were extracted following 10-min centrifugation in a bench centrifuge at 2500 rev/min and stored at -20°C until assayed. Plasma levels of triglycerides, cholesterol, LDL, HDL, creatinine, hemoglobin, fasting glucose and albumin were determined with laboratory standard techniques in Clinical Laboratory of Shastin Memorial Hospital. Serum levels of the VCAM-1 and IL-1 were measured by an enzyme-linked immunosorbent assay (ELISA) using commercially available standard kits *(Quantikine human sVCAM-1; IL-lbetta Research & Diagnostic Systems, USA)* in Microbiology and Immunology Laboratory of the HSUM. Serum NO, and NO," levels were measured by the Griess reaction *(Quantikine human Nitic Oxide, R&D Systems, USA)* as followed with manufacturer's protocol. The assay was reliable and reproducible with inter-assay and intra-assay variation coefficients of 3.4% and 4.0%, respectively.

Coronary Angiographic Analysis

Images ofthe coronary tree were obtained in routine standardized projections with the digital Hitachi HD1520TM, Philips TV monitoring system for the angiographic diagnostic. Percent diameter reduction of a coronary stenosis was calculated by comparing the minimal stenosis diameter to the diameter of the reference segment (an angiographically normal segment proximal to the lesion) measured in millimeters.

Doppler ultrasound examination

All participants' extra-cranial vessels including common carotid artery, external carotid artery, internal carotid artery, proximal part of subclavian artery and vertebral artery, were checked on both side of the participant for any atherosclerotic change by Multi-Dop® T (Compumedics Germany GmbH, The DWL^{K}Doppler Company, Germany).

Statistical analyses

Statistical analyses were made by SPSS-14. Differences between the means ofthe groups were analyzed by Student's / test. Correlation between the CAD, serum NOx, VCAM-1, IL-1 levels and other parameters were analyzed by statistical values were evaluated by two tailed significance and $P<0.05$ was considered statistically different. The data were shown as mean ± SD.

RESULTS AND DISCUSSION

Baseline Characteristics of Study group

Demographic and clinical data of patients with and those without rapid CAD progression are presented in Table 1. There were no significant differences in family history of cardiovascular disease, treatments,or standard biochemical results on total Cholesterol and LDL cholesterol between groups.

However, history of stable angina was more frequent in patients with macroangiopathy. We analyzed a total of 46 lesions (mean, 1.53 per patient); 24 (52%) were located in the left anterior descending coronary artery, 10 (21 %) in the circumflex coronary artery, and 12 (27%) in the right coronary artery with angiography. In Doppler ultrasonography examination, 90% of lesio'ns are located in the bifurcation of left subclavian artery. The baseline biochemical results of patients with and those

without macroangiopathy are presented VCAM-1, IL-1 and Triglyceride levels were significantly increased in case group compared with controls. There were significant differences between study groups in age, mean of blood pressure and level of inflammatory molecules (p<0.05). The body mass index significantly differed between control and case groups (p<0.001) and had seen greater association to macroangiopathy changes (r=.353).

Table. 1 Baseline characteristic

PtrameteD	Wiftmil	W1A (n-60)	St*gnifc vice oftrvup dlUBIUUt
Agt (yeu)	44 4*54	482*66	p<0001
Histoiy of previous treitmattforCVD	1880%	2460*/.	p=039
Anurmuu of stable sneiiu	33.70*/.	4490*/.	p-0.177
Family kv?tcsy of CVD	7.SO*/.	1.40*/.	p-0098
Alcohol consumption	20%	37.70'/.	p=0O18
Smoking	23.70*/.	21.70*.'.	p-0.772
Systolic fclooi pressure (mm Hg)	1086*134	1224*213	
Diastolic blood pressure (mm H{)	73*96	83.4*123	
BMI (l^m')	25*3.4	29.4*76	
CKolejtorolCmg/dL)	1933*358	197.9*466	p=0460
Triglyceride (mg(dW	886*27 9	1021*30 7	p<005
HDL (mg/dLI	292*85	251*10.2	p«001
LDLCmg/dL)	1464*338	1525*442	p=0338
lrterleukm 1 (pg/mL)	907*68.5	154 5*701	p<005
Nitnc oxide (|lM)	196*12	172*98	p*034
VCAM^rtiL)	382±112	472*232	p<005
Total protein	748*54	732*4 7	p<006
Afcunun	443*49	413*53	p<0001 •
Cmlitint	643*11.4	70*19.1	p«005
FVwmnjlum Scon	1.23*198	539*721	p<0001

Table 2 presents the associations of soluble adhesion molecules, inflammatory markers, and coronary risk factors to CAD. Age *(r = 0.301)* male sex *(r=0.427),* diastolic blood pressure *(r=0.431),* triglyceride *(r=0.224)* and HDL *(r=-0.213)* were significantly correlated with presence of the plaques, while no correlation observed with LDL, total cholesterol and nitric oxide.

Endothelial dysfunction and inflammatory factors

Level of serum NOx was lower than normal limit as shown in both control and case groups (Table 2). Serum mean NOx values were *(17.2±9.8)* uM in the CAD patients and *(19.6±12)* uM in the healthy controls without any statistical significance *(P=0.342).* In addition, serum NOx levels was not associated with presence of plaques *(r~0.111, P=0.162),* but significantly correlated with soluble VCAM-1 *(r=-0.384, P<0.05)* and triglyceride level *(r=0.544, P<0.001).* Levels of sVCAM-1 showed a strong correlation with IL-1. Other risk factors such as diabetes, history of CAD and hypertension were significantly associated with levels of sVCAM-1 but not with levels of lipids including LDL and total cholesterol.

Table 2. Pearson correlation between prevalence of plaque and variables

Risk/actors		***sig.(2tailed)***
Age	0301	p<0 001
Diastolic blood pressure	0.431	pOOOl
Total Cholesterol	0.061	NS
Triglyceride	0.224	p<005
HDL	-0.213	p<0.01
LDL	0.079	NS
Total Protein	-0.151	p=0 065
Albumin	-0.284	pOOOl
Creatinine	0.186	p=0.023
IL-1	0.432	p<0 05
VCAM-1	0 238	p<0.05
Nitric oxide	-0.111	NS

After calculating with binary logistic regression (Table 3), age (PO.OOl), family history of CAD (P=0.017), high blood pressure (P=0.002), sVCAM-1 (/><0.001), and Pramingham risk score (P=0.01) were independent predictors of CAD. Furthermore, when we calculated Pramingham risk score patients with macroangiopathy had a 5-fold higher risk of developingrapid CAD progression (1.23±1.98) than control patients (5.39±7.21).

Table 3. Factors associated with progression of carotid atherosclerosis

Psnmters	*OikMo*	*p- icki*	*ma*	
			Low 1	*Upper*
Age (year)	**1.113**	**1 001**	1.048	1.182
Gender	**0.111**	**(001**	0045	0.275
Histcry of previous treatment forCVD	**1417**	***t 3B4***	***mi***	3.104
Anamnesis of stable angina	**1.562**	**1 176**	0.819	2981
Family hystory of CYD	**0156**	***I 070***	0.021	1.167
Dias blood pressure (mmHg)	**1.095**	***I 001***	1055	1136
BMIfkg/m*)	**1.208**	**C 001**	1.102	1.323
Cholesterol (mg/dL)	**1.003**	**11.458**	0.995	1.011
Tnglyceride(mg/dL)	**1.016**	**0 008**	1004	1.028
E L (mg/dL)	0954	**J 080**	0.920	0989
LDL(mg/JL)	**1.004**	**0 337**	0.996	1.013
Interleukin 1 (pg/mL)	**1.015**	**0 047**	1.000	1.029
Nitnc oxide (/<M)	0979	**0 340**	0938	1022
VCAM-1 (ng/mL)	**1182**	**0 015**	1033	1352
Albumin	0.890	**0 001**	0831	0.953
Creatinine	**1.026**	**0 029**	1003	1.050
Framingham Score	**1311**	**<t 001**	1127	1.525

DISCUSSION

This study was performed to investigate whether the molecular and biochemical risk factors were associated with the presence of confirmed coronary artery atherosclerotic changes in the Mongolian population. The major finding of this study is the decreased NO level in both control and study groups without significant difference. It can be result of the several reasons. First, study age group included subjects between 40-60 years old with high risk of endothelial dysfunction even they do not have visual atherosclerotic plaque with diagnostic equipments. Second, both angiography and dopplerography analysis are not sufficient to determine endothelial micro injury and alteration. We determined only macro changes in vascular system, thus we could not exclude subjects with micro changes from control group. Third, it can be noticed that magnitude of vascular endothelial dysfunction in healthy subjects free from symptomatic cardiovascular disease is associated with reduced level of NO.

NO level can reflect developing endothelial dysfunction through eNOS and possibly iNOS. Because plasma NO levels are likely to reflect NO synthesis via both eNOS and the neuronal NOS isoform.[10] Taken after overnight fasting, serum NO levels of this study can reflect the basal and endogenous NO generation. Another important finding of this study is the report ofno relationship between serum NO levels and the occurrence of CAD in the Mongolian population. Most of previous studies showed impairment of NO level increased during endothelial dysfunction and coronary artery disease progression. Out of patients with macroangiopathy, 44.9% had a positive anamnesis of hypertension in our study. Hence, present data supports suggestion from previous studies that blood pressure may work in tandem to increase cardiovascular risk in Mongols. Data from basic research suggest a central role of inflammation in the genesis of hypertension and that hypertension in turn induces a proinflammatory response. Hypertension, one of the risk factors of coronary artery disease, decreases NO bioavailblity by promoting oxidative stress, increases ROS by stimulating NADPH oxidase and promotes atherosclerosis. In experimental systems, activation of endothelial cells is associated with a loss of the biologic activity of endothelium-derived nitric oxide, an effect that accelerates the inflammatory process and also promotes local thrombosis and impairs local control of vasomotor tone /13/. Consistent with these experimental studies, recent studies have provided evidence that inflammation is associated with an impairment of nitric oxide dependent responses in human subjects/l 4/. Furthermore, our data demonstrate that sVCAM-1 and IL-1 levels revealed the stronger association with presence and future coronary artery disease acceleration (Table 3). The results suggested that inflammatory factors can be one of the leading causes of CAD among Mongols, besides aging, hypertension and male sex. Also, those inflammatory molecules measured in our study are elevated in patients with macroangiopathy and at high risk for future by Pramingham risk score. Even patients with low total cholesterol and LDL levels were found to be at significantly higher risk, with elevated sVCAM-1. Despite the strong correlation between ICAM-1 and IL-1 *(r=0.544)*, impairment of NO level, a marker of endothel'al dysfunction was significantly associated with VCAM-1 level *(r=-0.384)*. Bacterium, virus and metabolic disorders and other reasons, which can modulate acute and chronic inflammations in human body, might alter endothelial function by stimulating a systemic inflammatory response or by directly invading endothelial cells and altering their function /l 5-1 6/.Those inflammatory triggering factors can easily find their host body to develop an inflammation, especially in Ulaanbaatar city where air pollution level is much higher than accepted limit.

Although this study found lipid levels within normal range rather than increased, the decrease was more pronounced for high-density lipoprotein that is atheroprotective, rather than increased level of LDL and triglycerides. This alteration in lipid ratio might increase atherosclerosis risk,even significant cor-relation with presence of plaque observed only in triglyceride level, while total cholesterol and LDL level were non significant with vascular changes. According to positive correlation with CAD, obesity induced oxidative stress and adipocytokines including A-SA A, TNF-a, 1L-6 which can accelerate endothelial dysfunction through inflammatory

process, monocyte infiltration and dyslipidemia.[1718] This would have allowed the contribution of metabolic syndromes that occur in obesity, can impair endothelial dysfunction and lead to atherosclerosis. In our study, almost 30% of patients were overweighed in case group and its significant relationship to CAD incidence can explain some of possible link of accelerating atherosclerosis among Mongols. In conclusion, among Mongols, pathogenesis of atherosclerosis is might be mostly explained by inflammation mechanisms in addition to traditional risk factors. From traditional risk factors age, family history of CAD, gender and dyslipidemia have more effect in atherosclerosis development among Mongols. There is now significant evidence to suggest that inflammatory factors alter endothelial dysfunction and accelerate atherosclerosis in Mongolian population and this information may offer new strategies for diagnosis, prevention and treatment for this life threatening disease.

Limitations

Our study limited by the small sample of the study, limited age group and participants were only from capital city where life style differs from rural area of Mongolia. To evaluate precise leading mechanism of atherosclerosis, one time cross-sectional study can not be sufficient and this will require long-term prospective follow up study on this case.

ACKNOWLEDGEMENTS

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THE STUDY OF THE DISTRIBUTION OF CELL SIZE IN PRIMARY LIVER CANCER IN MONGOLIAN PATIENTS

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Abstract

Morphometric study was made in Basic 4 types of Primary Liver Cancer (PLC) most prevalent in Mongolian. So the average indexes were classified by gender studied the spread by assimetric distribution rule expressed the observation and theary frequency ehicidated using Paerson's square test and then have reached following results.

The distribution curve of the average cell size in trabecular and acinar types of PLC has low slope and broad base. Therefore, these types of PLC are characterized by slow progression and moderate malignancy. In contrast, light cellular and pleomorphic types of PLC are characterized curve, which is the sing of high malignancy and poor prognosis.

Key words: primary liver cancer, trabecular type, acinar type, pleomorphic type, light cellular type.

INTRODUCTION

Each year about 1 million 250 thousand people die of liver cancer in the world *l\l.* However, countries differ significantly with the respect of the disease incedence and prevalence. In high risk countries of Africa, Southest Asia, Far East and thecaribean liver cancer is the first leading type of cancer, while in other countries it is less prevalents ***111.*** In Mongolia liver, gastric, lung, esophageal and cervical cancer are the five leading types of cance with the liver cancer being most prevalent. The incidence of liver cancer is increasing annually, and it also, is becoming the leading cause of cancer morbidity and mortality *111.* An average standardized incidence of liver cancer for 1996-2000 is 46.95 per 100.000 population in Mongolia, which places the country among regions with high incidence of the disease *141.*

Researches have noted the significance of studying liver cancer cytology in choosing prevention and treatment strategy *151.*

The main objective of the current study was to assess histometric characteristics of PLC cells and their distribution. The reasearchers assessed average cell size in trabecular, acinar, light cellular and pleomorphic types of PLC by gender and interpreted the findings in the light of Maxwell's asymmetric distribution rule. The difference between observed and expected frequency was elucidated using Pearson's chi square test.

MATERIALS AND METHODS

In study liver tissue of 99 patients who had live resection surgical department of National Cancer Center during 1997-2003. Was stained by the method of Haemotoxilin-Eosin and Zangizon and studied distinquishing types of PLC.

Linear morphometric characteristics of liver tissue were studied using Nikon microscope (Japan) and MOB* 15 ocularmicrometer/7-11/. Liver cell were modeled using hexagonal prism and average cell size was calculated /8/.

Average cell sizes in types PLC most prevalent in Mongolian patients have been identified stratified by gender. The findigs have been interpreted in the light of Maxwell's asymmetric distribution rule, and the difference between observed and expected frequency was elucidated using Pearson's chi square test /l 2-14/.

RESULTS

Trabecular type of PLC

For figure 1, 2 they have shown average spread of

trabecular in Mongolian people. The trabecular type is the one kind of primary liver cancer. In figure 1- man, picture 2 - woman who have trabecular type.

In result of the research the stead of trabecular type has been spread out by asymmetric spread so the spread is willing to diverge to right side of median. The observation and theory frequency of cell occupation (trabecular type of primary liver cancer) for the men c^2 5= 8.271 < c^2 $_s$t = 19.68, for the woman c^2 6= 4.33 < c^2 $_{st}$ = 4.575.

There is no difference between observation and theory frequency. So it means our result of research is true (P<0.001).

Figure 1.

Average spread of cell of trabecular type for men

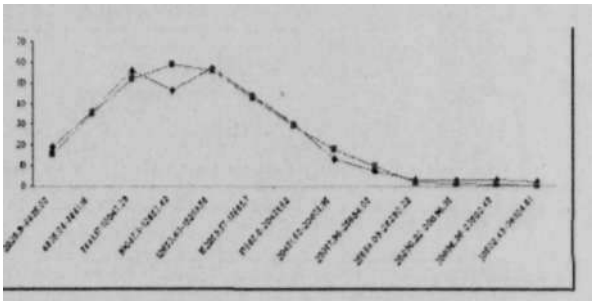
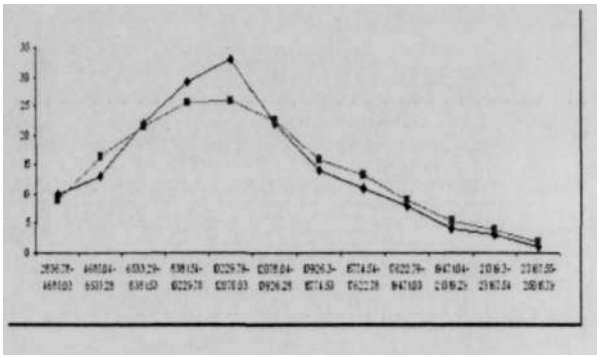


Figure 2.

Average spread of cell of trabecular type for women



For figure 3, 4 shown average spread of cell occupation of acinar type of primary liver cancer in Mongolian people. In figure 3 - men, figure 4 - women. In result of the research; cell occupation spread of acinar type of primary liver cancer is leaning to the right side of median by Maxwell's assimetria spread. The observation and theory frequency occupation's difference (acinar form of primary liver cancer). For the men c^2 5= 2.63 < c^2 $_s$t = 3.07, the for women c^2 6$^=$ 3.405 < c^2 $_s$t = 3.822. There is no big probability difference between obsevation and theory frequency, it means our research is true.

Figure 3.

Average spread of cell of acinar type for men

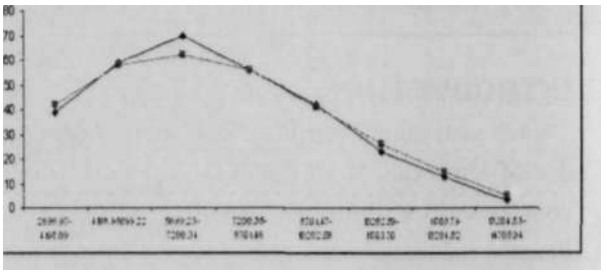
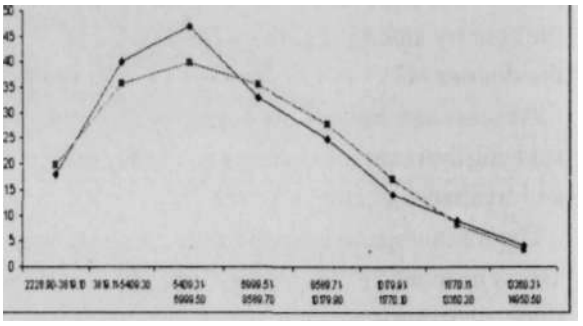


Figure 4.

Average spread of cell of acinar type for men



Here we see these two spreads by syndrom of biology stress, the bottom is crooked - short and wide. So liver cancer is calm, lower harmful!. It is in our research requlority.

Light cellular type of PLC

For figures 5, 6 shown average spread of cell occupation of light cellular type of primary liver cancer in Mongolian people. In figure 5 - men, figure 6 - women. In result of research' eel occupation is leaning to right side from media by Maxwell's assimetria spread. The observation and theory frequency of cell occupation's difference (light cellular type of primary liver cancer) for the men $C2Q = 2.458 < c2_{st} = 2.7$, for the women $C2Q = 4.028 < c2_{s}t = 4.67$. There is no statistic difference between observation and theory frequency ($p<0.001$). So it means our research is true.

Figure 5.
Average spread of light cellular type for men

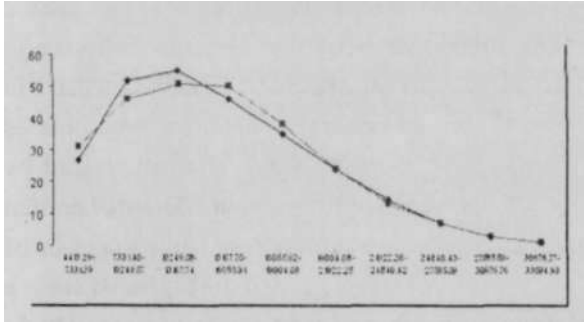
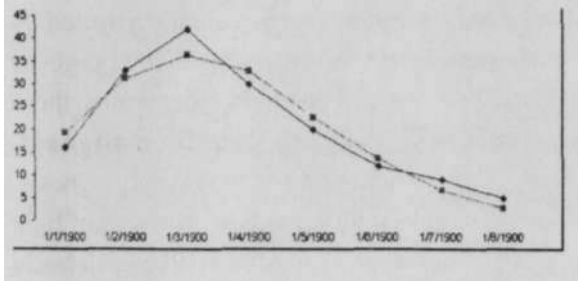


Figure 6.
Average spread of light cellular type for men



Pleomorphic type of PLC

For figure 7, 8 shown average spread of cell occupation of pleomorphic form of primary liver cancer in Mongolian people. In figure 7 - men, figure 8 - women. Cell occupation spread of pleomorphic type of primary liver cancer is leaning to the lright side of median by assimetria spread. The observation and theory frequency of cell occupation's difference (pleomorphic type of primary liver cancer) for the men $C2Q = 1.3 < c2_{S}$ $= 1.61$, for the women $c2g = 5.386 < c2_{st} = 5.578$. There is no difference between theory and observation frequency.

In syndrom theory of biology stress, average spread of light cellular and pleomorphic's cell occupation is leaning to the right side from crooked median, sharply becoming higher and also becoming two tops. It seems that the period of these forms, diseases are in quick process and highly malignant.

Figure 7,
Average spread of pleomorphic type for women

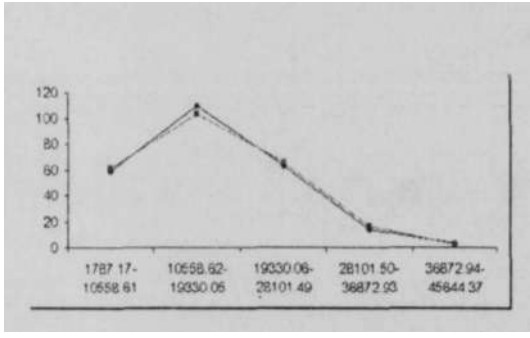
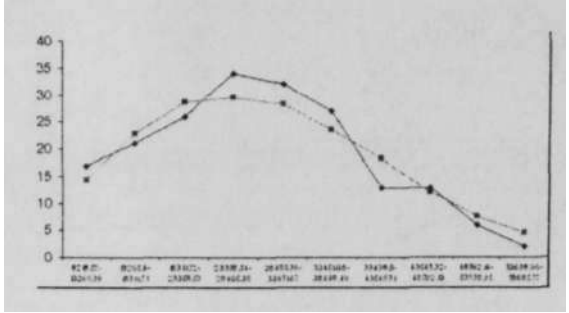


Figure 8.
Average spread of pleomorphic type for men



Hepatocellular dysplasia

For the figures 9, 10 shown average spread of cell occupation of dysplasia period. In figure 9 - men, figure 10 - women. In result of the research; in period of dysplasia, spread of liver cell occupation is spreading out by Maxwell's assimetria spread. The observation and theory frequency of cell occupation's (dyspasia) difference for the men $C2Q = 6.305 < c2_{st} = 6.393$, for the women $c2_0 = 2.375 < c2_{st} = 3.070$.

There is no statistic difference between observation and theory frequency (pO.OOl).

Figure 9.

Average spread of hepatocellular dysplasia for men

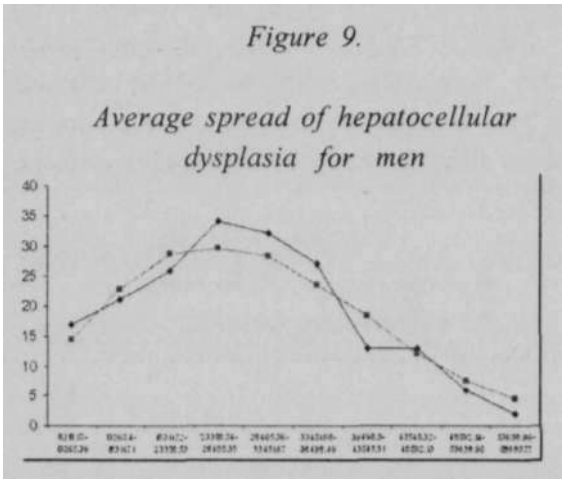
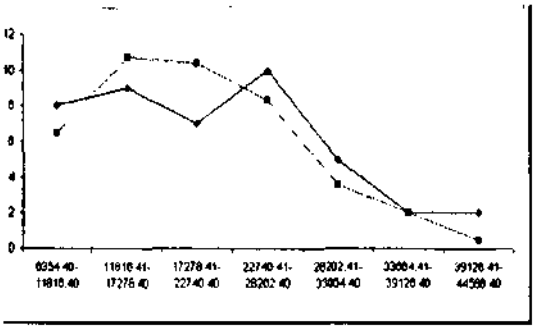


Figure 10.

Average spread of hepatocellular dysplasia for women



DISCUSSION

The study of the distribution of cell size in most prevalent cellular types of primary liver cancer (PLC) has demonstrated that the distribution of an average cell size in light cellular PLC is asymmetric, and the distribution curve is right-skewed and has two peaks.

There are strong requlatory mechanisms to keep internal body medium balanced, and damages to the system cause disease states. Researchers note that errors in adaptation mechanisms, which demonstrate the relationship between normal and pathogenic, lead to certain diseases /l 5/.

The results of the study have been interpreted in the light of the theory of general adaptation syndrome developed by famous Canadianresearcher G.Selie /16/. According to this theory, the distribution curve of cancer cell size can be plotted against the stages of general adaptation syndrome, namely;

1. Warning stage
2. Resistance stage
3. Exhaustion stage

The distribution of the average cell size in hepatocellular dysplasia can be explained in the light of the theory of general adaptation syndrome as follows. First, warning stage is characterized by gradual and weak stimulus, wich affects the normal resistance levels. Second, resistance stage in of general adaptation syndrome illustrates a correspondence between cancer inducers and body adaptation mechanisms, i.e. the capacity of the organism to resist cancer. Therefore, trbecular and acinar types of PLC are characterized by longer resistance to cancer inducers, which nevertheless eventually lead to exhaustion of adaptation energy and death.

In light cellular and pleomorphic types of PLC internal body mechanisms are greatly affected by cancer inducers, causing rapid drainage of adaptation energy and death. In other words, these two types of PLC are highly malignant, unresponsive to treatment and have poor prognosis. Research findings with regards to prognosis of light cellular PLC are controversial /l 7-19/, which could be explained by the differences in the nature and

duration of inducer effect, and the adaptability of the organism.

In conclusion, the distribution of average cell size in trabecular, acinar, light cellular and pleomorphic types of PLC is assimetric. Light cellular and pleomorphic types of PLC are highly malignant, unresponsive to treatment and have poor prognosis.

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THE ISSUES FOR IMPLEMENTATION OF QUALITY MANAGEMENT AND CONTROL IN NATIONAL PHARMACEUTICAL MANUFACTURING PROCESS

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Abstract

The National Drug Policy of Mongolia indicates the intention to develop a national pharmaceutical manufacturing and throughout assistance from government for elaboration of the GMP for Pharmaceutical manufacture and performing it in production process. The GMP is new item in pharmaceutical manufacturing practice in Mongolia and implementation of that connected with non completion of the legislative habitats yet. Therefore, the query for one thing the elaborating of pharmaceutical manufacturing requirement and legitimately warrants in standard dimension is foremost issue.

The rationale of this study was founded in elaboration of mode for the quality management modification and reconstruction of national pharmaceutical manufacturing process, future development posture connecting with foreign countries experience, leaning and oncoming to the international level and to be improve that in consistent with GMP requirement.

Key words: GMP - Good Manufacturing Practice, GLP - Good laboratory Practice. GSP - Good Storage Practice, GCP - Good Clinical Practice

INTRODUCTION

Many countries in World dominantly direct the attention to a personnel, environmental condition, construction, equipments of pharmaceutical manufacturing process and can properly carry out a leading the management and the supervision for all process, onset of raw materials to selling the finished products in market place. And so, are providing the quality assurance of drug and they can procure the own countries pharmaceutical needs and perform the GMP requirements for export. As well as, is established the possibility to work in collaboration in international level and region *l*\ 1 -16/.

If, counterfeit and substandard drugs were conquering the 5 per cent (for 32 million USD) of pharmaceutical market in 1991, they are increased 3 times in 2004 and the counterfeit and substandard drugs began to occupy the 15 per cent of world drug market. As professional publication and so and mass media began to inform this bearing has a direction to may be increased in last years. The international pharmaceutical market experiences show a circulation of the counterfeit and substandard drugs in many countries of World and particularly they have been easy to pierce into drug market in developing countries /2-10/. Therefore, there is considerable signification to approbate the domestic pharmaceutical manufactures, actualize and adjust the national drug policy for accommodation of national security and prevention from counterfeit and substandard drugs entrance to Mongolia and should be implement the GMP in national pharmaceutical manufacturing process. Accordingly, the issues for improvement of the supervision for all production process, onset of raw materials to the finished products/4-6/.

Aims and objectives

Under aim of the study was trended to analyze the present situation of national pharmaceutical manufacturing process and study the GMP experience, leaning of foreign countries and determination of mode to implement it in own manufacturing process, elaboration of national standard and its implementation.

For achievement the aim of study were put forward following objectives as:

1. To implement the dissection in present condition and activities of habitats pharmaceutical manufactures;
2. To investigate comparatively the specifics and factors of GMP during it's implementation to foreign countries Pharmaceutical Manufacturing;
3. To elaborate and relay the National Drug Manufacturing Standard for Mongolian pharmaceutical manufactures

MATERIALS AND METHODS

For evaluation of Mongolian pharmaceutical manufacturing process at present time, were selected 36 habitats pharmaceutical manufactures as research materials and 16 pharmaceutical plants from 9 countries as comparison investigation subject. And analyzed using the archive material involved the structure of drug procurement sector of Mongolia, Health Law and Drug Law of Mongolia, GMP of European and ASEAN countries, the action report of national pharmaceutical manufactures for 1998-2004, archive material of State Specialized Supervision Agency, materials of I-V symposium on National Drug Policy, "State policy on Drug", Mongolian statistical information for 1993-2004. Health statistics brochure(2004).

The methodology of the study

We used the estimation methodology of circumstance, descriptive and instant methodology of notice investigation and survey investigation methodology, depending from goal and subjects of the study.

The statistic operation of the investigation outcome

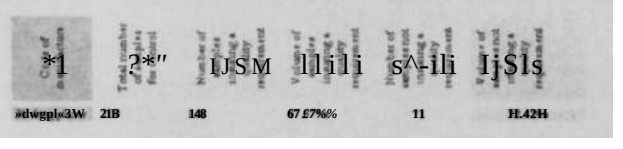
For operation of investigation material were used computer program as Microsoft Windows. Microsoft Excel-2000, SPSS-10.0 for social science.Present condition estimation of national pharmaceutical manufacturing process was established under the actual number, average indicates (maximum and minimum limit), m-average mistake, s- standard variation etc.) For consideration of pharmaceutical plants comparison with GMP were used t criterion - coefficient of probability or coefficient of credence, p- level of priority or probability.

RESULTS AND DISCUSSION

The outcome of investigation on current situation of national pharmaceutical manufacturing process

By investigation of pharmaceutics producing by own country phamaceutical plants, selling and growing of that were determined the number of about 400 name's product are increased for each year and 23.8% of new product, 30% of essential drugs, 20% of importing drugs should be produced in habitats pharmaceutical plants and this condition can inset the mite in drug procurement of population. But, there is situation on stagnant of production and realization because of not yet quality and selling and low circulation. At present time 52 name of own plants product or 10 per cent of all pharmaceutics are imported from foreign countries under the same name and pharmaceutics with the same pharmacological activities because of insufficient regulation for limitation of import by registration. This situation detains the national pharmaceutical manufacture development and governmental policy not yet for regulation of current negative condition.The summary of investigation in quality assurance of own pharmaceutical products is extended in Table 1 (1998-2004).

Table 1



The investigation for estimation of standardization adherenced in own pharmaceutical manufactures shows the 267 standards are used in pharmaceuti-

cal plants. 7.1% of them were approved during 1970 - 1980, 31.3% - during 1980 - 1990, 50.8% - during 1990 - 2000 and 10.7% were approved during 2000 - 2004. And 60 per cent of them are needed the changes.

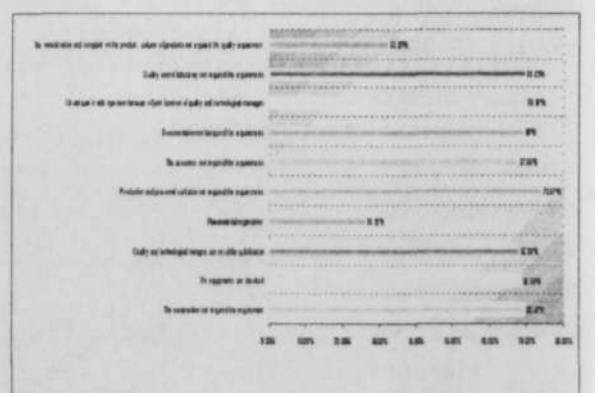
The national standard is legislative documentation exactly must to be conduct. The summary of the investigation shows the standards, which carried out in pharmaceutical plants can not conform current the scientific and technological and legislative requirement. And in the future should be improve and increse the standardization level to extend the pharmaceutical product assurance to international level.

In Realization of Ensure compliance will current legislation and decission on the drug manufacturing process: In picture 2 introduces the realization of the Drug Law reference on "The will prohibited the pharmaceutics, without state registration, for use" possess 71,4% and it depends from un fixing the GMP requirements in own pharmaceutical plants. There are needs to elaborate the national standard for national pharmaceutical manufactures and insure in legitimation and activate the registration of product from manufacturer, which content GMP requirement.

During the determination of future object by estimation current stiuation of own country pharmaceutical manufacturing process looks that drug quality is cardinal issue of pharmaceutical process. We have the estimation on that for decision of quality assured drug procurement increasing by implementation the the GMP in pharmaceutical manufactures and it adjustment to market must be involve the government participation and mangement. The comparative study on foreign countries realization GMP into drug manufacturing feature with Mongolian circumstance

The estimation of own pharmaceutical manufacture's activity by creterion of essential GMP component conducting in foreign countries shows the 69.7% have the construction not required, 68.66% of equipments are obsoleted, 67.98% of quality assurance and quality control managers are need the training for qualification and 59.44% of managers for quality assurance are execute own function with quality control managers function, 26.13% of raw materials involved in state registration and 67.75% not required hygienic and sanitation requirement. The Figure 1 introduces the 68.22% of own country pharmaceutical manufactures can not required the pharmaceutical manufacturing GMP requirements.

Figure 1. Summary of investigation on the Mongolian pharmaceutical manufacturing activity by GMP criterion extending in foreign countries



To see through to outcome of comparative research work: National pharmaceutical manufacturing process comply without national GMP rulesjaw and jural environment, Manufactures are in not purposed premises, obsoloted equipments, inadequate in requirement, specialized human resources insufficient, and their training inadequate, because of them national products quality could not reach to importing medicaments quality level. Academician Nyamdavaa noted the National pharmaceutical policy of Mongolia and said: "The Control of Drug and Biopreparation quality and use of medicaments must be first significance and could be elaborate the method and management. This issue could be developed in special project and it accordance with principle of WHO (WHA 22.50) of 22nd session assembled in 1971 on « The Control principles of medicament», « The Rule of Drug production and drug quality control» and « The Management of drug production and the principle of drug control » and the recommendation of GMP /16/. It is in conformity with the aim of the study. Many countries on the world developing of drug production controlled the long way from the entering of raw materials to the use of medicament. The principles of GMP (Good manufacturing Practice) from WHO. Mongolia has to pursue the general Principle of GMP".

All this report on national pharmaceutical manufacturing GMP, the observation of formulation requirements in drug production to standards level and the development of national pharmaceutical manufacturing was been urgent issue.The result of questionnaire survey shows about the urgent issue ofintroduce GMP into national pharmaceutical manufacturing The summary of questionnaire survey shows about the urgent issue of introduce GMP into habitats pharmaceutical manufacturing in Table 2.

Table 2.

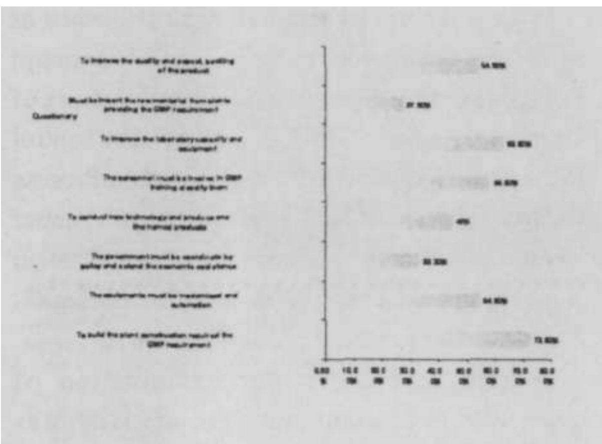
The result of questionnaire survey shove about the urgent issue of introduce GMP mo national pharmaceutical manufacturing

AnM'trt	Anara-2	Aiw>-3	Anjwti 4	Amuo-5	An*nt-o	Arwvtr T
TtMiapaitJiiv a«tanlna l>av*d«aiild; influadlo poduct aajily	Cjiirt».j tqupninf •* objclmdmd a-cfcin	TV-.. KoBanKil iirtmhrio CUPuTiw- *.***../""	Ttefttndad udwdvid faitrovaioc itfudiiuliay	C«»«y«" libtanayicr.oi yittndnct aaandth. aai«im»fld	Quufinkoi *of* pmonid n ocl yil ind not iD*dVfdin uaongvOMP	*fun* «nri»"»«il rotdamra JI^^,„j ^^J,?
•I5..10".	"«.«••	:J.2C".	.'"IO"!	-6.<S0*.	5-.60<t	S4.W.

We have estimation on that for improvement of product quality, must provide the measurements to implementation of GMP and decide above named problematic issues.

The Result of questionnaire survey about the issue of how to introduce GMP into habitats pharmaceutical manufacture extends in Figure 2.

Figure 2. The Result of questionnaire survey about the issue of how to introduce GMP into habitats pharmaceutical manufacture



The formulating and introduction of national GMP standard observing in drug manufacturing process and practice

On MNS 5524:2005 national standard contending in pharmaceutical manufacturing process

Since 2004 began build joint, with international investment and with long term credit financing "Munkhin Tun"," IVCO "," Mongol Sino Je " and "Tsombo" contented the requirements GMPHowever, is beginning conduct the national ratio, the elaboration and conducting the national GMP standard need to be as legislatively approved in national level.

During the elaboration of project for "National Standard (GMP) for Pharmaceutical manufacturing process " in collaboration with working team in 2005 by the order No.23 of Health Ministry. Since 2002 can investigate 2 times model GMP of WHO and GMP for manufacturing process in Russian Federation, China and countries of Europe and ASEAN, Japan and Malaysia providing the condition in our country and to erflect the opinion of professional organisations and specialist connecting to this problem. The MNS 5524:2005 standard on general requirement for Pharmaceutical manufacturing process, established by us in the results of our study gives the possibility on legislative totake inpestion in manufacturing process, placeman, organization having the authority for special accession and for managing the pharmaceutical production.

The mode for implementation of GMP in national pharmaceutical manufacturing process

We made the estimation in current situation of national pharmaceutical manufacturing process for detection the consequence of own country pharmaceutical product unrequirement to execute own function with quality control manager's function, 26.13% of raw materials involved in state registration and 67.75% not required hygienic and sanitation requirement introduced that own country pharmaceutical plant's product can not require the international standard requirement. Therefore, for improvement of quality management and the activity of national pharmaceutical manufacturing process in Mongolia must to implement the components of GMP requirements illustrated in Figure 3 step by step under the plan.

Figure 3. Requiremental contents of GMP components

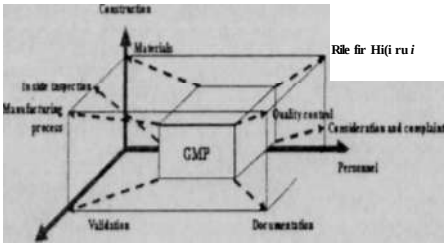
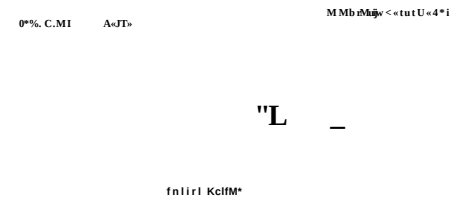


Figure 4. The basic principle of GMP in Pharmaceutical manufacturing. Regulations for manufacturing control and quality control



In the results we destined to introduce by scheme in Figure 4 on requirement to complexly implement the quality management as to be have the construction, a equipment contending the international standard requirement, educated and qualified personnel, import of raw material from manufacturers contending the GMP requirement, quality control laboratory having the capacity in international level, documented and validated production process, hygienic and sanitation of production environment extending the requirement, jointed structure for deciding the consederation and complaint.

The contents for implementation of GMP in pharmaceutical manufacturing and inspection organization of European and South East Asian cointries step by step under the recommendation of WHO conformed with our decision and estimation.

The general principle of manufacturing rule is the manufacturer must implement the structure requiring the drug quality and can involve the manager and personnel to production process. The GMP is used for as stdandard, which have the possibility the check the activity of pharmaceutical manufacturing and that included in compnents of pharmaceutical product quality certificate's schem in international trade of WHO.

Therefore, in scheme 1 illustrated the condition for inspection in case demand when decided to start the pharmaceutical manufacturing.

The Basic principle of GMP is scientific, concordant and coherence system to detect a risk, which may because in production process since raw material untill finished product, estimation, inspection and management of that during pharmaceutical quality improvement. Therefore, should be adherence the pharmaceutical manufacturing management, under which will be contented the pharmaceutical quality assurance by examination and pharmaceutics can be produced by drug quality standard. The mode for implementation of GMP in own country pharmaceutical manufacturing was defined and implemented in IVCO pharmaceutical manufacturing plant.

The outcome of research work published as "The Drug quality control" guideline," The control in Pharmaceutical manufacturing and the rule of Drug production " (GMP) guideline, "The control list" of drug production. Pharmacy and the Process on Drug process (In 1 st Supplement shown) under recommendation and participation of Academician Dungerdorj., associate professor Erdenetsetseg.G, Ph.D, doctor of medicine Damdinsuren A.

Also, check list for examination of pharmaceutical manufacturing acitivity was elaborated and in the sphere for improvement of pharmaceutical manufacturing management was

conducted the estimation of requirement and rating emancipated in knowledge and practice of quality assurance and quality control managers and was conducted the investigation for protection from risks of bacterological contamination can be caused through the product. And was elaborated the guideline for improvement the hygiene and sanitation of personnel and infection protectorated and were developed they in practice.

The practical implementation of quality control management in IVCO pharmaceutical manufacturing in reconciiiment of GMP requirement

Table 3. The mode for promotion of quality management structure in national pharmaceutical manufacturing

Component;	Mode for implementation
In the concerning of product ion constmction	• Must to plan certain agenda to affed the Standard level (GMP) and condud in manufacturing process step by step and use specific constudion or reconstrudion purposal materials and lay down lawn in surround Could equip ventilation system with specific filter HEPA to affed requirement level
In the concerning ofHumw resource	• All workers from manufudures must be trailed on theoretical and practical basic knowledge Moreover , must be organized the specific training, related their functional activities and estimated their results The irammg should be conduded continualy • Should send perscone! to foreign countries for exploring their experiences and to train short termly, to educate m mner country specialized specialist
The concerning of equipments	• The manufactures rrust have full or half automatic processing and equipments, should be afforce the concerning and record each time
In the concerting of drug raw materials	• For implementation of modem new tedmology produdion must improve the control for raw materials, and have to import the raw materials from manufacture with GMP standard, will warrant by confidential laboratory in the base quality certificate • The raw material, accomodate substances and finished products are stored separately m different places depending from that's properties because that have the risk to be changed and that must to have special mark m colors as red, green and yelow For example By the rule of good storage pradice (OSP) during the temporal stamg the product, from which got the sample for laboratory analysis, could be have the yelow mark, the produd required the quality requirement and decided to sent to produdion process could be have the green mark, produd not required the quality requirement and prohibited to sent to production process could be have the red mark
The demand of hygiene and sanitary on production and workers The validation The documer:lali<B	• The Pharmaceutical manufacturing have to specific featured sanitary rules and must test every production line and evaluate contamination risk and monitor and record • All workers from produdion must involve health check seasonly Workers must disinfect hands with modem disinfection substance, mist enter by air shower way into production zone • The all step of produdion process must be approved and the manufacture should be have the specialized personnel who will make the validation • The certified document must to mtrodjce on that initial material contents the requirement, fundion of techniquies is yet and personnel can do the fundion • The data on production stage must recorded in the technological management and control screen and controlled Part of products is documented and appended in produdion file Therefore there is possibility to extend the quality assurance
Inside control Quality assurance of	• The consolidated structur of quality management consist of quality control laboratory (chemical , biological), technique control service (inter - production line controller, arbitration control) From raw materials preparation to final produd must control each part of manufacturing

We conducted the estimation in current condition of pharmaceutical manufacturing, for determination of correlation and combination between consequence and circumstance of that, own country product can not required the international standard requirements. Also, we elaborated and implemented in practice the national standard 5524:2005 on general requirement extending to pharmaceutical manufacturing under the ASEAN countries experience of conducting the GMP in pharmaceutical manufacturing process by recommendation of WHO for improvement of quality control management in pharmaceutical manufacturing.

For improvement of quality control management in IVCO pharmaceutical manufacturing under the national standard MNS 5524:2005 on general requirement extending to pharmaceutical manufacturing process in adherence the GMP principle and involves the production managers and all personnel for extend drug quality and conducts the assurance all stage for drug production since raw material.

As result of the investigation work the GMP was complexly implemented in IVCO pharmaceutical plant. The IVCO pharmaceutical plant can adjust the national pharmaceutical product conforming international standard requirement in the results of complexly implementation of GMP requirements in production by conducting the manufacturing in special construction, using the equipments conforming international standard requirement, getting the raw material and container from manufacturers conforming the GMP requirements, conducting the permanent in side inspection, documentation and assurance in each production stage by specialized personnel, using the LAL test method of analysis for product quality control.

In conclusion, for Mongolian national pharmaceutical manufacturing management, 67.98% of human resources, 69.47% of construction, 68.66% of premises and equipment, 69.65% of quality control laboratory, 73.87% of raw materials and 67.75% of processing activities. hygienic and sanitary condition in manufactures or 68.22% of total manufacturers can not affect the GMP requirements conforming in many countries in World.

Practical recommendation and guideline descriped the mode for implementation of GMP in national pharmaceutical manufacturing under the experiences of some foreign countries and GMP tendency of ASEAN countries and WHO.

In the results of the research, the national standard MNS 5524:2005 on general requirement conforming pharmaceutical manufacturing and quality management structure of IVCO pharmaceutical plant was improved in reconcile of GMP requirement and implemented in practice. And there were defined the possibility to produce national pharmaceutical product conforming the quality of imported pharmaceutical product in the same name.

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TRACE ELEMENTS IN HUMAN HAIR OF PATIENTS WITH LIVER DISORDERS

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Abstract

Human hairs ofthe cirrhosis, acute viral hepatitis patients and healthy people in Ulaanbaatar, capital city of Mongolia, were analyzed for the presence of heavy elements by PIXE spectrometry using 2.5 MeV proton beam at the Tokyo Institute of Technology Van de Graaff Laboratory. The samples were dissolved in a mixture of nitric acid and hydrogen peroxide. Then a 20ml aliquot was dropped on the Nuclepore Track-etch Membrane. The IAEA Reference Hair IAEA-086 certified reference material was used in order to verify the accuracy ofthe method and the results were in a good agreement with the certified values. To determine the interaction between nine elements in hair, correlation coefficients were evaluated for several pairs of elements. In the group of healthy control groups, no correlation between elements was identified. Opposite to this, the strong positive correlations were observed for Zn and Ca or Fe; Mn and Ca or Ti; Sr and Zn or Fe of patients hair. In the present study, the mean concentrations of Ca, Ti, As and Sr in Mongolian patients were higher than those in the hair of normal people in Japan, Mongolia, Iran and Indonesia. The levels of Cu, Zn and Mn concentration in hair of normal people were almost the same for all the cohorts.

Key words: PIXE, trace element, human hair, liver disorder

INTRODUCTION

The content of trace elements in a human hair provides valuable information on the functioning of various organs. In recent years, the chemical analysis of trace element levels in hair has become popular for monitoring of environmental exposure /1-2/, evaluating heavy metal deposition *131,* assessing nutritional status, and diagnosing diseases /4-5/. The advantage of hair sampling lies in the simplicity of its treating without intrusion, and easy handling and storing for extended periods. Unlike urine or blood samples, which may reflect the subject's momentary situation, hair could give the information on the actual exposure over a period of months or even years *12-6-11.* It is of common practice prior to analysis to dissolve hair in order to obtain homogeneous samples. Though it might be treated as a destructive method, the advantage of homogeneity is broadly recognized and hair dissolution in acids ha~s become a worldwide experimental practice /8-10/. Also decomposition of organic matter is an important part for the determination of heavy metals in biological samples. The Particle Induced X-ray Emission (PIXE) has been widely used for elemental analysis along with neutron and proton activation analyses (NAA, PAA). By applying the PIXE method with an appropriate simultaneous multielemental method to water and hair samples, elements of interest can be easily determined in ppm to ppb, even sub-ppb, level irrespective of elements. This is more advantageous than these nuclear processes. Analysis of human hair using this method was

performed by several authors /2-I1-12/. The objective of the present study was to determine the concentration level and distribution of elements in the human hair of the cirrhosis and acute viral hepatitis patients in Ulaanbaatar, capital city of Mongolia. This data will serve a basis of diagnosis of ailment or disease.

METHODS AND MATERIALS

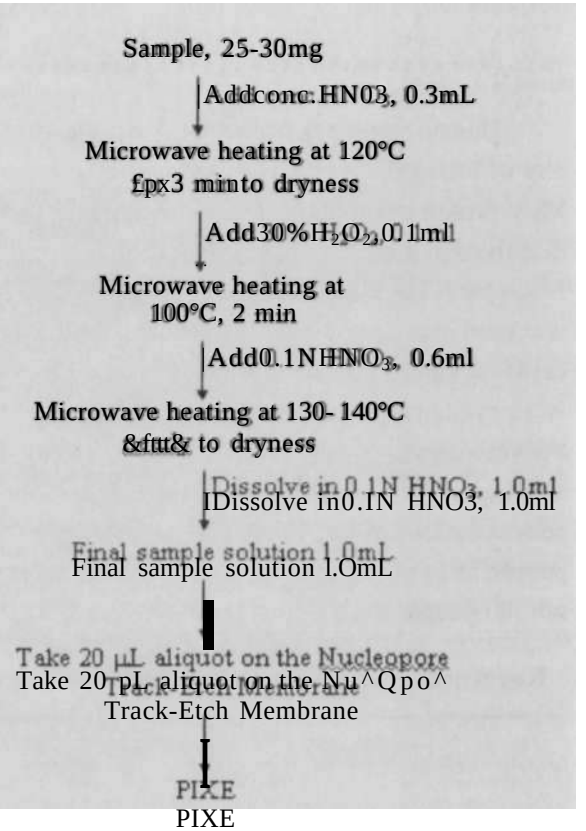
Sample preparation **for** making **the** efficiency curve

For the purpose of plotting the efficiency curves two targets were prepared to reflect the peculiarities of high and low energy regions. Targets for irradiation were prepared according to our previous procedure. For a high energy region a 20il-aliquot of mixed solution containing Co (20ppm), Zn (20ppm), Se(40ppm), Se (80ppm), Cd (200ppm), andZn(lOOppm) was directly dropped on and air-dried on the Nuclepore Track-Etch Membrane. For a low energy region a target containing P(40ppm), Na (59.8ppm), Mg(60ppm), Al(40ppm), and Ca(20ppm) was prepared in the similar manner.

Procedure of analysis

Twenty-seven scalp hair samples in Mongolian people were collected from the same place on the backside of head, namely from the occipital region using a pair of stainless steal scissors. The age range of individuals was 19 to 54 years old (mean: 37.2). Samples were stored in sealed plastic bags, which were marked with personal information regarding age, sex. hair color and doctor's diagnosis of diseases. The main problem of using hair is external contamination. The World Health Organization (WHO), United States Environmental Protection Agency (USEPA), and International Atomic Energy Agency (IAEA) have recommended using hair as an important biological material for environmental monitoring/13-14/. The samples were thoroughly washed to remove external contamination by 1% soap solution and rinsed with distilled water. Then they were placed for one hour in acetone and finally washed again by distilled water and air-dried. The samples were dissolved in a mixture of nitric acid and hydrogen peroxide. The flow chart of procedure is illustrated in Figure 1. Hair samples were taken of 25-30mg in a glass beaker and added a 0.3mL aliquot of ultra pure nitric acid. The digestion was carried out by heating the sample in the microwave oven for 3 minat 120°C. Then to the residue was added 0.1 mL of 30% hydrogen peroxide and heated at 100°C for 2min. A 0.6mL aliquot of 0. IN nitric acid was added to the residue and evaporated almost to dryness at 130-140°C.

Figure 1. Procedure for PIXE analysis of human hair samples



The residue was dissolved in 1 .OmL of 0.1M $HN0_3$ to produce a final sample solution. The standard reference material IAEA-086 human hair was digested as above and diluted in the same manner. A 20ml-aliquot of final test solution was directly dropped and air-dried on the Nuclepore Track-etch Membrane.These samples were irradiated by the 2.5MeV proton beam from the single-end type Van de Graaff accelerator following the method reported previously /l *SI.*

Detector set-up for PIXE

The proton beam was collimated to give about 5 mm in diameter at the collimator exit. Emitted X-rays were analyzed using the ORTEC Si (Li) detector (active volume 0.45cm\ effective diameter 10mm, thickness 5.67mm, distance from window 7mm, FWHM of FeK_a X-Ray 180eV) with a 1 mm polyethylene absorber and CANBERRA Si(Li)

detector (effective diameter 4mm, thickness 3mm, distance from window 5mm, FWHM of FeK X-Ray 160eV) without an absorber. The 1mm polyethylene absorber was employed to diminish lower-energy X-rays. The beryllium window was 25mm in thickness for both detectors. This set-up made effective to determine heavy elements by the former and light elements by the latter. All the chemicals of analytical grade were supplied by Wako or Kanto Pure Chemical Co., Ltd., and used without further purification. Deionized water was prepared using a Millipore model Milli-RX equipped with RO and ion-exchange membrane filter.

RESULTS

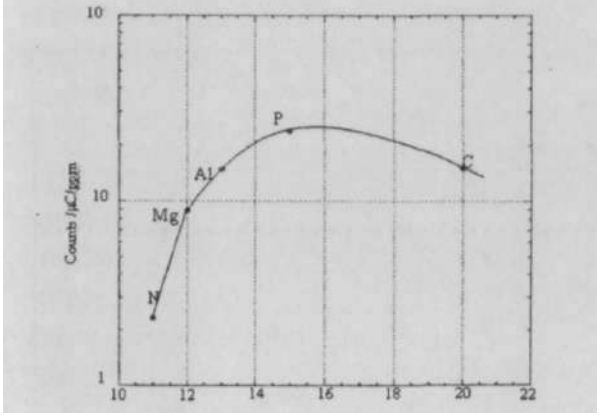
Calculation of elemental concentration

The mainstream of the experimental procedure is based on normalization of the K_a X-ray peak intensity of element to associate charge value in mC.

For intensity (I) corresponding to element M was normalized to the mixed standard of itsconcentration in ppm and associated charge value. The determined concentration of element in sample solution [Ml , was then calculated by the following equation (Figure.2).

$$[M]_{sample} = \frac{I_{sample}(counts/\mu C)}{I_{mixed\,std}(counts/\mu C/ppm}\ (ppm);$$

Figure2. Efficiency curve for Na to Ca

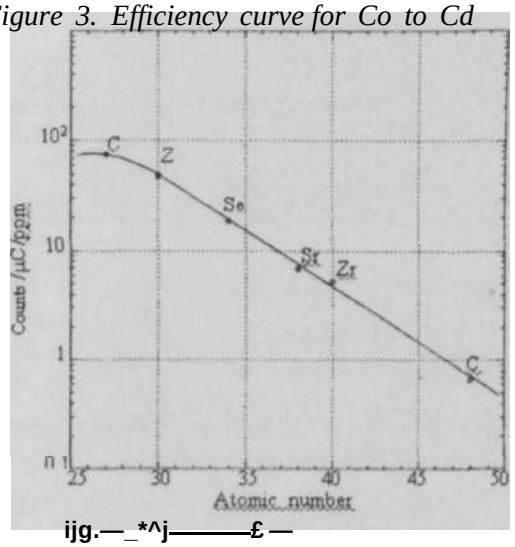


$$M_{hair} = \frac{[M]_{sample} \times V_{solution}(mL)}{m_{hair}(g)}\ (mg/g);$$

where $V_{solution}$, is volume of solution prepared (lmL), and m_{hair} is the mass of human hair in grams used for an elemental analysis.

The efficiency curves for these elements are shown in Figure 2 and 3. For elements with the atomic number lower than , Fe, an attenuated X-ray intensity was observed due to absorption by polyethylene. For elements with the atomic number greater than ,$_g$Ni, the curve monotonically slopes from ,$_0$Co to $_{48}$Cd. (Figure 3.)

Figure 3. Efficiency curve for Co to Cd



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Determination of trace elements in human hair

Figure 4 (a) and (b) show the typical X-ray spectra of a human hair Sample ID#5 in low and high-energy regions, respectively. It clearly indicates peak of As along with other transition and alkaline earth metals. PIXE analysis cannot make difference between III and V-valent arsenic. Figure 4 (a) gives a well-identified peak of S coming from the remaining organic matter of hair, sulfide or other compounds of trace elements in human hair which disturbed tha analysis some of the elements like Na, Mg and Al. The intensity of K_a X-ray was corrected for contribution of the K_0 X-ray line of the adjacent element, according to the method described previously /l 6/. In Figure 4(b), the X-ray peaks of Ni and As were poor because there are small concentration in the testing sample solutions. The elements of Ti, Mn, Fe, Ni, Cu, Zn, As, Br and Sr were identified along with the first row transition elements from $_{22}$Ti to $_{3g}$Sr without overlapping. The statistical errors for sample ID#5 (ls)were 2.5,48.1,25.9,2.2, 15.9, 8.7, 1.26, 30.7, 13.9andl2.7%forCa,Ti,Mn,Fe,Ni,Cu,Zn,As,

Br and Sr respectively. The large error will be due to low amount of the element.

The accuracy was checked by the analysis of a standard reference material, IAEA-086 human hair, including statistic and repeat errors, whose elemental concentrations are presented in Table 1. Errors mainly come from the preparation of targets for irradiation, spectrum fitting, and partially from the detection efficiency and the values of transmission of the X-ray absorber. The value of the integrated beam current required for the present method is around 4-5mC. The results obtained were in a good agreement with the certified values.

Table 1. Comparison of elemental concentrations (mg g'J in IAEA -086 standard sample and certified values

	This ivork	Certified value
Ca	81±11	112111
Cu	1.98+0.34	17610.13
Fe	20.1+3.2	12.311.5
Mg	13.514.2	17.7+30
MB	0.88+O.15	0.9610.03
Sc	1.5+0.2	1.4+0.2
Se	0.12±0.06	0.10+0 02
Zn	18.3±2.5	16.711.1

Concentrations of elements determined by using equations 3.1 and 3.2 are presented in Table 2. From the present results, it can be seen the levels of elements Ca, Ti, Fe, Ni, Cu, combined concentration of As (+Pb) and Sr are higher in the patients of liver disorders than those observed in the normal people. The high concentration levels of Ni and As observed in the patients of liver disorders will be related with the fact that these elements are carcinogenic.

The elemental concentrations in biological samples vary considerably due to geographical differences, nutritional status, and environmental factors. The present results were compared with other results reported by several researchers and the ranges of world wide mean values. Table 3 shows the comparative results of the elements in human hair. The mean concentrations of Ca, Ti, As and Sr in Mongolian patients were higher than those in the hair of normal people in Japan, Mongolia, Iran and Indonesia. The level of Cu, Zn and Mn elements is not different between these countries. The concentrations of Ca, Ti, Ni, As, Br and Sr in hair of the patients were found to increase over that of normal Mongolian people reported by other researchers. It is noteworthy that concentrations of Ca, Ti, Ni, As, Br and Sr in the human hair of the cirrhosis and acute viral hepatitis patients were higher than Mongolian normal human hair. Some researchers have reported that cancer of the respiratory tract can be attributed to the inhalation of nickel compounds /17/. It is shown, that difference of average contents of determined elements in hair of healthy people and patients, in most cases,statistically not significant. More interesting information has given the correlation analysis between contents of determined elements. The interaction was calculated among nine elements in hair correlation coefficients.

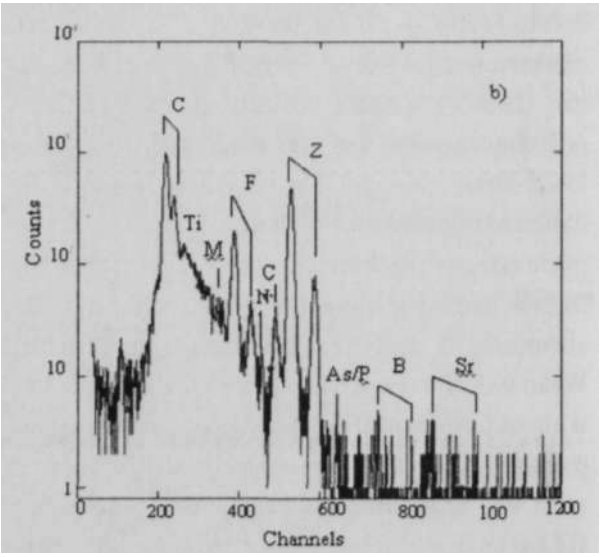
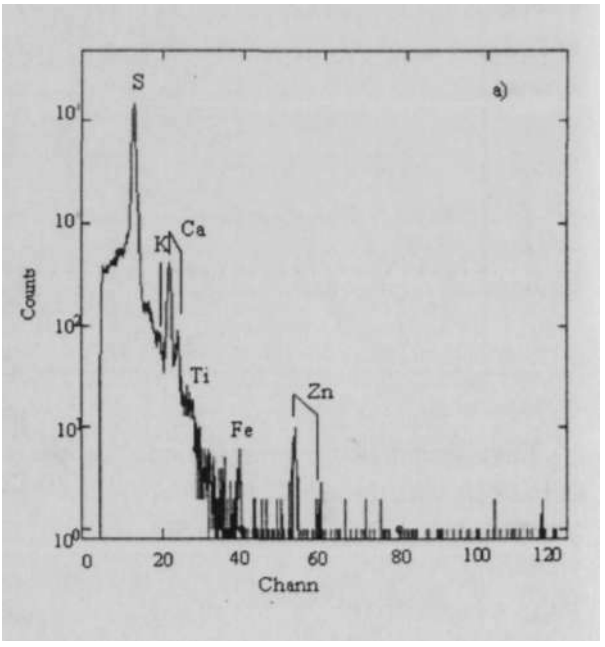


Figure. 4 .FIXE spectra of human hair sample ID 5 in (a) low and (b) high energy region.



At the level of significance equals P=0.05 correlations between the elements that play an important role in the biological system was obtained in human hair. The type of correlation, positive or negative, is also indicated. According to this test, the closer |rj values are to 1, the stronger is the correlation, for a significance p=0.05. In the group of healthy control groups, no correlation between elements was identified. The positive correlations were observed for Zn and Ca or Fe; Mn and Ca or Ti; Sr and Zn or Fe of patients. The correlations of Mn with other elements, e.g. Ca, Ti may suggest that Mn substitutes for those elements in human hair. Zn also demonstrated positive correlations with other elements which is known to occur in many important metal-enzymes. The correlation matrix gives us information about relation ships between two metals but does not take into consideration of the presence of other elements.

DISCUSSIONS

The trace elemental analysis is carried out in the human hair of the cirrhosis, acute viral hepatitis patients and healthy people by employing PIXE technique using 2.5MeV proton beam from the single-end type Van de Graaff accelerator. The hair samples were brought into solution by using a mixture of nitric acid and hydrogen peroxide. Then a 20ml aliquot was dropped on the Nuclepore Track-etch Membrane for the irradiation. The IAEA Reference Hair IAEA-086 certified reference material was used in order to verify the accuracy of the method and the results were in good agreement with the certified values. From the present results, it can be seen that the mean concentrations of Ca, Ti, As and Sr in Mongolian patients were higher than those in the hair of norma! people in Japan, Mongolia, Iran and Indonesia. The levels of Cu, Zn and Mn concentration in hair of normal people were almost the same for all the cohorts. The concentrations of Ca, Ti, Ni, As, Br and Sr in hair of the patients were found to increase over that of normalMongolian people reported by other researchers. It is noteworthy that concentrations of Ca, Ti, Ni, As, Br and Sr in the human hair of the cirrhosis and acute viral hepatitis patients were higher than Mongolian normal human hair. To determine the interaction between nine elements in hair correlation coefficients were calculated. The strong positive correlations were observed between Zn and Ca or Fe; Mn and Ca or Ti; Sr and Zn or Fe. This means that correlation analysis might serve as an important issue associated with analysis of liver disorders. For correctly assessing the role played by the trace elements in initiating, promoting or inhibiting liver disorders in human hair, there is a need for acquisition of more data by trace elemental analysis from several investigations of this type undertaken in different regions. These data successfully applied at the Department of gastroenterology, Shastin Central Clinical Hospital of Mongolia for serving a basis of diagnosis of ailment or disease.

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CESARIAN SECTION RATES AND COMPLICATIONS IN MONGOLIA

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Absract

The respective impact of obstetrical and surgical factors has rarely been analyzed and no study has been attempted in this area in Mongolia. This retrospective study was carried out in 3524 (5% of all deliveries) women cases, who underwent cesarian section between 1996-2000. The data obtained through the questinnaires with 113 questions on 29 parameters and was evaluated statistically. The incidence of cesarean sections is continuously increasing (8% and above), while the surgical complications have not decreased (47,8%). PROM (15,8%), insufficiency of the utrine scar (15,5%), and associated diseases with pregnancy (12,2%) constitute the leading indications of cesareans. The frequency of post-cesarean infection complications is high (17,4%-30.4%). Perinatal mortality occurred in 35.2% of cases. The number and rate of all cesarian deliveries, primery and repeat, rose 1996-2000 in Mongolia and mother and child morbidity rates were correlated with the severity of obstetrical manifestations and delay of care.

Keywords: postpartum complications, post-cesarian infection

INTRODUCTION

The prognosis of emergency cesarean section is poor for both the mother and child in developing countries. The analysis of clinical records of women delivered with cesarean sections have shown that recent increase in cearean rates neither improved maternal or newborn health nor decreased maternal or perinatal mortality, but significantly reduced the professional skill arsenal of obstetricians and midwives/1-3/.

Compared with vaginal delivery, the risk of woman dying during the cesarean section is 10-26-fold higher. According to V. Unzeitig *IAI,* postpartum infection is present in a every eighth women undergone abdominal delivery.

The leading morbidity after cesarean surgery is the uterine infection. To prevent this complication, it is required to reduce the number of unnecesarry cesarean sections and, most importantly, improve the fetal monitoring and management of labor, introduce vaginal birth after cesarean (VBAC) or any other uterine surgery and improve prophilactic measures against infection.

Therefore, the present study was intended to address the most common indications for and risk factors of emergency cesarean delivery, direction of the national cesarian rate and prognosis of complications and the posibilitiesof improvingthe outcome of cesarean section, prevention of infection or management of women with uterine scar to date, because no study has been attempted in this area in Mongolia.

MATERIALS AND METHODS

Retrospective study: We did a retrospective analysis of the clinical records of the women delivered at the First maternity Hospital of the Ulaanbaatar City, and at the Maternity units of the general hospitals of Khovd,Arkhangai, Khuvsgul, Khentii and Umnugobi aimags during 1996-2000, a total of 70,490 women delivered at these hospitals including 3,524 women who undergone cesarean sections, which count for 5% of deliveries. The model questionnaire recommended by the WHO to assess the surgical complications in obstetrical practice has been modified according to the country

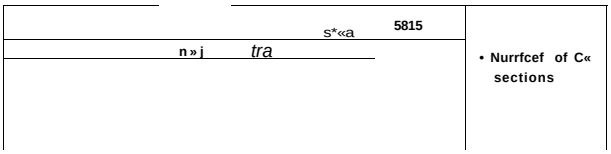
situation. The modified version had 113 questions on 29 parameters, and the data obtained through thequestinnaire.

Statistical analysis: All case-hystories were evaluated and analyzed by statistical exact Fisher's test and univariate and multivariate stepwise regression analysis. P values of <0.05 were considered significant.

RESULTS

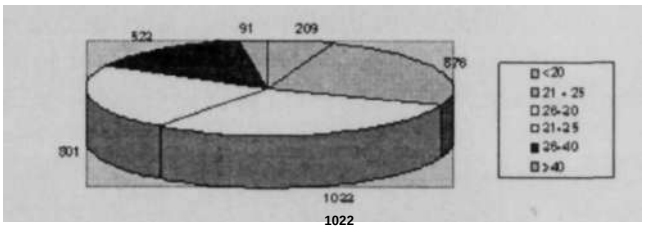
During 1996-2000, a total of 233,831 gave birth in Mongolia including 14,365 (5,7%) who were delivered by cesarean section. In 1996, 51,456 women gave birth including 2,101 (4,1%) who had undergone cesarean. However, in 2000, out of 51,276 deliveries 3,815 (7,4%) had cesarean. Thus the cesarean section rate has increased from 4,08% to 7,44% or by 3,36%.

Figure 1. The number of cesarean section during 1996-2000 in Mongolia



During 1996-2000, a total of 70,490 women delivered at these hospitals including 3,524 women who undergone cesarean sections, which count for 5% of deliveries.

Figure 2. Age of women delivered by cesarean section



From the figure2, it draws a special attention that 5.9% (209) ofwomen were younger than 20 years old. Out of these 209 women, 50 (23,9%) became pregnant before the legal age of marriage and underwent cesarean sections. Overall, 53,9% of women were 21-30 years old which is related to the highest fertility rate in this age group.

Among the subjects of the study, 82,2% were first-time cesareans. Among 628 women (17.8%) undergone repeat, 2nd or third, cesarean sections, 568 (16,1%) became pregnant within 1-1.5 years after the previous cesarean section and 58 (1,6%) within 1.6-2 years indicating relatively high incidence of repeat cesareans.

The retrospective study has shown that cesarean indications have the following structure: Premature rupture of membranes (PROM) - 15,8%), insufficiency of the scar of the previous cesarean section - 15,5%, severe conditions associated with pregnancy —12,2%, severe pre-eclampsia refractory to the medical treatment and eclampsia -10,7%, prolonged pregnancy with low Fisher score - 6,4%, primipara at age older than 28 - 5,7%>, prolonged labor -5 ,4%.

Out of 557 cases of PROM, in 10%, cesarean was performed within the first 6 hrs of PROM, in 60% within 6-12, and in 30% after 12 hrs. In other words, in 90‰ of cases, the surgery was performed on potentially infected uterus.

In the second place among the indications of cesarean sections, repeat cesareans constituted 15,5%) of cases and in most of the cases, the uterine incision was performed by Eltsov-Strelkov method with catgut sutures.

A total of 431 women undergone cesarean section because they have presented with health conditions associated with the pregnancy. Among these women: 63,6%> - presented with renal and urinary tract infections. 16.9% - cardiovascular disease, 5.1% - gastrointestinal disease, 4.6% - neurological disorders and 2.6%) - respiratory tract and endocrine disorders respectively.

There were 193 (5,5%>) cases of abnormal fetal position, including 87 (2.5%>) shoulder presentations, 67 (1.9%) breeches with estimated birth weight of above 3,500 gs, and 39 cases of (1.1%) extended head presentations.

Fetal asphyxia was the cause of cesarean indication in 297 cases (8.5%>). The majority of fetal indications were made after the onset of delivery, thus the interventions were made late and number of newborn had Apgar scores below 5. This was observed at both rural and Ulaanbaatar hospitals.

Among 324 cases (9.6%) of cesarean sections due tocephalopelvic disproportion, 5.1% (180) had II and III degree contracted pelvises, 2.4% (85) had surgical repair of the cervix or pelvic floor, 1.4% (50)-history of pelvic trauma, 0.4%> (15)-pelvic

and uterine abnormality and 0.3% (9) - history of III degree perineal tear.

Bleeding due to placenta previa and abruptio placentae constituted 126 (3,6%) cases. There ere 58 cases (1.6%) of placental abruption and 48 cases (1.4%) of placenta previa including 20 cases (0.6%) of lower segment placentas.

There were 37 complications observed in the total number of cesarean section. In 21.5% (5) it was hemorrhage, in 17.4% (4) - metritis, in 17.4% (4) - peritonitis, in 13.0% (3) - endometritis and in 4.3% - other complications.

Re-laparatomy was performed in 18 cases (0.5%) of all cesareans or in 48.6% of all complications because of bleeding, uterine or adnexal purulent inflammatory disease, generalized peritonitis or dehiscence of the uterine repair.

All women who received cesarean section were grouped in three groups according to the type of uterine wound repair. The first group comprised 2,023 cases (57.4%) operated by the Eltsov-Strelkov method, which uses two layers of separate sutures. The second group had 993 women (28.2%) who were repaired using a combined method of first layer performed with separate mucosa-muscle sutures and the second layer with a continuous muscle-muscle suture. The last group had 508 (14.4%) cases operated with continuous mucosa-muscle sutures. All three groups used catgut suturing material and the wound then was closed with the visceral peritoneum.

Using sutures very close one to another and closing the peritoneum causes reduction of the blood circulating in the wound area and edema around the sutures delaying the regeneration process due to lack of oxygen and necrosis. The average bed occupancy of women undergone cesarean section with catgut sutures was 13,7±0,7 days.

Overall, 35,5% of cases (1,254) lost up to 500 mis of blood, and 64,5% (2,273) lost 501 mis and more amount of blood. Hypo and atonic uterine bleeding during and shortly after the surgery was observed in 36 cases counting for 4.0% of all cases. Associated renal and urinary tract diseases, cardiovascular diseases and gastrointestinal disorders tended to lead to coagulatory disorders, including the disseminated intra-vascular coagulation, contributing to heavier blood loss.

One third of women who had cesarean sections revealed the history of having one, two or more abortions including spontaneous abortions, and one of twenty women had a previous cesarean. Half of women who had cesareans mentioned a history of an inflammatory disease of internal genital organs.

Table 1. Birth weight of the newborn delivered by cesarean section

Weig	8 9	000 o	1001 2000	B 8	3001 4000	Over 4001
Number	32	23	69	953	2179	268
%	0,9%	0,7%	2,0%	27j0%	61,8%	7,6%

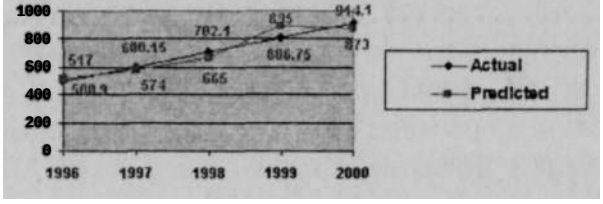
Table 1 shows that out of 3,524 women delivered by cesarean section 3,6% had babies of up to 2000 g or preterm infants. They were mainly delivered in emergency situations to save mother's live independently of the survival chances of the newborn. These babies contribute to 35,2% of perinatal mortality. Ten percent of babies over 200 lg of birth weight were asphyxiated and 15% had trauma indicating the lack of technological fetal diagnosis capacity and timely comprehensive interventions to improve the fetal status.

The cesarean section rate trend was calculated using the following formula

$$na + c\sum t^2 = \sum y \qquad b\sum t^2 = \sum yt$$
$$a\sum t^2 + c\sum t^4 = \sum yt^2$$

and it shows an increasing trend over the forthcoming years.

Figure 3. The cesarean section rate trend



With the increase of cesarean rates , no trend of decrease in maternal mortality ratio (MMR) has been observed. Actually this increase leads toward increased MMR. For instance, during and after cesareans uterine infection occurred in 30,4% of cases, uterine hemorrhage - in 21,5%, generalized peritonitis occurred in 17,4% which lead to the

subtotal or total hysterectomy and in 2,8% mothers died. Early identification and monitoring of women with high risk of undergoing cesarean section, and comprehensive and intensive prevention from potential complications, including appropriate evaluation of the maternal and fetal health would increase the proportion of elective surgery and thus reduce maternal and perinatal mortality.

DISCUSSION

The increase in absolute numbers of cesarean sections as it can be seen from the figure 1 is linked to the continuous changes in indications of cesarean section. However, it is also influenced by the fact that many obstetricians nowadays regard cesarean as a simple and available procedure and by overall increasing numbers of surgical solutions in the modern obstetrical practice.

Among 3,524 cesarean sections, 54,2% were emergency and 45,8% were elective. The predominance of emergency cesareans indicates that procedures without thorough preparation served as condition for increased number of infections and violation of infection prevention guidelines.

The maternal mortality reviews have shown that although modern preventive and therapeutical methods have been extensively applied, major causes of maternal deaths occured in relation to abdominal delivery consist of hemorrhage and post-operative infection /5-8/. Cesarean section ought to be very safe. In order to resolve this issue, firstly, the number of unnecessary surgical interventions should be reduced by improving the evaluation of the fetal status and timely management of the complications of labor and delivery that will allow vaginal birth after cesarean section (VBAC) and, secondly, the incidence of infections can be reduced by improving the prevention and treatment of post-operative complications including the optimization of the cesarean repair technique that creates the best condition for wound healing process.

One of every four women undergoing cesarean section have had a previous cesarean because of fear of uterine rupture through the scar. Increasing incidence of repat cesareans has been highlighted by a number of authors /9-1*II*.

With the increase of cesarean sections, the incidence of post-operative infections has also a tendency to increase. In Mongolia, the frequency of post-cesarean infection complications is high (17,4%-30.4%). The results of our study are in line with the conclutions made by many Mongolian researchers /14-20/. Our study has shown that prevention of post-operative infection after cesareans should be comprehensive but individualized for each woman, and should start before the surgery. The recommendations of the study by F.A. Smekuna /20/ also confirm our conclussions.

However, according to our findings, the most important prevention measures take place during the surgery. These measures include to do a proper coagulation of bleeding vessels in the fatty layer under the skin, use a correct incission on the uterus (Derfler's method), evacuate fetal head carefully, choose the optimal method for uterine repair and rinse the abdominal cavity with an antiseptic solution during the surgery.

The second most important aspect of the cesarean section is the regeneration of the tissue around the uterine wound. This is very important for two reasons, firstly, the deshiscence of the uterine repair in case of infection provides the opportunity to a local infection to spread in the abominal cavity. Secondly, poor prognosis for the outcome of consequent pregancy and labor as poor healing of the wound can cause uterine rupture /21-23/.

Our results agree with that complete recovery of the uterus from the cesarean section often depend of the repair method and suturing material /24-26/.

In conclusion: The incidence of cesarean sections is continuously increasing (8% and above), while the surgical complications have not decreased (47,8%). PROM (15,8%), insufficiency of the utrine scar (15,5%), and associated diseases with pregnancy (12,2%) constitute the leading indications of cesareans. Maternal and newborn health institutions should comply with the preventive scheme in order to decrease the incidence of complications linked with cesarean sections.

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ORIGIN OF MOXIBUSTION

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Abstract

Moxibustion although nowadays adopted in other countries, is a curative method which was unique to Mongolia. It is well-suited to our continental, cold and changeable climate and to nomadic living conditions. A very ancient report on Mongolian Traditional Medicine was noted in the "Huang Di Neijing" the book of Traditional Chinese Medicine written more than 2000 years ago. According to this book, moxibustion came from beyond the north of China. North of China is Mongolian territory and it is known to have very cold climate, people who eat dairy products and who live in the open, meaning nomadic people or the dwellers within felt walls, ac=cording to another text. Another interesting fact is brought to light in the fifth chapter of the Root Tantra of "The Secret Oral Tradition of the Eight Branches of the Science of Healing" (Four Medical Tantras in all), collected by Yuthog Yontan Gonpo the elder (First great Tibetan doctor). He noted that "Mongolian moxa cauterisation (Khorji-Meza) was a treatment for disorderly khii otherwise wind"[1]. Mongolian moxa consists ofFoeniculum vulgare tied up in felt, after which it is immersed in hot oil and applied points of the body associated with the wind. These historical facts testify that moxibustion therapy was first invented and used by Mongolian people, and was then introduced to China over 2000 years ago. It follows then, that Mongolian moxibustion was the precursor of both Chinese and Tibetan moxibustion treatment.

Key words: Moxibustion, Hunnu Empire, "Four Medical Tantras" and "Huang Di Neijin"

INTRODUCTION

In order to free themselves from the suffering of ailments, the ancient Mongolian ancestors instinctively used sharp-edged stones and applied heat, readily accessible resources in their natural surroundings, to relieve the aching parts of the body. Thus they learned that disorders of the body surface or internal organs could be relieved or cured by stimulating certain other areas of the body. Eventually, through the accumulation of such experience, our ancestors discovered that principles in the cure of disease could be deduced, and that theories of treatment, could be established which, in turn, gave rise to the systematic development of the techniques of moxibustion.

Materials and Sources

1. The Quintessence Tantras of Tibetan Medicine, Ithaca, New York, USA, Snow Lion Publications, 1995 (translated by Dr.Barry Elark)

2. The Yellow Emperors Classic of Medicine, (with commentary MaoshingNi). Boston and London, Shambhala, 1995.

3. "Ancient Mongolian Moxibustion" manuscript in Vertical Mongolian script

RESULTS

Moxibustion although nowadays adopted in many countries, is a curative method which was unique to Mongolia. It is well-suited to our continental, cold and changeable climate and to nomadic living conditions. Mongolians call it heat therapy. During the 8[th] century C.E. the principal oriental medical

book "Four Medical Tantras" advocated to "heal wind (mania) using smear (to apply a medical ointment etc) massage and Mongolian (Khor) moxibustion" in its chapter 5 and named "Methods of Treatment".

However, although the above mentioned phrase is considered to be the most respected source, there is some information about moxibustion methods used by Mongolians in Tibetan texts. We therefore intended to prove the recording studying different sources.

The oldest information about Mongolian moxibustion is recorded in the Chinese medical text "Huang Di Neijin", compiled in the period of the Han Dynasty, after almost 2000 years. The "Huang Di Neijin" consists of two sections: 'Suwen' meaning "Questions Organic and Fundamental Nature" and "Zhen Jing" meaning "Classics of Acupuncture". "Suwen", though, represents the whole "Nuang Di Neijin" in the historical field. The following phrase was written in the chapter entitled "Methods of Treatment". "Their build is too stout and huge and their internal organs are hurt by the cold. In this situation the most convenient treatment is moxibustion. Therefore, moxibustion is said to originate in the North".

According to "Four Medical Tantras", Mongolian moxibustion treatment was called Khorji Meza. The scholar and great master Lunrig Dandar (1831-1920) first defined Khorji Meza. He described as follows: First, they prepared a paste mixing Foeniculum vulgare with oil. Then, they put the paste on a stone (spar), and placed it on aching points.

Inner Mongolian researchers have been successful at finding old medical sutras. For instance, in 1992, Dr. Duvan Gombojav came upon a manuscript about moxibustion written in vertical Mongolian script and published it under the name of "Ancient Mongolian Moxibustion". The unknown author of this book determined 177 moxibustion available points (belcher in Mongolian) of which 22 points are on the head, 25 are on the hands, 28 are on the front side of the body, 80 are on the back and 22 are on the legs. The book had 27 pages.

Comparing the writing style and terms used in the "Ancient Mongolian Moxibustion" with those of Erdeniin tovch by Sagantsetsen, Duvan Gombojav, the moxibustion textbook was inferred to be written nearly 300 years ago. In addition, he noted that Mongolian moxibustion methods differed from Chinese and Tibetan methods.

DISCUSSION

During 198 B.C., to Han Dynasty accepted the Hunnu Empire created a contracted defining the two countries borders. According to the contract, territory to the north of the Great wall belonged to Shanyu, while territory to the south of the Great wall belonged to the Han Dynasty.

The Hunnu's territory during this time period reached Baigal nuur to the north, the Great wall to the south, II tarvagatai to the west, and Korea to the east. Early Mongolians, who roamed over such a wide land with a variety of climates, surviving on a diet of only meat and dairy products, were more likely to suffer from cold related diseases. The origin of moxibustion treatment was a therapy for cold related diseases, as was recorded vividly in "Huang Di Neijin". Other evidence (History of Mongolia. Volume 1. Establishment of Hunnu Empire) states that all of the Hunnu would only eat meat and dairy products while using animals' skins for clothing. Thereby, it is reasonable to assume that the ancestors of Mongolians first developed moxibustion and put it into medical practice. B. Jigmed (1985,2000), Sh. Bold, M. Ambaga (1999. 2000), Burenhuar, Delger (1999), Sh.Bold (2005, 2006) noted this hypothesis in their workshops.

Moreover, early the Mongolian ancestors, "Uhuni" burned artimesia frigida next to patients or applied them with hot stones. Also, they had the patients lie in burning grass (Ts. Shagdarsuren 1991). Later, a Persian historian Pashid Al-Din proved it again in his work "Sudar- yin Chuulgan". He wrote that nomads of Xianbi State could preserve the ancient treatment methods. In fact. they applied a hot stone to the patients, covered them with water, and let them lie on ploughed ground. The Hunnu tribe inhabited the territory during the 2nd century C.E. Thus, the hot stone moxibustion method was transmitted to Xianbi

State. (According to the investigation of their names and languages, it was proved the two tribes had the same origin (G. Sukhbaatar, 1992). The moxibustion method was received by the Tureg Khanate, the dominating tribe of the period. Afterwards, during the Uigur's period (745-840), it spread onward to Tibet.

While studying "Ancient Mongolian Moxibustion", we came across terms such as khii (wind), shulsun (phlegm) or shar (bile) and shilusun, demonstrating that the ancient Indian medical theory of Ayurved "vata, kapha and pitta" gained popularity among Mongolians as well as being a main theoretical and practical medical guide. Prior to this a school based on "Astanga Hrdayam"', the theories of khii (wind), shar (bile) and badgan (phlegm) blossomed in Mongolia. After the 17th century, terms like rlung, mkhris pa, badkan began to be used "Four Medical Tantras" entered Mongolian medical practice.

The terms khii, shulsun, shulusen are sometimes noted ask khii, shar, shulusen in the "Ancient Mongolian moxibustion". In the 1930s, a translator Sharavsenge (Guush) rendered the terms rlung, mkhris pa and badkan as khii, shar and shulusun when he translated sutra ' Altangerel" from Tibetan and Uigur into Mongolian. These terms were discussed in the chapter entitled "curing all kinds of diseases", and introduced Ayurveda medicine. Thereby, the key terms of Ayurved medicine "vata, kapha and pitta" were transletad as "khii, shar and shulusen" in Mongolian during the 14th century.

Therefore, we conclude that moxibustion therapy, which was practiced broadly during the Hunnu period, was passed on from generation to generation. It was introduced to China during the Chinese Warring States' period (475 B.C.), to Tibet during the Uigur's period (745- 840) and finally could became an independent medical method during the Yuan dynasty combining some key elements of Ayurveda.

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COMPARISON OF POLYDIOXANONE AND SILICONE PLASTIC IN THE PREVENTION OF ADHESIVE OTITIS MEDIA

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Abstract

The purpose of this study was to compare polydioxanone sheets with silicone plastic sheets in the middle ear to find out inexpensive ideal material to prevent readhesion of tympanic membrane to the promontory, to stay for long enough time until middle ear mucosal line regenerated and to absorb itself after regenerating of middle ear mucosa. Polydioxanone sheets were placed in 24 middle ears and silastic sheets were placed in 12 middle ears during ear surgery to prevent readhesion of tympanic membrane. The result of this study demonstrate that polydioxanone sheets are as effective and as well tolerated as silicone plastic sheets in the middle ear.

Key words: atelectatic ear, tympanic membrane, tympanic membrane retraction, grades of membrane retraction

INTRODUCTION

Adhesion of tympanic membrane to the promontory /inner wall of middle ear/ may occur after ear surgery particularly in atelectatic ears because of poor eustachian tube function and removal of mucosa from the promontory during surgery/3-11-12/.

Silastic sheets /silicone silastic sheet/ have been used in middle ear surgery for many ears to prevent readhesion of tympanic membrane to the promontory. These sheets are usually placed on the promontory before graft placement and may be removed at the time of revision surgery if necessary /3-4-10-14/. Every patient doesn't need revision surgery and has to stay for life time with foreigh body in the ear. Silicon sheets are generally well tolerated, but they are subject to occasional extrusion, encapsulation, or foreign body reaction /3-11/. The ideal barrier to adhesion formation would be a nonreactive, flexible, absorbable substance that would obviate long term toxicity consideration. A number of synthetic materials are used as suture materials and have established their credentils as well-tolerated biomaterials. Polyglycolic acid /Dexon/, polyglactin 910 /Vicryl/, polyglycolidetrimethylene carbonate /Maxon/, polycaprolactone, and polydioxanone /PDS/ five absorbable synthetic ploymers that are widely used as suture materials in surgical practice now/l-3-8-9-13-15/. An absorbable material that is quickly resorbed would not keep the middle ear space open long enough for the middle ear epithelium to regenerate. The longest lasting of the above 5 materials is PDS which lasts approximately 50 longer than dexon and twice as long as vicryl. All of the above materials are absorbe through hydrolysis. Polydioxanone has been shown to be well tolerated in a variety of surgical settings *IX-ll.* It may be a material that is as well tolerated as silicone plastic in the middle ear, in addition to being persistent enough to promote regrowth in the postoperative ear before resorbition.

The purpose of this study was to compare polydioxanone sheets with silicone plastic sheets in the middle ear to find out inexpensive ideal material to prevent readhesion of tympanic membrane to the promontory, to stay for long

enough time until middle ear mucosal line regenerated and to resorb itself after regenerating of middle ear mucosa.

MATERIALS AND METHODS

The study was covered 36 patients with adhesive otitis media who need surgical treatment. The average age of our patients was 12 years and sex was about equal 12 /46.2%%/ females and 14 /53.8%/ males.

Polydioxanone sheets were placed in 24 /66.7%/ middle ears and silastic sheets were placed in 12 /33.3%/ middle ears during ear surgery to prevent readhesion of tympanic membrane. Gelfoam was occasionally necessary to maintain the flap's position /Table 1/.

We have used silastic sheets which were prepared specially for ear surgery. Polydioxanone sheets for the study were prepared by melting PDS 4.0 suture in an oven at 130°. The suture was than platened in a press to the appropriate thickness and cooled to room temperature. The resulting sheet was then cut to the size of 0.3x 0.3 sm in diameter. The polydioxanone plastic disk were steam sterilized and kept packs until use.

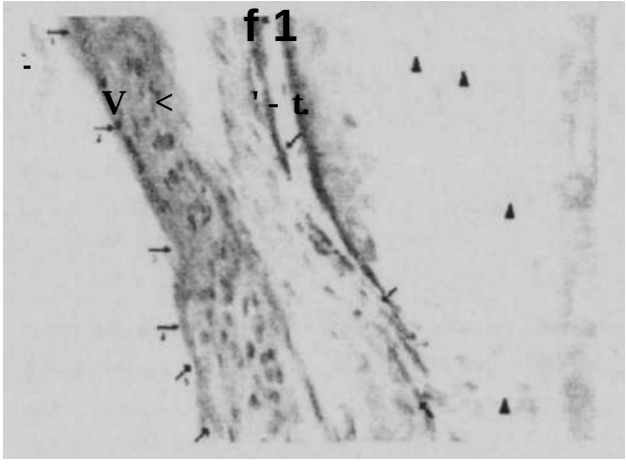
Table 1. Placed materials in the middle ear to prevent readhesion of tympanic membrane after surgery

Material						
PDS sheds		Gelfoam		Silastic sheets		
N	%	Fi	%	N	%	!
~~24	667	36	6M	12	531	

Ear packs were removed out on 9th day after surgery in all patients. Granulation tissue was present in ears /2.7%/ which were implanted with PDS. There was no significant difference in numbers of ears with vascularization, swelling, wound effusion around the tympanic membrane / healing process/ and adhesion formation between 2 groups or between time periods by the Fisher exact test.

When the 2 groups were compared with each other with the respect of healing process and formation of tympanic membrane the p values were 0.370 at 14th day, 0.630 at 21th, 1.00 at 30th day after surgery /Table *21*.

Figure 1: Patient L. 16, m. Hystological investigation from middle ear mucosal line after 7 month of surgery. Intympanic cavity placed polydioxanone sheet to prevent adhesion of tympanic membrane to inner wall of middle ear space. Re growth of middle ear space.



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3 ears from polydioxanone implants group and 1 ear from silastic implants group were examined during second look operation hystologically at 7th month postoperatively. Polydioxanone sheets weredisappeared on 7th month after surgery in 2 middle ears during second look operation /Figure 1/.

DISCUSSION

The investigation of various biomaterials for use in the middle ear has been in story of continuing progress since the 1950s, but the use of silicone plastic sheet has remained fairly common since the beginning of this field.There have been few reports of extrusion of these sheets.Neverthless, the pressure on silicone products has been growing , and the time may come when silicone plastic sheets are no longer widely available for use. Silicone is certainly noted for its persistence and one approach to overcome this inherent defect is to use absorbable sheet that is well tolerated. The absorbable suture materials all have extensive track

records of exellent tissue tolerance. Ideally such material would persist long enough to alow regrowth of epithelium in the mesotympanum but could not cause long term problems simply because of its absorption.Gelatin film has been used in this role but, because of its rapid absorption , may not be a suitable candidiate for a material to keep the mesotympanum open long enough to allow epithelial regrowth.lt is also stifferthan polydioxanone when implanted. As previously stated , there are a number of materials that are potential candidates for absorbable sheeting in the middle ear.The absorbable suture materials all have extensive track records of excellent tissue tolerance. Of the five suture materials mentioned, the most flexible is polydioxanone. Polydioxanone is also the longest lasting of the materials, with small fragments lasting as long as 6 month, whereas the other materials are all absorbed by 3 to 4 month. The feasibility of using polydioxanone sheets may therefore be established by merely showing that they are as well tolerated as the silicone products.Most ear surgeons would agree that silicone plastic sheets are fairly well tolerated in the middle ear. Our study was disigned to detect differences between two products in terms of tissue tolerance and ability to prevent adhesion of tympanic membrane in operated ears. No significant differences were detected between the 2 groups with respect these two parameters. Therefore polydioxanone is as well tolerated as silicone plastic in the middle ear.

In conclusions, there are no significant differences were detected with respect to the tissue tolerance in ears implanted with polydioxanone and silastic sheets during ear surgery to prevent adhesion formation. Polydioxanone sheet was as well tolerated as silastic sheet in middle ear and it was stayed long enough to promote regrowth in the postoperative ear before resorbtion.

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THE MANAGEMENT OF HYDATIDIFORM MOLE IN THE MONGOLIA

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Abstract

Gestational trophoblastic disease is a common gynecological disorder in Mongolia. It have come to conclusion that these diseases account for 2.9% of all cancers in women. The preferred method of evacuation is suction curettage. Partial moles in our study comprised 31.6%. This is potentially malignant and needs follow up for a complete mole. In the management of the invasive mole, chemotherapy should not be withheld in the presence of metastases and failure of regression of hCG. The role of prophylactic hysterectomy and prophylactic chemotherapy in the management of molar pregnancies is discussed in contrast to selective preventive chemotherapy in patient at Risk appears appropriate. Chemotherapy remains the main modality of treatment for gestational trophoblastic tumours.

Key words: Hydatidiform mole, partial and complete mole, gestational trophoblastic disease, tumour, methotrexate (MTX)

INTRODUCTION

Gestational trophoblastic disease is a common gynecological problem in Mongolia and in the region. The true incidence in Mongolia is, however, not known because of the lack of Tumor Register *l\l*. The National Oncology centre, Ulaanbaatar, is a major referral centre for gynaecological malignancies in the country. During the 10 year period 1992-2001 a total of 254 cases were managed in the gynaecologic oncology ward of the hospital. The risk of choriocarcinoma after hydatidiform mole is higher than after an abortion or normal pregnancy. Without optimal management and follow-up of hydatidiform mole, the risk of choriocarcinoma will be increased.

MATERIALS AND METHODS

A retrospective analysis was made on the outpatient and inpatient clinical records, including the results of the tests of patients admitted to the NOC during 1992-2001. The study questionnaire had 44 variables and over 200 alternative responses. The data was entered into an EPI-6 computer program.

The retrospective analysis method was also used for the assessment of the results of histological study on uterine samples tested during the past five years. The following is a description of the forms of gestational trophoblastic disease and the changes in therapy that has occurred during the time of the study.

The statistical analysis was performed using the SPSS 10.0 program.

RESULTS

The TBD cases were classified according to the WHO guidelines as hydatidiform mole and chorioepithelioma. The study comprised 40 cases (15.7%>) of chorioepithelioma and 214 cases (84.3%) of hydatidiform mole.

The analysis of the initial diagnosises of patients showed that 71.4% had different diagnosis before being referred to the NOC (67.8% for hydatidiform mole and 75% for chorionepithelioma). Among the patients who were previously addmitted to other hospitals, 88% were admitted in one ocasion, 6.3% in two occasions and 9.6% in 3-4 occasions.

Before being addmitted to the NOC, 13.8% of patients were diagnosed as miscarriage and 9.1% as dysfunctional uterine bleeding indicating that early TBD symtoms such as cessation of the menstrual periods, vomitting, nausea, hyperpigmentation of skin and vaginal bleeding present significant challenges for differential diagnosis.

The causes varied depending of the types of TBD. In 68.7% of hydatidiform moles the cause was not clear, while remaining 31.3% of cases presented after miscarriage, induced abortion, delivery or ectopic pregnancy. In 32.5% of chorioepitheliomas the causes were unclear, while 22.5% of neoplasms developed after induced abortion or hydatidiform mole

Overall 45.3% of patients with TBD have had induced abortions, 37% having 1-2 abortions and 8.3% having 3 or more abortions. If among patients who had abortions in the chorionepihtelioma group, 50% have had 1-2 terminations of pregnancy, the majority of those in the hydatidiform mole group experienced 3 and more terminations of pregnancy.

Among all participants, 50.4±6.3% presented vaginal bleeding, 32.7±5.9% presented lower abdominal pain in association with other symptoms, 5. 1±2.8% had hypertermia and 3.9±2.4% had some symptoms of gestosis.

Asherman's Syndrome occurred in 2 of our patients; after lysis of intrauterine synechae fertility was restored /5/. Although others *161* have reported acute respiratory distress to occur in 2 per cent of cases, we have not encountered any. Although all patients had no evidence of choriocarcinoma 3 years later *111,* but we had 6 evidences after 6 month to 2 years. Our study demonstrated, for subsequent malignancy in patients with pregnancy at 40 years and over that the RR was 1.2. We found that in 32.6 per cent of our cases complete emptying of the uterus was not achieved at the first attempt.

The results showed that there were certain risk factors which were more likely for women to present with chorioepitheliomas than with hydatidiform mole. Those findings are as follows:

Women older than 40 years have OR=2.31

Women with history of 5 or more pregnancies OR=1.21

Women who had 5 or more deliveries OR=2.38

Women with a history of induced abortion OR=1.41

Women with history of miscarriage OR=1.03

DISCUSSION

The classic mole or complete mole has a 46 XX karyotype and a partial mole has a triploid karyotype (69 chromosomes). In our review of the records the true incidence of partial hydatidiform mole in Mongolia is unknown because of under-reporting, lack of awareness, lack of detailed routine histopathological evaluation of placenta and products of conception evacuated at abortion *191.* Szulman and Bagshave /10-11/ claimed that choriocarcinoma has been associated with partial hydatidiform mole. Looi and Sivanesaratman /l 2/ reported malignant evolution with fetal outcome in patient with partial hydatidiform mole. The partial hydatidiform mole in the late can move to potentially malignant.

In the diagnosis of hydatidiform mole, the uterine size is often not consistent with the number of weeks of gestation. Typically in about 25% of the cases the uterus is smaller than would be expected with the gestational age. In the majority of cases the uterus is larger. Illustrative of this, one of our cases *141* had a 30 weeks enlarged uterus at 15 weeks gestation; the mole and fetus were seen on ultrasound. Once the diagnosis of hydatidiform mole is confirmed (by ultrasound) the uterine cavity is evacuated, suction curettage is the preferred method. The use of an oxytocin drip (10-20 units in 500ml saline) commenced soon after induction of anaesthesia helps the evacuation and minimizes the risk of uterine bleeding. Prevention of malignant sequelae should be the aim, thus complete emptying of the uterine cavity is essential *111.* Because of the number of patients who still had tissue within the uterus, in spite of others /3-4/ seeing no merit in a second uterine evacuation, we have advocated a routine repeat curettage 1 week after primary evacuation of the mole. The availability of good resolution ultrasound machines can help select more objectively the cases that would require a second evacuation. The danger of

repeated curettage is the development of Asherman's syndrome.

It is well known that embolisation of trophoblasts occurs during uterine contractions (stimulation by oxytocics, uterine evacuation and hysterectomy). In the early 1980s, we felt that prophylactic intravenous methotrexate (50mg in 400 ml saline) infusion during evacuation of a mole or hysterectomy for mole would help eliminate these emboli and thus help solve problems of follow-up and late diagnosis. We have now stopped the above practice and, instead follow-up patient with serial hCG after uterine evacuation practice, selective preventive chemotherapy in those patient who we consider are at risk of developing choriocarcinoma is applied.

Some researchers reported the rate of subsequent malignancy in patients with pregnancy at 40 years and over is 3 '/: times of those below 40 years of age; similarly, the risk of malignancy was higher with increasing parity age *HI.* Thus, we advocated prophylactic hysterectomy in these 'high risk' cases. For many years, it has been routinely practiced. When radioimmunoassay for hCG became available in 1999, we have stopped performing prophylactic hysterectomy

We did not see any cases of malignant mole. In the practice conserving the uterus in patients with molar pregnancy, a pathological diagnosis of invasive mole can not be made, the diagnosis of myometrial invasion is not always possible with abdominal or vaginal ultrasound.

Deep myometrial invasion can result in uterine perforation and massive intraperitoneal haemorrhage. The areas of haemorrhage and necrosis in the uterine wall can be confused with choriocarcinoma /l 3/.

Gestational trophoblastic tumours are potentially curable. Good results in gestational trophoblastic tumour can only obtained by referral to specialized centres; this will help in accurate diagnosis, determining the extent of the disease and institution of appropriate chemotherapy.

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COMPLICATIONS OF THE SURGICAL TREATMENT OF UPPER GASTRIC CANCER

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Abstract

Such a complication the leakage from esophageal anastomosis alone accounts for 25-60 percent of mortality following the upper gastric cancer surgery. Although the surgical technique is often accountable for the complication, a number of other factors such as anatomical peculiarities of esophagus, level of esophageal excision, degree of esophageal involvement and surgical approach play role in it.

The current study investigated the esophageal leakage complication based on the records of 137 patients who underwent surgical treatment for upper gastric cancer at the National Cancer Center (NGC) during 1994-2002. Irrespective of the type of surgery, anastomoses with the use of stapler result in twice as less complications as manual methods, and no difference is observed in complication rates between gastric resection and total gastrectomy.

Key words: gastric cancer, surgery, gastrectomy

INTRODUCTION

One of the most life-threatening and common complications of the surgical treatment of upper gastric cancer is leakage from esophageal anastomosis/l-2/. This complication alone accounts for 25-60 percent of mortality following the upper gastric cancer surgery. Although the surgical technique is often accountable for the complication, a number of other factors such as anatomical peculiarities of esophagus, level of esophageal excision, degree of esophageal involvement and surgical approach play role in it /4-7/. Although the introduction of a stapler into esophageal surgery in 1980s significantly improved surgical outcomes, leakage complication issue has not been resolved fully since surgeon's clinical experience, intuition and skills are especially important in the process /9-11/.

MATERIALS AND METHODS

The current study investigated the esophageal leakage complication based on the records of 137 patients who underwent surgical treatment forupper gastric cancer at the National Cancer Center (NCC) during 1994-2002. (58- upper gastric resection, 74-total gastrectomy , 5- lewis surgery)

RESULTS AND DISCUSSION

The above time period has been divided into three periods according to the introducton of new surgical techniques and methods.

Table 1. Mortality due to esophageal leakage

Period	Number of patients undergoing surgery	Post-surg c*l mortality			
		Totjl		Of tnem. dui 10 leakage	
		Number	**	Number	*Vi*
1(1004-1006)	24	7	29213 9	4	10,7 £3,3
11(1097-1000)	»	1	21613.5	4	108127
iii(5oM)-2biU)	76	11	146130	S	7 0123
Tom	157	26	19013 4	14	102126

The table above demonstrates a two-fold decrease in post - surgical esophageal leakage in the 3rd period compared to the I^{s}'.

The relationship between mortality due to post - surgical esophageal leakage and the extent of the surgery is demonstarted in the following table.

Table 2. The relationship between mortality due to post-surgical esophageal leakage

Type of surgery	Number of ljatients undergoing surgery	Mortality due to esophageal leakage Number	
Upper gastric resection	58	5	8,2+2,3
Total gastrectomy	74	7	9,5125
. Lewis surgery	5	2	400+4.1
Total	137	14	102+2.6

Mortality due to esophageal leakage is the highest for Lewis surgery (40,0±4,2%). This could be related to small number of such surgeries in general and inherent complexity of the surgery itself.

The frequency of esophageal leakage depends on the degree of esophageal involvement and surgical approach, which is demonstarted in the following table (E - esophagus, C - gastric cardia).

Table 3. The frequency of esophageal leakage depends on the degree of esophageal involvement and surgical approach

Sutgical appro ac h and degree ot esophageal invoTvemtnt		Numtiti of pjttnts	EsoptijgQJl lcjkjge Numtxi	*
Abdominal approach	K->ew	54	0	6
	§ <•) S(.)	78	6	103*2.6
	Totjl	(M	1	7.6323
Tbftiwo-abdominal approach	E *i)* «-)	0	1	11.1±2.7
	E (•) C(.)	21	3	143*3.0
	Total	56	4	133*2.0
LtwMf surgtry	E O C()	2	1	600*4.3
	E W BM •	3	1	333±4.0
	Totjl	S	2	400*4.2
Tctil	EO«>	35	2	5.7J2D
	E (•) C(«)	105	15	13.7*2,0
	Totjl	<37	14	102*2.0

The above data suggests that esophageal leakage is common in upper gastric cancer with the involvement of esophagus. However, there is no significant difference between complication rates in patients with gastric resection and total gastrectomy. We also studied the relationship between the complication rate and anastomosis technique (manual or with the use of stapler) taking into the account the surgical approach. The results are demonstrated in the following table.

Table 4. Relationship between esophageal leakage rate and surgical approach and technique

Surgical approach	Aiwstqmo»S technique ~r*w- Numb op«tjt td	Mortatit* rate O)	* Numb " optrjt • d	Mortality ut* w	WitS the Numb , f op.l* td	of stapler MortattW rate fit)
Abdominjl	102	8(7.612.0)	70	7(1001214)	32	1(3 1*1.4)
Ihoraco. Jbdommjl (I.H)	50	4(133*2.0)	51	3(14313.0)	0	1(11.1*2.5)
XtjftUK*'Jb do mir. jt (right)	*	2 (40*4 1)	*i*	1 (50*42)	5	1 (33314.0)
Tcptjl	13?	14(102*25)	05	11(11.6*27)	44	3(0 8*2.1)

Esophageal leakage rate is l .7 times less when a special stapler is used compared to manual anastomosis. Furthermore, the above difference is 3.2, 1.3 and 1.5 when abdominal, left thoraco-abdominal and right thoraco-abdominal approaches are used, respectively.

The results of the study suggest that there is no relationship between the complication rate and the extent of the surgery. This is demonstrated in the table below.

Table 5. Comparison of the mortality rate due to esophageal leakage and the extent of the surgery

An art or. *ot* rs teefmkjue	Upper gastric resertion Number operated	Mortality iat«	Total gastrectomy Number operated	Mortality iat« (*)	Total NufU*. operated	Mortality rate (*>
Manual		S (11012.7)	54	0(11812.7)	8?	11(11.812.7)
With tie use of stapler		1 (3.311.0)	*H*	2(8,012.3)	44	3(0.8*2.1)
T«U		0(0.932.5)	*lb*	9 110512.6)	ly>	14 f10.2*2 5)

Use of stapler in upper gastric cancer surgery reduces mortality due to esophageal leakage 1.4-3.2 times.

In conclusion esophageal leakage is comparatively common in patients with upper gastric cancer with the involvement of esophagus. In one hand, this could be related to the need for resection well above the upper cancer boundary. On the other hand, resection of the stomach stretches and restricts the movements of gastrointestinal organs. This potentially explains fewer esophageal leakages after surgeries with abdominal approach.

Use of stapler in esophageal anastomosis not only significantly reduces the duration of the surgery,

but also allows the performance of the operation in the conditions of closed abdominal cavity.

Irrespective of the type of surgery, anastomoses with the use of stapler result in twice as less complications as manual methods, and no difference is observed in complication rates between gastric resection and total gastrectomy.

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