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Comparison of Amniotic Fluid Alpha-Fetoprotein and Gel-Acetylcholinesterase Tests With Fetal Blood Contamination

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Abstract: *The addition of 5% fetal serum, equivalent to 1.5 ml fetal blood in 20 ml of amniotic fluid, can result in a false positive amniotic fluid AFP test. The qualitative AChE test requires the addition of more than 3 ml of fetal blood to be abnormal. We recommend a repeat amniocentesis whenever both tests are positive despite the presence of fetal blood, but this may be avoided when the presence of fetal blood appears to explain a slightly elevated AFP (≥+3 SD<+5 SD) and the AChE and sonogram are normal. (Thai J Obstet Gynaecol 1989; 1 :1-5)*

Key words: alpha-fetoprotein, acetylcholinesterase,fetal blood contamination

Neural tube defects (NTDs) include anencephaly, spina bifida and encephalocele, most of which can be diagnosed in the second trimester by two amniotic fluid (AF) tests, alpha-fetoprotein (AFP) assay and acetylcholinesterase (AChE) analysis. AChE can be measured quantitatively or analysed qualitatively by gel-electrophoresis[1-4].The latter is frequently used in combination with AFP assay[5], and a laboratory engaged in the diagnosis of NTDs should probably perform both tests[6].

Because the concentration of AFP in fetal serum is between 100 and 200 times higher than in AF, false positive AFP tests can result from fetal blood (FB) contamination. The AChE test appears to be less influenced by FB contamination [1,4,7,-11], although some reported false positive results have been attributed to this. Maternal blood contamination does not affect either the AFP or AChE test[10].

The present study was designed to compare the amount of FB contamination required to produce an elevated AF-AFP and a positive AChE gel - electrophoresis test.

Materials and Methods

Fetal blood was collected from the umbilical cord of a normal 24 weeks infant delivered prematurely because of an incompetent cervix. Clear AF was obtained from a 17 weeks gestation with a normal AFP level and AChE test. 1%, 5%, 10%, 25% and 50% dilutions of cord serum were made in AF.

AChE electrophoresis was carried out by disc technique as previously described[10]. Two tests were run on each sample; the first without and the second with the specific AChE inhibitor BW284C51. A positive result was defined as a clear band in front of the non-specific cholinesterase which disappears with addition of the specific inhibitor. Positive and negative controls were included.

AF-AFP was measured by radioimmunoassay using a double antibody technique[10].

Results

AF-AFP levels, the equivalent concentrations of FB and the effects of different amounts of FB contamination on the qualitative AChE test are shown in Table 1 and in Fig. 1. By the definition used, the AChE test was not positive until the concentration of FB exceeded 10%. However, a faint but specific band was seen at concentrations of 5% and 10%.

The 17 weeks gestation AF sample used as diluent contained 1.03 mg% AFP and was negative for AChE. AFP measured 9.84 mg% in the cord serum at 24 weeks gestation and the AChE was clearly positive (Fig. 1).

Table 1. AFP levels and AChE results at different concentrations of FB contamination

Fetal serum in %	Equivalent [1] FB in %	FB in 20 ml of AF in ml	AFP in mg% and (SD)	AChE result
1	1.5	0.3 [2]	1.09(<2SD)	0
5	7.5	1.5	1.91(+2-3SD)	±
10	15.0	3.0	3.29(>+5SD)	±
25	37.5	7.5	6.84(>+5SD)	±
50	75.0	15.0	8.64(>+5SD)	±

[1] Packed cell volume 33%

Mean FB count 2.8 x 10^9 rbc/ml

[2] 20 ml of AF contaminated with 1% FS contains 0.3 ml of FB or 8.4 x 10^8 rbc

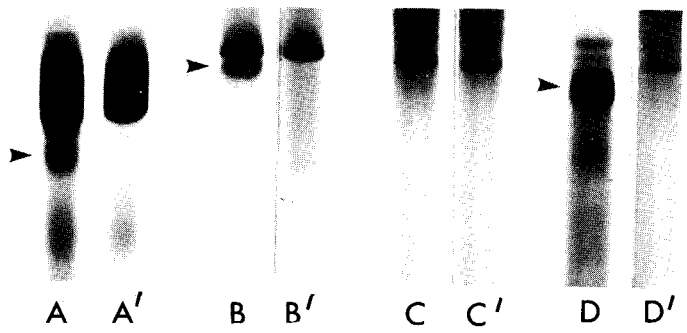

Fig 1 (a) AChE gel electrophoresis. AA'= cord blood, BB' = AF from open NTD, CC' = AF from normal 17 weeks pregnancy, DD' = AChE positive control.
In each pair the left hand tube contains no inhibitor and the right hand tube contains the specific inhibitor. ▲ denotes specific AChE band.

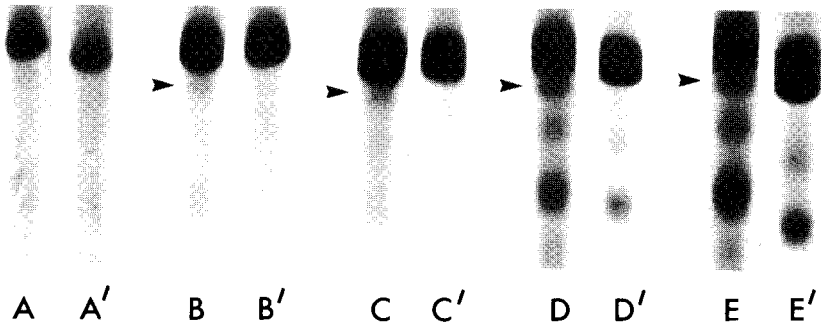

Fig. 1 (b) AChE gel electrophoresis. AA' = AF with addition of 1% cord serum, BB' = AF with addition of 5% cord serum, CC' = AF with addition of 10% cord serum, DD' = AF with addition of 25% cord serum, EE' = AF with addition of 50% cord serum. B and C show a faint specific band.

Discussion

Most fetal abnormalities which affect AF-AFP levels produce elevations which measure more than 5 SD above the mean. However, levels of between +3 and +5 SD are suggestive of some abnormality. In a recent analysis of 34,000 routine second trimester AF-AFP assays, the risk of a fetal abnormality was 22.6% when levels measured between +3 SD and +5 SD and 86% for those above +5 SD. Contamination with FB accounted for 36% of 72 false positives in the former group and 68% of 19 false positives in the latter group. A second test, less sensitive to FB contamination, could help identify these false positives, and in some instances might avoid a repeat amniocentesis. A qualitative AChE test using gel electrophoresis appears to fulfill this role and in our experience is much less affected by FB contamination than AFP. However, false positives have occurred with this test, usually with heavy FB contamination. In the series

reported above, we had 8 false positives with AChE, 7 apparently due to FB contamination.

In this study, an unequivocally positive AChE test occurred only with the addition of more than 10% FB. This was equivalent to more than 3 ml of FB in 20 ml of AF, an unlikely event since this amount to about 25% of the total fetal blood volume at 17 weeks gestation. At this level of contamination, the AF-AFP measured more than +5 SD above the mean. Additional dark bands in front of the specific AChE were also very suggestive of blood contamination (Fig. 1). The very faint band noted on the AChE gel with 5% and 10% FB contamination usually did not interfere with interpretation of results. All open NTDs produced a clear band which disappeared with addition of the specific inhibitor. A difference in the response of AFP and AChE to FB contamination would be even more apparent earlier in gestation because AF-AFP levels are about 20 times higher at 17 weeks compared with 24 weeks. Although AChE levels in AF at 17 weeks are not recorded, studies in other species, as well as higher levels in premature human gestations, show some decrease with gestational age, but this decline appears to be much less than for AFP.

From this study we conclude that repeat sonography and amiocentesis is indicated whenever the AF-AFP measures $\leq +$ 3 SD and the AChE test is positive, regardless of FB contamination. However, if the AF-AFP measures between +3 and + 5 SD above the mean, and the AChE is negative, a repeat amniocentesis may be avoided if FB is present, providing careful sonography excludes the presence of NTDs or other defects.

Acknowledgements

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If women with conditions not associated with hyperprolactinaemia are treated with Parlodel, the drug should be given in the lowest effective dose necessary to relieve the symptoms; this is in order to avoid the possibility of suppressing plasma prolactin below normal levels, with a consequent impairment of luteal function. In patients to be treated for mastalgia and nodular and/or cystic breast alterations, malignancy must be excluded by appropriate diagnostic procedure. There have been occasional reports of gastrointestinal bleeding in acromegalic patients, both in those treated with Parlodel and those given a different or no medication. Until further data are available, acromegalic patients with a history or evidence of peptic ulceration should preferably be given alternative treatment. If Parlodel must be used in such patients they should be instructed to report promptly any gastrointestinal reactions. 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In addition, constipation, drowsiness and, less frequently, confusion, psychomotor excitation, hallucinations, dyskinesia, dryness of the mouth and leg cramps have been reported during high-dose treatment with Parlodel. All these side effects are dose-dependent and can usually be controlled by a reduction in dosage. Episodes of reversible pallor of the fingers and toes induced by cold have occasionally been reported to occur during prolonged treatment, particularly in patients previously exhibiting Raynaud's phenomenon. **Presentation:** Tab 100.

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AIDS Antibodies Screening Test in High-Risk Population of Southern Thailand: Preliminary Report

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Abstract: *We screened the high-risk population with no clinical evidence of AIDS for HIV antibodies by ELISA during February to October 1988. Among 8,895 cases of the high-risk population in 7 provinces who volunteered for the study, 40 (0.45%) of them were initially positive by ELISA. Confirming by Western blot, 26 were positive and 14 negative. The prevalence of HIV infection in the high risk population of Southern Thailand was 26 (0.29%) of 8,895 cases. (Thai J Obstet Gynaecol 1989;1: 7-10)*

Key words: AIDS antibodies, high-risk population

The Acquired Immunodeficiency Syndrome (AIDS) is caused by the human immunodeficiency virus (HIV), also called the human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV). Among the people who have been infected by this virus, more than half of those with the disease have died. The actual case fatality rate approaches 100%. AIDS affects all groups and classes of people. although some are at special risk. Distribution of the disease is worldwide.[1]

HIV infection has now spread through large urban areas, mainly through sexual relationships. As far as sexual transmission is concerned, it is heterosexual, in spite of the primary epidemic outbreak in the occidental world that focused interest toward male homosexual group, the first exposed to AIDS. At present we know that heterosexual transmission is important and bidirectional, even if transmission from female to male has seemed to be more difficult to occur, as it is common in sexually transmitted diseases (STD). Transmission risk to a heterosexual partner is between 20 and 70%. The virus is present in semen and in cervico-vaginal secretions during the entire menstruation cycle. Vertical transmission from mother

to child, through placenta or during delivery is frequent,about 50%.[2]

The Region 12 VD center, is in charge of STD prevention and control in 7 southern provinces of Thailand; Songkla, Satun, Pattani, Yala, Narathiwas, Trang and Phatthalung. There is a recognized need for a serological assay for HIV that could be used for epidemiologic studies and screening of defined populations. Ideally, such a test would be reproducible, specific, sensitive, relatively inexpensive, timely and noninvasive. After mandatory blood tests on high risk populations from February to October, 1988, we then analyzed the preliminary application by the enzyme-linked immunosorbant assay (ELISA) in our laboratory

Materials and Methods

Serum samples were obtained from subjects; prisoners, prostitutes, drug addicts, and homosexual men. Specimens were transferred from the VD units of 7 provinces to the laboratory in the VD center. The serology screening tests for AIDS virus antibody were analyzed by the enzyme-linked immunosorbant assay (ELISA), Organon Teknika, and the positive ELISA tests were sent to Bangkok for confirmation as specific by Western blot. It also confirmed the validity of ELISA blood testing and suggested that ELISA-positive, Western blot-negative blood may not be infectious[4].

Results

The screening data for the voluntary high-risk population in 7 southern provinces is showed in the table below.

The total number of blood test was 8,895 cases. The prevalence of HIV positive (ELISA) was 0.45% (40 of the 8,895). The positive-screening tests were confirmed by Western blot, and the prevalence of positive Western blot was 0.29 % (26 of the 8,895 cases). Among 40 patients with HIV positive only 26 (65%) were Western blot positive.

Table 1. Results of ELISA for HIV antibodies

Provinces	Groups	No.tested	No.positive	Per cent positive
Songkla	prostitutes	5,027	7	0.14
	prisoners	491	3	0.61
	drug addicts	124	14	11.29
	homosexual men	4	0	-
Satun	prostitutes	127	0	-
	prisoners	198	1	0.51
Pattani	prostitutes	564	2	0.35
	prisoners	115	3	2.61
Yala	prostitutes	125	0	-
	prisoners	193	0	-
Narathiwas	prostitutes	1,279	5	0.39
	prisoners	114	2	1.75
Trang	prostitutes	273	1	0.37
	prisoners	101	2	1.98
Phatthalung	prisoners	160	0	-
Total		8,895	40	0.45

Discussion

Weiss et al,[5] in their article on a screening test for HIV antibodies, reported a specificity of 98.6% (false positive 1.4%) and a sensitivity (true positive) of 97.3%, excluding borderline tests results. These values of specificity and sensitivity are quite impressive, but they are, in reality not practical. Borderline results can not be excluded in actual practice as they may give an erroneous impression of the performance of the test and laboratory personnel.

Because of the performance of the test and manpower, our laboratory as well as the others need a confirmatory assay to be applied to those testing seropositive. It must be printed out that the current test (Western blot) is labor intensive and technically difficult. Screening of low-risk population will probably start before a practical confirmatory test is avialable. In the meantime, how should the seropositive groups be handled? Should the confirmatory test, when available, be used for borderline cases to try to reclaim some of the large number of blood tests that fall into the borderline category?

The problems of interpretation common to all laboratory tests include the specificity, sensitivity, positive and negative predictive values of each test[6]. Specificity refers to the likelihood of a test being able to predict that a person is free of infection. Sensitivity refers to the likelihood of a test being able to determine that a person is definitely infected. The high specificity (true positive rate) will increase the percentage of positive predictive value, especially in the high-risk population, but the predictive value will decrease in low-risk population. Thus, the predictive value is dependent not only on test sensitivity and test specificity, but is even more closely related to the prevalence of the disease[7]. Many authors recommend that all positive tests for HIV be confirmed by more specific methods when obtained in low-risk population.

It is believed that the greatest hope for stopping the spread of HIV infection lies in the voluntary cooperation of those at higher risk, their willingness to undergo testing and to alter their personal behavior and goals in the interests of the community[8,9]. However, voluntary testing is not enough. Voluntary identification, education, and counseling of infected persons are the most effective means of encouraging the behavioral changes that are necessary to halt the spread of AIDS[10].

Although there is a low prevalence (0.29%) in our region, continuing spread of HIV in IV drug users, prostitutes and prisoners is expected. The use of the test remains controversial because of public perceptions about AIDS, the technical limitations of the test, and the sheer magnitude and diversity of the tests present and their projected applications. So surveillance, which involves both passive reporting and the active search for information, provides data on the prevalence, incidence and distribution of disease or infection in the population. Such data can be used to monitor the spread of a disease, to shed light on the mechanisms of transmission of infectious agent, to

help in designing public health measures to prevent the spread of a disease, to evaluate the effectiveness of interventions and to guide planning for the provision of facilities. Data of HIV infection and related diseases are critical to all aspects of coping with the epidemic[11].

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Study of AIDS Prevention Strategies in a High-Risk Population

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Abstract: *Although Acquired Immune Deficiency Syndrome is not yet epidemic in Thailand, there is evidence that AIDS is spreading to Asia. Because the disease is most likely to first establish itself among high risk groups, it is important to develop educational programs to promote accurate knowledge of AIDS and preventive health behavior. This study will test three educational strategies among high risk group to develop cost-effective AIDS-prevention education. The study will be of benefit to others who are interested in AIDS education strategies. (Thai J Obsted Gynaecol 1989;1:11-19)*

Key words: AIDS prevention, high risk population

In January,1988 the Ministry of Public Health in Thailand received reports of a cumulative number of 240 cases of infection with the AIDS virus, HIV (human immune deficiency virus). Two months later, that number had nearly doubled to 450. Although increased surveillance activities probably account for some of the increase, it is clear that the spread of AIDS is occurring rapidly.

In 1984, the first case of Acquired Immune Deficiency Syndrome in Thailand was diagnosed in a Thai male homosexual. Since then, the spread of the infection has been similar to that of North America and Europe. Homosexual men are most at risk followed by intravenous drug users and much less by female prostitutes and blood donor recipients. However, given the large sexual services in Thailand and the large number of foreign tourists who patronize this industry, it has been predicted that the infection will soon spread more rapidly among the general heterosexual

population through female prostitutes[1,2].

Establishments offering sexual services have existed in Thailand as long as there has been a cash economy. Outside Bangkok these establishments are of two basic types; brothels and massage parlors. Brothels are located in both rural and urban settings and charge inexpensive fees while massage parlors are found in provincial capital towns and are more expensive. The sexual services offered in both establishments are the same but the massage parlors attract a more affluent out-of-town clientele. Despite their name, massage parlors, in fact,are brothels where a variety of sexual services are offered at negotiated and set prices. Sexual intercourse commonly takes place in massage parlors.

Khon Kaen town in the heart of Northeast Thailand is typical of most provincial towns in Thailand. Because Khon Kaen is the regional center for the northeast it is somewhat larger than the average town and attracts both Thai and foreign professionals for conferences and development projects. Khon Kaen is also promoted as a tourist site and there are two jet flights from Bangkok to Khon Kaen daily. There are three massage parlors there.

These three massage parlors were selected for an applied research study to test the effect of educational interventions about AIDS for AIDS-preventive behavior. Massage parlors are a more appropriate site than brothels because sex workers in massage parlors are more independent and better educated than the prostitutes in brothels. In addition, the massage parlor worker is more likely to come into contact with out-of-town carriers of HIV than brothel workers.

The long-range objective of this study is to increase AIDS-preventive behavior through an increase in the understanding of how AIDS is spread, how dangerous AIDS is and how infection can be prevented.

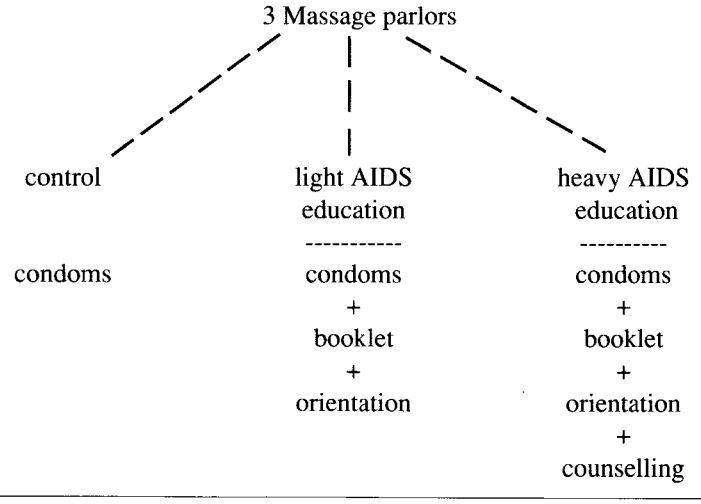
The short-term objectives are to test which of two educational interventions is the most effective to increase the awareness of AIDS and to increase the use of condoms among the sample of massage parlor workers.

Materials and Methods

The three Khon Kaen massage parlors provide convenient locations for a controlled experimental design involving two treatments and a control (Figure A). The massage parlors in Khon Kaen are typical of those found generally in Thailand. There is a cocktail lounge on the ground floor for customers to sit and ponder their choice of one of the 20 to 30 masseuses who sit behind a glass partition facing the lounge area. The AIDS education was conducted shortly before opening time in the room where the masseuses sit.

The two treatments were designed to compare light and heavy educational interventions. The light treatment consisted of group orientation on AIDS, a slide show, an educational brochure and providing 20 condoms per masseuse per week. The heavy treatment contained all of the above inputs plus counselling. The counselling was conducted with small groups of masseuses during a pe-

Figure A. Research design



AIDS education	Time (months) 1	2	3	4	5	6
heavy	OX	X	O	X	X	O
light	OX		O			O
control	O		O			O

O denotes self-administered questionnaires filled out
X denotes educational interventions provided

riod of three months after the baseline survey. The baseline questionnaires were used as a basis for the content of the counselling. Areas of weak knowledge were reviewed and a strong emphasis was placed on the importance of AIDS prevention by using condoms. The sessions were conducted by medical staff of the Family Planning Unit of the Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University.

Originally it was planned to conduct individual counselling in a nearby clinic. Appointments were made for each worker in the heavy treatment massage parlor. The strategy had to be modified, however, when very few of the workers kept their appointments. It was decided to conduct intensive education in small groups (three to four individuals) in the massage parlor.

The control group received only condoms but no education. However, it is very likely that workers in the two experimental parlors had an opportunity to share their knowledge with workers in the control. The study did not attempt to document contamination of the control.

Short questionnaires were filled out

by all the massage parlor workers at the beginning of the project. The same questionnaires were applied three months and six months later. Only those workers who filled out the baseline questionnaire were asked to fill out questionnaires in the two follow-up rounds (post-test 1 and post-test 2).

In all three massage parlors, the workers were offered free blood tests to screen for HIV infection and syphillis. Although the screening was not intended as part of the research assessment, this service was offerred to gain the cooperation of the managers of the massage parlors. All workers chose to have the blood tests and all three managers of the massage parlors cooperated fully with the investigators. One aspect of the managers' cooperation may have affected the experiment, however. During the period of study there were several news, reports on the threat of AIDS in Thailand. This resulted in a decline of customers at the massage parlors. Thus, the manager of the parlor receiving the heavy educational treatment posted signs saying that all his workers were AIDS free (based on the results of the pre-test blood screening). While this announcement might result in an increase of patrons it could also have the effect of reducing condom use because of a perception of no risk. This potential bias should be kept in mind when interpreting the results and in designing a similar AIDS educational program.

Including preparation, the study required ten months. The actual implementation took place over six months, from July to December, 1987. All the clinical, counselling, data collection and analysis were conducted by staff of the Family Planning Unit of the Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University.

Results

Through the excellent cooperation of the managers of the three massage parlors and the workers themselves, the study was successfully carried out. In all, 311 self-administered questionnaires were properly completed and returned to the investigators.

Because no new massage parlor workers were admitted to the study after it began, there is only attrition to the original total of 130 workers from the three parlors (Table 1). By the first post-test of questionnaires (three months later), 104 workers from the original sample remained and, by six months there remained 77 workers, an attrition rate of 20% at three month and 40% at six months. This attrition was equal for the three establishments.

The mean age of the workers is 24 for all three groups and ranges from 18 to 35 years. The panel of respondents who were present for all three rounds had been working at the massage parlor an average of one year to 18 months. It may be significant that the control sample had a shorter duration of employment than the two experimental groups. The range in duration of employment is exceptionally wide, from 6 to 41 months in the control, 6 to 121 months in the light treatment and 5 to 51 months in the heavy treatment group.

Table 1 Selected background characteristics of Khon Kaen massage parlor workers

Items	Control			Educational treatment					
				Light			Heavy		
		post-test			post-test			post-test	
	pre	1	2	pre	1	2	pre	1	2
Number of respondents	42	30	22	40	34	24	48	40	31
Mean age (yrs)			24			24			24
Age range (yrs)			19-35			18-38			18-30
Mean duration of employment (mos)			12			18			16
Range in duration of empleyment (mos)			6-41			6-121			5-51

The top half of Table 2 presents results of AIDS awareness measurements over the three rounds. The percent who had heard of AIDS in August 1987 was over 80% in each group and increased to 100% after one round in the experimental and two rounds in the control. During the time of the research, there had been several noteworthy cases of AIDS reported in the media with daily installments in newspapers and television. Thus, it is difficult to attribute the early knowledge gains in the experimental areas to the educational intervention.

A more refined measure of AIDS knowledge is the series of twelve multiple choice questions that quizzed the respondents on information presented in the group orientation and the AIDS booklet (Fig. B). In the control, knowledge remained constant at 67% correct response whereas the heavy treatment group increased from 67% to 92% correct response. The light treatment showed a very slight gain in knowledge. The question most frequently answered incorrectly concerned the causative agent (a virus, not a bacteria) and the typical symptoms of AIDS.

The bottom half of Table 3 shows the (self-reported) respondent behavior over the duration of the study. The average number of episodes of sexual intercourse per week range from seven to eleven. There is some indication of a decline in frequency of coitus in the control group which began at a higher level than the experimental parlors. By the time of the second post-test, all three groups averaged eight episodes of sexual intercourse per week.

In this study, the workers were advised to use condoms in order to prevent AIDS, since reducing the number of sexual partners is not a realistic option for prostitutes. In this regard the educational intervention had a distinct impact.Condom use increased from 58%

Table 2 Selected AIDS knowledge and preventive behavior measures among Khon Kaen massage parlor workers

Measure	Control			Educational treatment					
				Light			Heavy		
	pre	post-test 1	post-test 2	pre	post-test 1	post-test 2	pre	post-test 1	post-test 2
Ever heard of AIDS (%)	81	90	100	85	100	100	85	100	100
Mean AIDS knowledge test score (12 = max.)	7.7	8.6	8.5	8.6	9.6	10.4	8.1	10.7	11.2
Mean number of episodes of sexual intercourse in past week	9.7	10.7	8.1	6.7	7.4	7.7	7.0	8.0	7.6
Percent of episodes of sexual intercourse in which a condom was used in past week (%)	44	49	48	51	66	64	58	67	72

pre: pre-test
Post-test 1: at three months
post-test 2: at six months

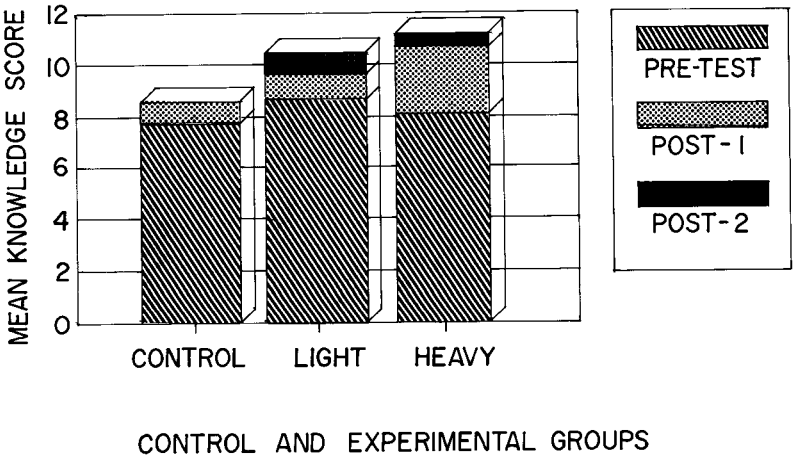


Fig. B Mean AIDS knowledge score by experimental and control

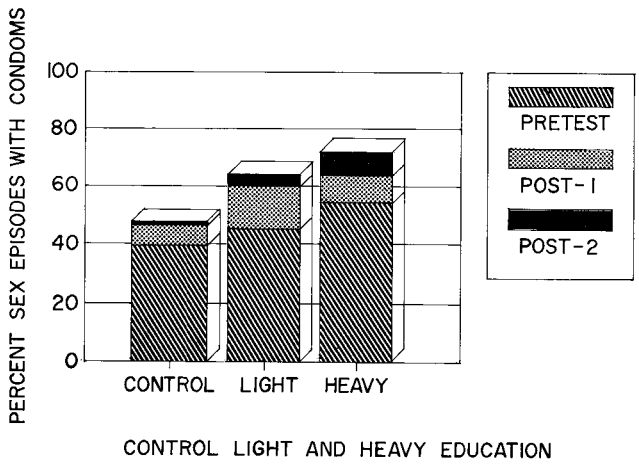


Fig. C Percentage of sexual episodes with condoms by control and experimental

to 72% of sexual episodes in the heavy treatment group and from 51% to 64% of sexual episodes in the light treatment. There was no corresponding increase in the control group which remained under 50% protected episodes for the duration of the study (Fig. C).

The counselling sessions provided the researchers with important insights into the perceptions, fears and motivations of the massage parlor workers. The following is a summary of comments on worker and client perspectives.

Reasons why clients do not want to use condoms (as expressed by the massage parlor workers):

1) Reduction of sexual feeling.

2) Condoms are tight and uncomfortable.

3) No need to use condoms if the worker is negative for HIV infection.

4) Clients prefer oral sex without a condom.

Reasons why the massage parlor workers did not want to use condoms:

1) The masseuse does not want to risk losing the client or a tip by suggesting him use a condom.

2) Condoms without a lubricant are uncomfortable for the masseuse.

3) Some kinds of condoms break easily.

4) Clients are mostly Thais and, therefore, of low AIDS risk.

5) The masseuse did not care whether she became infected or not; the need to make money is too great.

The results of the blood test did not find any HIV infection among the masseuses but there was a relatively high level of syphilis infection (Table 3). The fact that syphillis remains prevalent is an indication that increasing condom use to 70% of sexual episodes has only moderate impact on preventing STD.

Discussion

With a disase as deadly as AIDS, it seems that a rational response is to minimize one's exposure to infection[3,4]. However, rational health behavior depends on perceived risk, competing pressures against preventive health behavior

Table 3 Blood screening test results among Khon Kaen massage parlor workers

Blood tests	Educational treatment								
	Control			Light			Heavy		
	post-test			post-test			post-test		
	pre	1	2	pre	1	2	pre	1	2
Syphillis (% positive)	17	12	16	10	3	14	8	8	6
HIV (% positive)	0	0	0	0	0	0	0	0	0

and lack of power to take action. Although the questionnaire and counselling sessions did not systematically probe these issues, it is possible that the workers perceive little risk of AIDS because none of their co-workers have been infected. Also, economic pressure to maximize income militates against urging a client against his inclination to use a condom. Finally, in many cases the masseuse is young and of low education and, thus, lacks the assertiveness to protest if a client does not use a condom.

A follow-up study to this reseach is investigating these and other barriers to AIDS preventive behavior. Nevertheless, from the results of the present study the following points emerged:

1) Sexual worker turnover is high (40% at six months) and this suggests that educational interventions need to be one time only events and repeated over a short period of time.

2) It is possible to raise AIDS awareness and knowledge levels to a peak within three months and these will be maintained through at least six months.

3) The light education approach with a group lecture, slide show and brochure was just as effective in increasing knowledge levels as the heavy educational approach which added small group counselling.

4) To increase condom use, however, the heavy educational approach was more effective than the light educational approach.

5) Both light and heavy educational approaches were distinctly more effective in increasing condom use than no education at all.

6) Condom use must be increased to much higher levels than observed in this study if significant reduction of STD (and the risk of AIDS) is to be achieved.

7) Conducting blood screening can give the massage parlor worker and her client a false sense of security about freedom from the risk of AIDS. One rea-

son condoms are not used more is because the worker and her client know that she is not infected.

8) The poor quality of some brands of condoms are a barrier to their use.

9) The economic incentive and a sense of hopelessness among the workers are still important barriers to greater AIDS preventive behavior.

Acknowledgements

We are indebted to Mr. Tony Bennette for his valuable help in being our consultant of this research. We thank the owners and the managers of the massage parlors for allowing us to study their commercial sex workers. Particular thanks is extended to the university Research Coporation (URC) in supporting the budget for our study.

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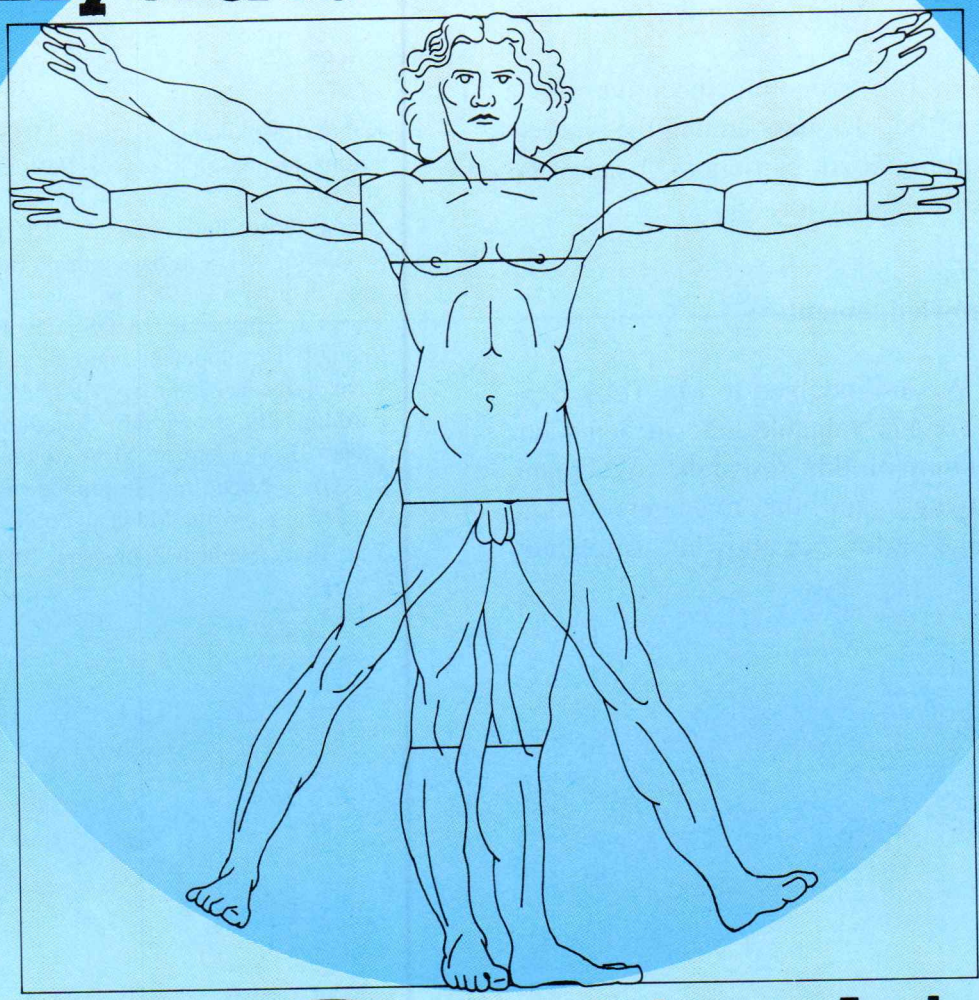

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Treatment of Mucopurulent Cervicitis with Doxycycline

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Abstract: *The study of treatment of mucopurulent cervicitis with doxycycline hyclate was carried out among 56 patients attending the Sexually Transmitted Diseases Clinic, Songklanagarind Hospital, from January 1 to December 31, 1987 to evaluate its efficacy. Those patients with infections of N. gonorrhoeae, herpes simplex virus, C. albicans, T. vaginalis and non-specific vaginitis were excluded. The characteristics of mucopurulent cervicitis included the presence of yellowish endocervical secretion and the presence of 10 or more polymorphonuclear leukocytes per microscopic field of 1000 magnifications. The patients were given 200 mg doxycycline hyclate orally initially followed by 100 mg twice daily for 8 days. Their sexual partners were treated likewise. Those receiving antibiotics within 2 weeks, pregnant women and women during lactating period and prostitutes were excluded from this treatment. A follow-up visit was scheduled 1-2 weeks after the completion of treatment. The results were, by self assessment, good and unchanged in 92.85 % and 7.14 % respectively. However, clinical evidence of yellowish endocervical secretion disappeared in 86.84 % with reduction of the presence of 10 or more polymorphonuclear leukocytes in 71.42 % (Thai J Obstet Gynecol 1989;1: 21-24)*

Key words: mucopurulent cervicitis, doxycycline

Mucopurulent cervicitis represents the portion of the iceberg which is largely on the clinical diagnosis of urethritis in males and on the treatment of the sexual partner of men with urethritis. Since mucopurulent cervicitis in females produces less symptoms than male urethritis it is of paramount importance in the control of the gonococcal and the clamydial infection[1]. With the presence of yellowish endocervical secretion and the increased number of polymorphonuclear leukocytes in smears from endocervical specimen such findings correlated well with isolation of C. trachomatis[2].

Broad spectrum antibiotics are employed to treat mucopurulent cervicitis, including doxycycline hyclate[3]. It was the purpose of this study to evaluate

the efficacy of doxycycline hyclate in the treatment of such a condition.

Materials and Methods

The study was carried out in the Sexually Transmitted Disease Unit, Songklanagarind Hospital from January 1 to December 31, 1987. The participants were sexually active women, 14-45 years of age, presented with one of the following: hypervaginal secretion not associated with mens, offensive vaginal discharge, and yellowish vaginal discharge.

The vaginal discharge was collected during vaginal examination and was examined for C. albicans, T. vaginalis and a smear was examined for predominant organisms. Endocervical discharge was also collected and examined for characteristics, cultured for N. gonorrhoeae and smeared for polymorphonuclear leukocyte count. The smear was dried and stained with methylene blue in conventional manner[4]. The polymorphonuclear leukocytes were counted under the microscope with magnification of 1000 in 5 nonadjacent fields. A specimen contained that 10 or more polymorphonuclear leukocytes was accounted for a significant finding of mucopurulent cervicitis. Those with infections of N. gonorrhoeae, herpes simplex virus, T. vaginalis, C. albicans and anaerobic vaginosis were excluded from the study.

The patients were given doxycycline hyclate 200 mg orally initially followed by 100 mg twice daily for 8 days, provided they were not pregnant or during lactating period and were not prostitutes. Their sexual partners were treated likewise. They were advised to return for follow-up examination 1-2 weeks after completion of the treatment. The results of treatment were classified as follows:

Good - both the clinical assessment and the laboratory testing were improved

Fair - clinically improved, but laboratory testing not improved

Stable - both the clinical assessment and laboratory testing were not improved

The patients were also asked for the adverse drug reactions or untoward side effects as well. Statistical evaluation was carried out by the Z-test.

Results

There were 56 women enrolled in this study. The epidemiological characteristics are shown in Tables 1 and 2. All patients returned for follow-up examination and the results of treatment are shown in Table 3. It can be seen that clinical improvement was achieved in 92.85%. However, by only examining the cervical secretion, the yellowish discharge disappeared only in 86.84 %. In considering the presence of 10 or more polymorphonuclear leukocytes decreasing, 71.42 % was achieved.

Only 5 patients reported as having had untoward side effects from treatment. These were dizziness, nausea, nausea and vomiting, experienced in 2, 1 and 2 patients respectively.

Table 1. The epidemiological characteristics

Symptoms	Before treatment number N = 56	per cent	After treatment number N = 56	per cent	P value
Hypervaginal secretion not associated with menses	54	96.42	24*	42.85	< 0.001
Foul smelling discharge	19	33.92	0		
Yellowish discharge	21	37.50	0		
Itching	24	42.85	0		
Discomfort	16	28.57	4	7.14	< 0.01
Dysuria	4	7.14	0		
Dyspareunia	1	1.78	0		
Post coital bleeding	1	1.78	0		

* 4 Cases with hypersecretion and 20 cases decreased in amount

Table 2 Microscopic findings of mucopurulent cervicitis

Symptoms	Before treatment number N = 56	per cent	After treatment number N = 56	per cent	P value
Mucopus	38	67.85	5	8.92	< 0.001
PMN leukocytes 10 or more	56	100	16	28.57	

Table 3. Results of treatment

Level	Number N = 56	Percent
Good	32	57.14
Fair	20	35.71
Stable	4	7.14

Discussion

As mentioned early that the aetiology of mucopurulent cervicitis is still unknown, specific treatment is, therefore, not yet established. However, as data reviewed had indicated, clamydial infection should always be suspected in women with mucopurulent cervicitis.[1,2] Since the diagnosis of clamydial infection by laboratory means are not feasible in some places, the antibiotics given should be those effective against C. trachomatis.

Among antibiotics used, tetracy-

cline hydrochloride or doxycycline are recommended by the Centers for Disease Control[5]. A high efficacy rate, 90-98 %, has been achieved with the use of oxytetracycline,[6,7] while the rate of 100 % with tetracycline[8].

Although it was reported that with the use of doxycycline for the treatment of mucopurulent cervicitis a 100 % efficacy rate was achieved,[3] the result of the present study seems to be slightly less effective. However, the use of doxycycline yielded a higher efficacy rate than our previous study[9].

Since the efficacy rate of treating mucopurulent cervicitis is high while the side effects are less, it is concluded that the present treatment regimen is simple and effective for use.

Acknowledgements

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Comparative Effects of 17-ß Estradiol Gel and Conjugated Estrogen on Climacteric Symptoms and Hormonal Levels in Oophorectomized Women

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Abstract: *The aim of this study is to compare the effects of estradiol gel and conjugated estrogen as treatment for climacteric symptoms and their effects on hormonal levels in oophorectomized women. The patients had hysterectomy and bilateral oophorectomy performed at least 6 weeks prior to estrogen treatment. They were randomly allocated into two groups. Group 1 (21 patients) received 17-ß estradiol gel 2.5 gm percutaneously once daily. Group 2 (21 patients) received 0.625 mg of conjugated estrogen orally. These were given for 3 weeks. Both groups had similar mean age, weight and height. After treatment the climacteric symptoms decreased in all patients. The patients reported that treatments were favourable. No significant adverse effect of the drugs was observed. Mean serum estradiol level in both groups increased to early follicular phase level. (from 11.05±8.01 and 10.11±4.48 to 67.83±64.32 and 59.89±42.96 pg/ml in group 1 and 2, respectively). In conclusion conjugated estrogen and 17-ß estradiol at dosage used in this study were comparable in clinical and hormonal effects. (Thai J Obstet Gynaecol 1989; 1:.25-30)*

Key words: 17-ß estradiol gel, conjugated estrogen, climacteric symptoms, oophorectomized women

The benefit of estrogen replacement therapy in postmenopausal women is obvious. It relieves climacteric symptoms and also abolishes or minimizes postmenopausal bone loss.[1-5] Oral substitution with conjugated estrogen is at present the most common therapy. But it is, however, claimed to be unphysiologic due to a higher level of estrone to estradiol ratio and high concentration of hormone in portal circulation, which will be further converted in the liver.[6] Recently percutaneous administration of 17 -ß estradiol in a gel form was introduced in Thailand, offering an alternative route to that of oral estrogen. Compared with

the oral treatment, percutaneous administration of estradiol may have theoretical advantage with respect to liver metabolism because the hormone will directly enter peripheral circulation without passing through enterohepatic circulation. There is, however, potential disadvantage related to the specific kinetics of this route.[7]

The aim of this study is to compare the effects of percutaneous 17-ß estradiol gel and conjugated estrogen given orally as treatment for climacteric symptoms and their effects on hormonal levels in oophorectomized women.

Materials and Methods

This prospective study was conducted at Ramathibodi Hospital during May 1987 to September 1987. Forty-two healthy women aged between 25 to 53 years, who had hysterectomy and bilateral oophorectomy carried out for benign causes, were recruited in this study. Their operations were performed at least 6 weeks previously. They had at least one climacteric symptom. All women did not receive any hormonal treatment for at least 3 months preceeding the study. None had a history of liver disease, vascular disease, diabetes, hypertension or any contraindication to estrogen therapy. The subjects were randomly allocated to two groups. A hydroalcoholic gel containing 17-ß estradiol (Estrogel®, Besin-lscovesco, France) was prescribed for the first group. The dosage was 2.5 gm of gel (1.5 mg of 17 -ß estradiol) applied once daily in the morning to the skin of the abdomen and left to dry for a few minutes before dressing. The second group received 0.625 mg of conjugated estrogen (Premarin®, Ayerst) in a single dose orally in the morning. Before starting treatment, all subjects were asked about the climacteric symptoms, and blood samples were taken for the assays of follicular stimulating hormone (FSH), luteinizing hormone (LH) and estradiol levels. All patients were instructed to record any complication in the treatment. After 3 weeks of treatment all subjects were evaluated for the improvement in symptoms and complication of treatment. Blood samples were again taken for the hormonal assays.

Serum LH, FSH and estradiol were determined by radioimmunoassay using commericial kits (Diagnostic Product Co, Los Angeles, CA). Student *t*- test was used to compare the mean value of clinical effects and hormonal levels between the two groups.

Results

There were 21 patients in each group. During the treatment 3 women in the "17-ß estradiol" group were lost to follow up for unknown reasons. Two subjects in the "Conjugated estrogen" group were excluded from the study due to the drug being taken irregularly.

There were no significant differences in mean age, weight and height for both groups (Table 1). Before starting the treatment, all subjects had serum estradiol level in the postmenopausal range with elevated level of FSH and LH (Table 2). The mean level of LH was higher in

Table 1 Pretreàtment clinical parameters

Parameters	17-ß estradiol n = 18 Mean ± SD	Conjugated estrogen n = 19 Mean ± SD
Age (yr)	43.11 ± 5.42	42.7 ± 3.79
Weight (kg)	52.43 ± 8.11	55.95 ± 6.90
Height (cm)	154.13 ± 4.29	152.32 ± 6.40

Table 2 Pretreatment hormonal levels

Hormones	17-ß estradiol n = 18 Mean ± SD	Conjugated estrogen n = 19 Mean ± SD
LH (mIU/ml)	123.61 ± 49.20	86.47 ± 43.39*
FSH (mIU/ml)	92.56 ± 24.01	83.79 ± 27.10
Estradiol (pg/ml)	11.50 ± 8.01	10.11 ± 4.48

* significant difference, $p < 0.05$

Table 3 Clinical responses of the treatment

Symptoms	17-ß estradiol		Conjugated estrogen	
	n	%	n	%
Hot flush	15/15	100	18/18	100
Sweating	13/13	100	18/18	100
Insomnia	9/11	82	11/11	100
Headache	6/8	75	6/7	86

n = number of patients with improvement of symptoms/ number of patients with symptoms before treatment.

the "17-ß estradiol" group. However, all subjects had LH level in the postmenopausal range.

After 3 weeks of treatment, the climacteric symptoms i.e. hot flushes and sweating subjectively decreased in all patients in both groups. Other nervous symptoms such as insomnia and headache had also lessened (Table 3). The patients did not complain about the treatment and judged the treatment as favourable in both groups. No significant adverse effect of the drugs was reported in either group.

Hormonal levels after 3 weeks of treatment changed significantly. Mean serum estradiol in "17-ß estradiol" group and "Conjugated estrogen" group increased from 11.05±8.01 and 10.11±4.48 to 67.83±64.32 and 59.89±42.96 pg/ml, respectively (Fig. 1). Mean serum FSH decreased in both groups (Fig 2). For serum LH, the level did not change significantly after treatment in both groups and remained in the postmenopausal range.

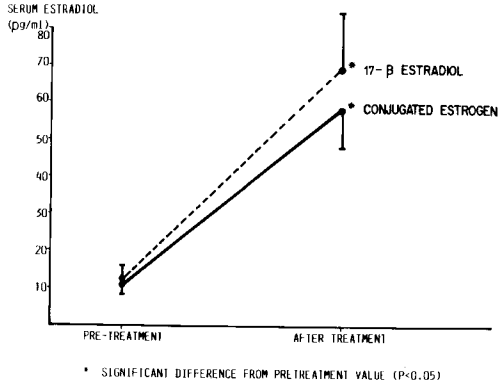

Fig 1. Serum estradiol before and after treatment

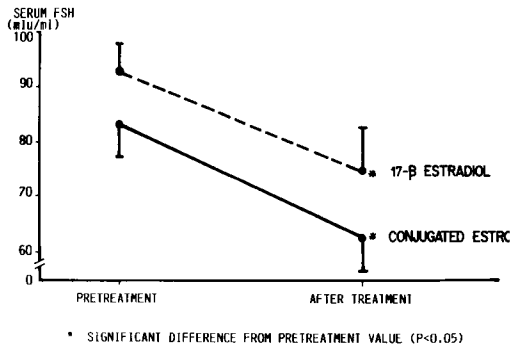

Fig 2. Serum FSH before and after treatment

Discussion

In this study, the effects of subcutaneous 2.5 gm of 17-ß estradiol gel and orally 0.625 mg of conjugated estrogen on climacteric symptoms and hormonal levels were compared. All subjects in both groups had decreased hot flushes and sweating, symptoms claimed to be due to estrogen deprivation.[8] Other symptoms which might be indirect effects from estrogen deficiency such as insomnia and headache were also improved.

The present study also showed that percutaneous administration of drug results in a significant absorption of estrogen. The peripheral estradiol levels after percutaneous dose of 2.5 gm of 17-ß estradiol were the same magnitude as after oral administration of 0.625 mg of conjugated estrogen and corresponded to the levels at early proliferative phase of menstrual cycle. The lowest daily dose of conjugated estrogen that consistently protects against bone loss was reported to be 0.625 mg.[9-11] So percutaneous 17 -ß estradiol at this dosage may be an effective preventive therapy of postmenopausal bone loss. The therapeutic effectiveness of estradiol level for relieving vasomotor symptoms was 40-50 pg/ml.[12] Thus, application of 2.5 gm of 17 -ß estradiol gel daily should be enough. In this study, however, there was a wide range of estradiol level after treatment which emphasized the necessity to individualize the dosage.[12] Several factors such as the application site, time of day, humidity and climate might effect the absorption of hormone through the skin. Previous studies about the use of percutaneous estradiol were conducted on Caucasians. The results may not be applicable to population in different regions. This study in Asian women, however, showed that the percutaneous administration of estrogen could fairly increase estradiol level.

After 3 weeks of treatment, both groups had significantly decreased level of FSH, but remained in postmenopausal range. This finding agreed with other studies that negative feed back of postmenopausal women is still preserved. [13,14] But it could not lower the level of the hormone to premenopausal level which could be due to insufficient level of estradiol.

In this study there was no reported side effects from treatment. There were no allergic reactions at the site of dermal application. All patients using subcutaneous 17-ß estradiol gel judged that the treatments were favourable.

Since the effectiveness of estrogen replacement therapy is obvious no matter what kind of estrogen is used, natural or synthetic estrogen, either in oral or in parenteral forms, might be considered as effective as long as they are given in sufficent doses. Percutaneous application provides an alternative to the oral route. Zondex[6] was the first to demonstrate that estrogens were absorbed through the skin of ovariectomized mice in quantities sufficient to produce estrus. The difference between the phamacodynamic of oral and percutaneous treatment is that following oral treatment, the intestinal absorption is rapid and yields extremely high concentration of hormone in portal

circulation. For topical administration of 17-ß estradiol, the hormone enters the peripheral circulation without passing the entero-hepatic circulation. The bypass of liver circulation may be beneficial since some side effects and risks associated with estrogen replacement therapy are known to stem from the hormone's impact on the liver.[5,6,13,15] Previous studies have shown that topical administration of 17-ß estradiol does not change the concentration of hepatic protein and does not so through the liver first. The conversion of estradiol to estrone, which is a consequence of the oral administration, is less pronounced so that estrone to estradiol ratio in the circulation will more closely resemble the physiological state of fertile women.[6,15,16] Estrone level was not assayed in this study due to technical problems. In comparison with the oral route, the increase in peripheral estrogen of percutaneous treatment was quite slow, less pronounced and had a longer maintenance of this level.[17]

In conclusion, both orally 0.625 mg of conjugated estrogen and 1.5 mg of 17-ß estradiol percutaneously were compared for clinical and hormonal effects. Further studies are needed to clarify the clinical significance of the theoretical advantages of topical estradiol application.

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Clinical and Metabolic Study of Triphasic Contraceptive Pill (Triquilar)®

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Abstract: *One hundred and forty healthy women were recruited for clinical and metabolic study. Each woman was instructed to take a triphasic pill at bed time. Forty-two percent of the volunteers completed 24 cycles for a total of 1847 cycles. The cycle control was quite satisfactory and no accidental pregnancy occurred. Changes in blood pressure and body weight were insignificant during the trial. Three cases showed an abnormal glucose tolerance test at six and nine months after taking pill. Fasting state serum transaminase, and bilirubin showed no sinificant changes of mean values, but significant decreases in alkaline phosphatase were observed at 3,6 and 12 months after taking the OC. Lipid metabolism, serum cholesterol, triglycerides and its fractions remained unchanged during treatment period. (Thai J Obstet Gynaecol 1989;1:31-38)*

Key words: clinical and metabolic study, triphasic contraceptive pill

Clinical trials of combined oral contraceptive pills have shown that they are effective and that they regulate the menstrual cycle with respect to intermenstrual bleeding, cycle length, duration and intensity of withdrawal bleeding. Levonorgestrel (LNg), a synthetic biologically active progestin, has been combined with ethinyl estradiol (EE) in three different dose ratios as a triphasic pill (Triquilar)®. The contraceptive effectiveness of this preparation has been shown to be high in previous studies.[1,2] Suppression of ovulation with the low-dose contraceptive is similar to that of high-dose fixed ratio preparations. A study of a small number of subjects in a recent report indicated that this compound has minimal influence on the metabolism of lipids and carbohydrates.[3] Changes in plasma concentrations of lipoproteins such as increased total cholesterol or LDL cholesterol, increased triglycerides of VLDL and reduced HDL cholesterol are

major risk factors for ischemic cardiovascular diseases. It has been shown that testosterone-derived progestogens reduce HDL levels in women.[4,5] A previous study demonstrated the positive correlation between mean changes in HDL or triglyceride levels, and the mean changes in sex hormone binding globulin concentration or the ethinylestradiol/levonorgestrel ratio illustrate that changes in HDL and triglycerides during OC treatment are influenced by the total estrogenicity of the drug used.[6] In short term use, results indicated there was no statistically significant difference between the mean values at baseline and during treatment of any lipids[3].

The relationship of oral contraceptive agents and the glucose tolerance test have been examined by many investigators with conflicting results being reported. Wynn and Doar[7] and others[8], using a variety of oral contraceptive agents over varying time, observed no difference in the fasting glucose levels in normal women associated with the use of oral contraceptive agents. Deterioration of glucose tolerance has, however, been reported by orthers[9,10,11].

Admittedly, many differences can be explained by the type of contraceptive agent used, the duration of its administration, the methods used and the characteristics of the patient group under study. Race and diet may influence the results. Most studies have been done in developed countries. We felt it worthwhile to evaluate this triphasic combination of LNg and EE in Thai women with special attention to effectiveness, cyclic menstrual beeding and metabolic changes.

Materials and Methods

One hundred and forty Thai women desiring oral contraception volunteered for this trial. The subjects had regular menstrual cycles before enrollment. They were healthy and under 35 years of age. No woman has used oral contraceptives or injectable hormonal contraceptives for at least six months prior to the study. A history was taken and a physical examination was performed before the subjects entered the study and every 6 months for its duration. The volunteers were seen at the Family Planning Clinic, Department of Obstetrics and Gynaecology, Chulalongkorn Hospital, every third cycle. Each subject was encouraged to record abnormal bleeding and any side effects that may have occurred in a diary card. The clinical characteristics of the volunteers are shown in Table 1.

Table 1 Clincal details of subjects participating in the study. Values are means ± SD, figures in parentheses are ranges

Age (years)	25.2	±	3.7
	(20	-	34)
Weight/Height^2	21.38	±	2.51
(Quetelet's index)	(18.9	-	23.9)
Blood pressure-systolic	103.1	±	15.6
diastolic	65.8	±	8.2
Cycle length (days)	29.7	±	2.6
	(25	-	38)
Menses (days)	4.6	±	1.1
	(3	-	7)

Metabolic studies were carried out in 20 subjects to evaluate the effect of the pill on carbohydrate and lipid metabolism. Blood samples were collected before and at 3,6,12, and 24 months of

pill intake. The subjects were asked to fast at least 12 hours before collecting blood. For the glucose tolerance test (OGTT), a 250 ml solution containing 50 g of glucose was given to each woman to drink within five minutes. Repeated venous blood samples were drawn at 0,30,60,90,120 and 180 minutes. Plasma glucose was determined by the glucose oxidase-perioxidase method which was previously described by Trinder[12]. The total area under the curve was calculated according to Wynn et al[7]. Fasting blood samples were allowed to clot and serum was separated. The lipid fractions in serum were separated by ultracentrifugation in a saline-density gradient modified from the previously described method.[13] The cholesterol content in each fraction was determined by means of commercially available kits (CHOD-PAP Boehringer-Mannheim, A.G.Mannheim, West Germany), while the triglyceride content was measured by the "Fully enzymatic (UV) test", using Boehringer-Mannheim reagents.

Liver enzymes, SGOT, SGPT, alkaline phosphatase and bilirubin were measured by the use of a LKB 8600 reaction rate analyzer. Reagents for determining liver enzymes were obtained from Boehringer-Mannheim. Statistical analysis of the results were performed by using student's *t-test* for paired or unpaired data, or the two-way analysis of variance as appropriate.

Results

Clinical Data

Of the 140 women who started the trial, the continuation rate at three month intervals is shown in Fig. 1 .49% completed twelve cycles and 24% completed 34 cycles for a total of 1847 cycles. No accidental pregnancy occurred during the study period. Possibly drug-related medical reasons accounted for withdrawal from the trial of 7.8% of the subjects. Table 2 presents the number of subjects who withdrew for medical reasons, personal reasons and of drop outs by cycle interval.

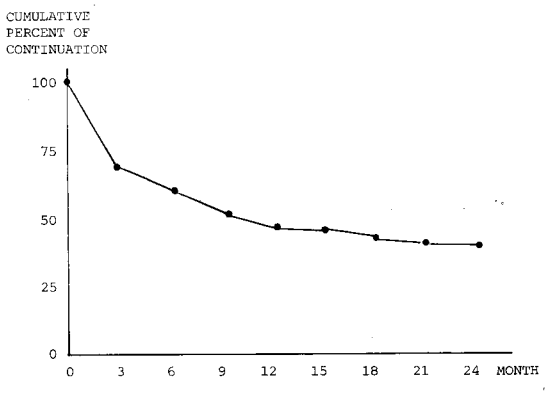

Fig. 1 Continuation rate at 3-month intervals. (1847 cycles)

Table 2 Reasons for discontinuation of trial

Reasons	Months of use								
	3	6	9	12	15	18	21	24	Total
Bleeding/spotting	-	-	-	-	1	-	-	-	1
Malaria infestation	3	-	-	-	-	-	-	-	3
Abnomal OGTT	1	2	-	-	-	-	-	-	
Weakness/weight loss	2	-	-	-	-	-	-	-	2
Nausea-vomiting	3	-	1	1	-	-	-	-	5
Plan pregnancy	-	-	-	2	2	1	-	-	5
Change method	2	1	1	1	-	-	-	-	5
Move away	6	2	-	1	-	-	3	-	12
Loss follow-up	23	6	2	2	-	2	1	-	37
Indigestion	1	-	-	-	-	-	-	-	1
Incorrect taking pill	7	-	1	-	-	-	-	-	8
Personal	4	-	-	-	-	1	-	-	5
Total	52	11	5	7	4	4	7	-	
Continuation	140	88	77	72	65	62	58	53	

Metabolic Data

Three cases showed an abnormal area under the curve (over 800) at six and nine months (Fig. 2). They were asked to stop taking the OC and a repeat glucose tolerance test was performed six months later. The glucose tolerance test results had returned to the normal range after cessation of the OC.

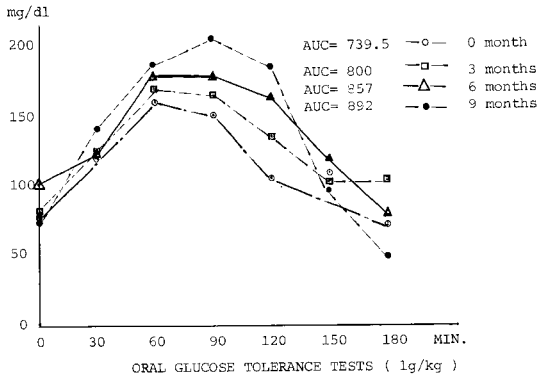

Fig. 2 Plasma glucose during oral glucose tolerance tests performed before and after treatment, An abnormal area under curve (AUC) over 800, demonstrated at 6 and 9 months.

The mean plasma values of glucose before and after OC therapy did not differ significantly in the fasting state. There were statistically significant changes of plasma glucose at 60,90,120,150 and 180 minutes after ingestion of gluclose (Table 3).

Fasting state serum transaminase (SGOT, SGPT), alkaline phosphatase and bilirubin were assessed in 18 subjects. There were no significant changes of mean values of transaminase and bilirubin in serum, but a significant decrease in alkaline phosphatase was observed at 3,6 and 12 months after taking the OC (Table 4).

Table 3 Plasma glucose levels (mean ± SD) and area under curve (AUC) at different time intervals after ingesting glucose (N=20). Figures in parenthesis denote range values. Asterisk denotes significant different levels.

	Changes in oral glucose tolerance test Times (min)							
Months	0	30	60	90	120	150	180	AUC
0	80.8 ± 8.3 (60-99)	117.1 ± 20.3 (86-153)	114.6± 36.5 (70-196)	92.3± 26.0 (52-160)	89.4 ± 14.0 (70-121)	81.8 ± 15.4 (50-113)	76.9 ± 13.4 (54-99)	574.0 ± 91.9 (421-728)
			**	***	****	***	*	****
3	80.2 ± 8.7 (70-108)	127.2 ± 18.8 (100-170)	136.8 ± 33.5 (77-204)	117.9 ± 33.8 (71-195)	109.8 ± 19.7 (87-151)	98.8 ±16.5 (71-133)	86.9 ±15.1 (55-107)	674.1 ±110.3 (495-889)
			*	****	***	****	*	****
6	80.1 ± 6.7 (65-92)	125.6 ± 20.4 (83-166)	135.0 ± 26.6 (88-176)	121.7 ± 29.6 (84-182)	110.0 ± 22.9 (74-161)	97.8 ± 16.7 (70-127)	88.2 ± 20.9 (57-136)	673.8 ± 98.7 (512.5-846.5)
		***	***	***	***	****		
12	81.7 ± 8.6 (69-97)	122.1 ± 17.5 (95-148)	134.1 ± 26.9 (85-201)	119.1 ± 28.3 (76-177)	130.2 ±13.2 (77-128)	93.8 ± 14.5 (63-120)	80.3 ± 14.7 (58-108)	653.3 ± 76.7 (498.5-788.5)
		***	***	****	***	*		****
24	83.5 ± 5.9 (75-92)	138.0 ± 15.6 (113-159)	153.5 ± 26.2 (114-207)	134.4 ± 31.1 (81-197)	114.7 ± 9.9 (99-123)	105.0 ± 14.7 (83-133)	89.5 ± 22.6 (57-140)	726.8 ± 79.9 (618.5-849.5)

* P < 0.05 ** P < 0.01 *** P < 0.005 **** P < 0.001

Table 4 Serum levels of bilirubin, alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic phosphoacetic transaminase (SGPT) in 20 subjects, all values are mean ± SD. Figures in parentheses are range values. Asterisk indicated significant changes at different levels

Changes in liver function tests (n=20)

	Treatment period (months)				
	0	3	6	12	24
SGOT (U/L)	9.11± 3.3 (5.0-16.2)	8.4 ± 3.3 (1.4-16.4)	9.0 ± 2.6 (5.7-13.9)	8.2 ± 1.9 (4.7-12.2)	8.4 ± 2.3 (6.2-11.8)
SGPT (U/L)	5.0 ±2.4 (1.8-10.5)	4.2 ± 2.5 (2.1-11.2)	4.5 ± 2.3 (1.9-9.3)	4.3 ± 1.2 (2.3-5.6)	3.4 ± 0.7 (2.6 - 4.5)
ALK (U/L)	21.1 ± 7.2 (12.1-39.2)	15.7± 4.2 (10.0-26.0)	16.3 ± 4.8 (10.4-24.6)	15.8 ± 4.9 (9.7-23.5)	17.5 ± 5.3 (13.4-26.8)
BILIRUBIN (MG/DL)	0.5 ± 0.2 (0.2-1.2)	0.4 ± 0.2 (0.2-0.9)	0.5 ± 0.2 (0.2-0.8)	0.4 ± 0.1 (0.2-0.8)	0.4 ± 0.1 (0.3-0.6)
	** P < 0.01		**** P < 0.001		

Table 5 Serum lipid (VLDL-cholesterol, LDL-cholesterol, HDL-cholesterol and total cholesterol) of 18 subjects, all values are mean ± SD and the concentration are in mmol/L

	Treatment period (months)				
	0	3	6	12	24
VLDL-C	0.32 ± 0.15	0.29 ± 0.12	0.34 ± 0.13	0.30 ± 0.13	0.31± 0.12
LDL-C	2.31 ± 0.69	2.21 ± 0.54	2.37 ± 0.62	2.49 ± 0.70	2.37± 0.58
HDL-C	1.12 ± 0.18	1.09 ± 0.21	1.09 ± 0.14	1.09 ± 0.25	1.22± 0.23
T-C	4.37 ± 1.03	4.22 ± 0.75	4.20 ± 0.57	4.25 ± 0.80	4.13± 0.56

Table 6 Serum triglycerides (VLDL-triglyceride, LDL-triglyceride, HDL-triglyceride and total triglyceride) in 18 subjects. All values are means ± SD and the concentrations are in mmol/L

	Treatment period (months)				
	0	3	6	12	24
VLDL	0.46 ± 0.24 (0.18-1.11)	0.43 ± 0.19 (0.19-1.00)	0.46 ± 0.18 (0.18-0.96)	0.44 ± 0.18 (0.04 - 0.81)	0.41 ± 0.17 (0.19-0.77)
LDL	0.27 ± 0.08 (0.16-0.53)	0.26 ± 0.09 (0.13-0.56)	0.28 ± 0.11 (0.14-0.57)	0.28 ±0.09 (0.14-0.51)	0.27 ± 0.08 (0.16-0.45)
HDL	0.20 ± 0.05 (0.12-0.29)	0.19 ± 0.05 (0.10-0.31)	0.02 ± 0.07 (0.09-0.39)	0.20 ± 0.06 (0.91-0.32)	0.21 ± 0.08 (0.07-0.36)
T-TRIGLY-CERIDE	1.09 ± 0.36 (0.59-1.83)	1.04 ± 0.31 (0.57-1.83)	1.08 ± 0.38 (0.50-1.85)	1.11 ± 0.30 (0.55-1.72)	1.18 ± 1.03 (0.50-1.68)

Lipid metabolism, serum cholesterol, triglycerides and its fractions remained unchanged during treatment (Tables 5 and 6).

Discussion

The introduction of a triphasic approach of oral contraception represents a

noteworthy contribution in contraceptive technology. The reduction in synthetic progestogen per cycle is accomplished by taking advantage of the well defined hormonal events during the normal menstrual cycle. The triphasic mode of administration gave promising results in cycle control and the present study showed stable menstrual cycles. There was a signficant reduction in cycle length and an increased menstrual flow during the first three months of use. The duration of bleeding was, however, significantly decreased after ten months of use. These findings may reflect the direct effect of synthetic steroid on the endometrium. Breakthrough bleeding and spotting during the trial of Triquilar® were reported in 1.2-10% of cycles[2,3]. Side effects of intermenstrual spotting led to discontinuation in one case. Cycle control was quite satisfactory.

Changes in blood pressure and body weight were insignificant during the trial. Side effects were difficult to interpret. Nausea, vomiting, dizziness and headache were most frequently reported in the first three cycles, abating subsequently. The continuation among patients in this study was low (about 50% at 12 months) when compared to earlier report[2]. One of the major problems for patient's discontinuation in the trial was loss to follow-up. This is difficult to interpret and we were not able to determine the reasons for drop out in most patients.

Triphasic preparations of ethinyl estradiol and levonorgestrel, with a progestogen content of less than that in any of the monophasic products, have been associated with a minimal effect on carbohydrate metabolism. The progestogen-estrogen ratio of combined oral contraceptive seems to be the major factor influencing metabolism[11,12]. Previous studies have shown that levonorgestrel will cause hyperinsulinemia in doses of 150 μg or more[14,15,16]. This effect occurs without necessarily altering glucose tolerance. The present study revealed that after three months of use there was significant increase in plasma glucose at 60,90,120 and 150 minutes. At 180 minutes after ingestion of glucose, however, the plasma glucose returned to a normal range. There were three cases that exhibited an abnormal glucose tolerance test, and they were asked to stop the OC. Three months later the glucose tolerance test result had become normal (Fig 3). It has been shown that progesterone is metabolised in the splanchnic bed (65%) and brain (35%)[17]. It is possible that the fasting blood glucose level may be altered by a central effect of progestogen on the brain[18]. The mechanism behind the influence on glucose metabolism by contraceptive steroid compounds is not fully known. There is evidence that pro-

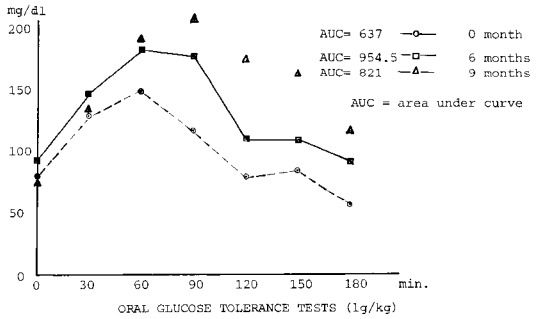

Fig. 3 Illustration of an abnormal area under the curve at 6 months after taking OC. Plasma glucose level (AUC) returned to normal range after stopping OC 9-month curve

gestogens alone or combined with estrogens induce a decrease in tissue sensitivity to insulin[14,19]. Moreover, the increased plasma cortisol levels found in women treated with oral contraceptives, may impair glucose tolerance as the result of an increase in hepatic glucose production and an inhibition of glucose uptake in peripheral cells[20].

The association between lipoprotein levels and coronary heart disease is well known[21]. In general, HDL-cholesterol levels are increased by estrogens and decreased by progestogens. There have been reports that triphasic compounds raise plasma triglycerides to a greater extent than low-dose monophasic ethinylestradiol/levonorgestrel combinations[12]. Recent studies have demonstrated that triglycerides remained unchanged in women with previous gestational diabetes[22,23]. Our present study confirmed previous findings in Thai women. Serum triglycerides remained unchanged after 24 months of OC use. It is of interest to note that serum lipids and triglycerides were thus unaffected by hormonal intake. This ocurred despite elevated glucose levels in some patients. Unchanged high density lipoprotein, low-density lipoprotein and very-low density lipoprotein cholesterol levels together with unchanged serum triglycerides levels during OC use appear to be favorable findings.[24]

A previous study has shown that liver enzymes and alkaline phosphatase levels were affected by estrogens and progestogens. They increased by higher progestogen and decreased with high estrogen[25]. If a decrease in the alkaline phohatase level indicates a decrease in cholestasis, this might be a further benefit of ethinyl estradiol/levonorgestrel triphasic agent. The present study showed a statiscally significant reduction of alkaline phosphatase levels. The transaminase remained the same.

We conclude that Triquilar® in a short term study has a low incidence of side effects, affords good cycle control and is effective. This low-dose triphasic pill may cause transient deterioration in gluclose metabolism but has no effect on lipid and lipoprotein levels. Changes in liver enzyme levels were minimal. To sum-up, the present study confirms that a triphasic principle and dosage of this preparation, affords good cycle control and is effective.

Acknowledgements

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The Epidemiology Of Uterine Cervix Cancer In Khon Kaen Province 1985-1987. First Result From A Population-Based Cancer Registry

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Abstract: *This study was carried out to determine the accurate incidence and magnitude of problems of uterine cervix cancer in Khon Kaen province population. Under the methods of population-based cancer registry of Khon Kaen province, every case of uterine cervix cancer diagnosed from every health service center in Khon Kaen during the period from January 1,1985 to December 31,1987 was notified to the cancer unit, Faculty of Medicine, Khon Kaen University, both in passive and active methods. After careful check by computer and unit's staff, cases were recorded in computer for further study.*

There were a total of 270 new cases of uterine cervix cancer reported in this three year period. The data showed it ranked first when compared with other female cancers. The crude incidence rates were 11.1,14.1 and 11.1 per 100,000 women per year for the years 1985,1986 and 1987 respectively. The age-standardized incidence rate, compared with standard world populations, were 14.8,20.7 and 16.1 per 100,000 per year for the years respectively for three years. The crude mortality rates were 2.2,1.3 and 0.8 per 100,000 per year for the years 1985,1986 and 1987 respectively. The age-standardized mortality rates, compared with standard world populations, were 3.7,1.9 and 0.7 per 100,000 per year for these years same. (Thai J Obstet Gynaecol 1989;1:39-46)

Key words: cervical cancer, epidemiology, cancer registry

Cancer is the third leading cause of death for Thais and is becoming a national health problem.[1] Cancer of the uterine cervix ranks first for all female cancers in every part of the country.[2] At present, there are no well established morbidity and mortality statistics for cervical cancer in Thailand. Most of

what is available are the relative frequencies from hospitals and institutes. This presentation is the first analysis based on the data from a population-based cancer registration.

Materials and Methods

Population at risk

Khon Kaen is one province situated in the northeast of Thailand, about 450 kilometers from Bangkok. It has a population of about 1.5 million , living in 20 districts located from about 30 to 150 kilometers from the city. The geographical and age distributions of the female population of Khon Kaen are shown in Tables 1 and 2. Most of them are Thai, Buddhist farmers with education only at primary school level. Their socio-economic status is low compared to other parts of the country.

Khon Kaen cancer registry

The Faculty of Medicine and Srinagarind Hospital, Khon Kaen University established a cancer unit, with one of its tasks the responsibility for cancer registration since 1984. The first hospital-based cancer registry was published in 1985 followed by annual reports up to 1987. The relative frequencies of cervical cancer at Srinagarind Hospital from the population-based cancer registry are shown in Table 3. The population-based cancer registry of Khon Kaen began on January 1,1988 as a prospective data collection. The objectives of the registry are to collect, store, analyze and interpret the data on cancer occuring in Khon Kaen. Other objectives

Table 1 Geographical distribution of female population in all age, Khon Kaen Province 1985-1987 *

Districts	Years		
	1985	1986	1987
Muang	146299	147949	150564
Ban Phai	72575	73283	73949
Pol	41543	41202	41540
Chumpae	43226	58625	59939
Nam Pong	48588	48603	49578
Kranuan	40770	40303	42325
Puvieng	50847	50821	51357
Nong Rua	40706	40550	41218
Chonnabot	24111	23880	24149
Munjakiri	45804	45815	46482
Nong Song Hong	33771	35001	32206
Wang Noi	19994	19598	19559
Sri Chompu	35429	35268	35729
Ubolratana	19029	18712	18992
Ban Phang	23881	23778	24174
Kao Saun Kwang	15159	15143	15528
Pra Yuen	15551	15344	15266
Wang Yai	13351	13375	13121
Puey Noi	9864	9421	9743
Puphaman	8949	9043	9150
Total	667200	763671	774569

*From Provincial Statistics

Table 2 Female population of Khon Kaen Province 1985-1987 age 20-79 *

Age	Years		
	1985	1986	1987
20-24	73000	73000	77600
25-29	58200	58200	59300
30-34	50000	50000	51600
35-39	42100	42100	43400
40-44	34800	34800	36100
45-49	29800	29800	30300
50-54	25400	25400	26000
55-59	19900	19900	20900
60-64	14900	14900	15500
65-69	10600	10600	11000
70-74	7300	7300	7400
75+	7300	7300	7500
All ages	667200	770800	783700

*From National Population Estimation

are to measure the incidence rates and long term cancer trends in Khon Kaen, set up the model for provincial population-based cancer registry in conjunction with the Thai National Cancer Institute for national cancer registration and assist in epidemiological research.

Table 3. Relative frequencies of cervical cancer at Srinagarind Hospital from hospital-based cancer registry

Year	Number of cases	Percentage of all female cancer	Percentage of all cancer
1984	255	35.19	19.38
1985	329	30.50	16.20
1986	416	32.00	16.40
1987	451	27.40	13.90

A case for the registry is defined as a malignant neoplasm not previously registered in any hospital or clinic. Exclusions were made for all premalignant diseases. All districts and regional hospitals including private clinics are requested to report new cancer cases to the cancer unit of Srinagarind Hospital. The cancer unit will then check the patients' names and identifications to be included or excluded as a new case. Death certificates will be checked at all hospitals, district offices and the central provincial office to compare with death certificates of Srinagarind Hospital and Khon Kaen Provincial Hospital.

Case-findings and diagnosis

In this study the personel from the cancer unit of Srinagarind Hospital went out to every hospital in Khon Kaen including district and central provincial offices to collect data. All new cases and deaths occuring between January 1,1985 and December 31,1987 of residents in Khon Kaen were included in the study. All data were carefully checked with data from the hospital-based cancer registry of Srinagarind Hospital.

Statistical methods

Crude incidence and mortality rates for a certain year were obtained from the total number of cases and deaths of cervical cancer in each year compared to the total number of female population in Khon Kaen province per 100,000 women. Age-specific incidence and mortality rates were obtained from the number of new cases and deaths from cervical cancer in each age interval from 20 to 79 years. The rates were expressed per 100,000 women. Age-standardized incidence and mortality rates were obtained from the summation of the expected cases of occurence in each age interval when compared to the standard world population in the same age group per 100,000. Case fatality rate of cervical cancer was obtained from the number of deaths from cervical cancer in each year divided by the total number of new cases in each year and was expressed in percent. Crude incidence and mortality rates for all districts in Khon Kaen were obtained from the total number of new cases and deaths for every district in each year compared to the female population for a certain destrict in a certain year.

Results

Incidence rates

Data for a total of 270 new cases

of cervical cancer were collected from all districts of Khon Kaen whose diagnosis were made between January 1,1985 and December 31,1987. Ages and yearly distributions of the cases are shown in Table 4. The age-specific incidence rates of cervical cancer in Khon Kaen from 1985 to 1987 are shown in Table5. The crude incidence rates from 1985 to 1987 were 11.09, 14.14 and 11.10 per 100,000 respectively. The age-standardized incidence rates as compared to the standard world population for 1985 to 1987 were 14.75,20.68 and 16.07 per 100,000 respectively (Table 6).

Mortality rate

Death from cervical cancer for the Khon Kaen resident population from 1985 to 1987 were 17,10 and 6 respectively. Age distribution for fatal cases are shown in Table7. The crude mortality rates from 1985 to 1987 are shown in Table 8 and were 2.2,1.3 and 0.8 per 100,000 respectively. The age-specific mortality rate are also shown in Table 8. Table 9 shows the age-standardized mortality rates of cervical cancer from 1985 to 1987 when compared to the standard world population, which were 3.7,1.9 and 0.7 per 100,000 respectively.

Table 4. Age Distribution of cervical cancer patients in Khon Kaen Province 1985-1987. From population-based cancer registry

Ages	Years			Total
	1985	1986	1987	
20-24	0	1	0	1
25-29	2	1	3	6
30-34	3	9	10	22
35-39	10	9	7	26
40-44	13	14	16	43
45-49	11	24	17	52
50-54	12	26	11	49
55-59	5	14	6	25
60-64	7	6	7	20
65-69	5	2	6	13
70-74	5	2	2	9
75+	1	1	2	4
Overall	74	109	87	270

Table 5. Age-specific incidence rate of cervical cancer in Khon Kaen Province 1985-1987. From population-based cancer registry

Age groups	Years		
	1985	1886	1987
20-24	0.00	1.37	0.00
25-29	3.44	1.72	5.06
30-34	6.00	18.00	19.38
35-39	23.75	21.38	16.13
40-44	37.36	40.23	44.32
45-49	36.91	80.54	56.11
50-54	47.24	102.36	42.31
55-59	25.13	70.35	28.71
60-64	46.98	40.27	45.16
65-69	47.17	18.86	54.55
70-74	68.49	27.40	27.03
75+	13.70	13.70	26.67
CR*	11.09	14.14	11.10

CR* = Crude rate per 100,000 population per year

Table 6. Age-standardized incidence rate of cervical cancer in Khon Kaen province 1985-1987, compared to standard world population. From population-based cancer registry

Age groups	Expected cases		
	1985	1986	1987
20-24	0.00	0.14	0.00
25-29	0.27	0.14	0.40
30-34	0.36	1.08	1.16
35-39	1.43	1.28	0.97
40-44	2.24	2.41	2.65
45-49	2.21	4.83	3.37
50-54	2.36	5.12	2.12
55-59	1.01	2.81	1.15
60-64	1.88	1.61	1.81
65-69	1.42	0.57	1.64
70-74	1.37	0.55	0.54
75+	0.21	0.14	0.27
ASR*	14.75	20.68	16.07

ASR*= Age-standardized incidence rate per 100,000 population per year (Compared to standard world populations)

Case fatality rates were computed and revealed as 22.97% , 9.17% and 6.90% respectively. Table 10 summarizes the incidence and mortality rates of cervical cancer in Khon Kaen from 1985 to 1987.

Geographical rates

Table 11 shows the geographical distribution of cervical cancer from 1985 to 1987 and Table 12 shows the crude incidence rates of those. Tables 13 and

Table 8. Age-specific mortality rate of cervical cancer in Khon Kaen Province 1985-1987. From population-based cancer registry

Age groups	Years		
	1985	1986	1987
20-24	0.00	0.00	0.00
25-29	0.00	0.00	0.00
30-34	2.00	0.00	0.00
35-39	2.38	2.38	0.00
40-44	8.62	0.00	5.54
45-49	0.00	6.71	0.00
50-54	11.81	23.62	3.85
55-59	5.03	5.03	4.78
60-64	33.56	0.00	6.45
65-69	9.43	0.00	9.09
70-74	27.40	0.00	0.00
75+	0.00	0.00	0.00
All Ages	2.21	1.30	0.77

Table 9. Age-standardized mortality rate of cervical cancer in Khon Kaen Province 1985-1987, compared to standard world population. From population-based cancer registry.

Age groups	Years		
	1985	1986	1987
20-24	0.00	0.00	0.00
25-29	0.00	0.00	0.00
30-34	0.12	0.00	0.00
35-39	0.14	0.14	0.00
40-44	0.51	0.00	0.33
45-49	0.00	0.40	0.00
50-54	0.59	1.18	0.19
55-59	0.20	0.20	0.19
60-64	1.34	0.00	0.00
65-69	0.28	0.00	0.00
70-74	0.55	0.00	0.00
75+	0.00	0.00	0.00
ASMR*	3.74	1.94	0.72

ASMR* = Age-standardized mortality rate per 100,000 population per year (Compared to standard world population)

Table 10. Morbidity and mortality statistics of cervical cancer in Khon Kaen Province 1985-1987

Statistic*	Years		
	1985	1986	1987
Crude incidence	11.09	14.14	11.10
Age-standardized incidence	14.75	20.68	16.07
Crude-mortality	2.21	1.30	0.77
Age-standardized mortality	3.74	1.94	0.72
Case fatality rate	22.97	9.17	6.90

* All figures are shown in the rates per 100,000 population per year, except for case fatality rate that is show in per cent.

Table 11. Geographical distributions of cervical cancer in Khon Kaen Province 1985-1987

Districts	Number of patients by years			Total
	1985	1986	1987	
Muang	23	32	22	77
Ban Phai	9	11	4	24
Pol	3	11	5	19
Chumpae	6	5	11	22
Nam Pong	3	9	6	18
Kranuan	2	0	5	7
Puvieng	4	4	4	12
Nong Rua	4	3	7	14
Chonnabot	4	7	0	11
Munjakiri	2	4	2	8
Nong Song Hong	3	4	2	9
Wang Noi	2	1	1	4
Sri Chompu	3	4	5	12
Ubolratana	1	2	2	5
Ban Phang	1	6	3	10
Kao Saung Kwang	0	0	1	1
Pra Yuen	1	2	2	5
Wang Yai	2	3	1	6
Puey Noi	0	1	2	3
Puphaman	1	0	2	3
Total	74	109	87	270

14 show the crude death rates in different districts.

Race, religion and marital status

Table 15 shows that 94.81 % of the patients were Thai, 95.56% of those were Buddhists (Table 16) and 98.52 % of the cases were married (Table 17).

Staging of Disease

From the available data, 13.97 % of the cases were in stage I, while 48.90 % of those were in stage II and III, 4.04 % were in stage IV and 33.09 % could not be staged or the data were missed (Table 18).

Histology

Table 19 shows the different histological types of cancer of which the most

Table 13. Death from cervical cancer in 20 districts of Khon Kaen Province 1985-1987. From population-based cancer registry

Districts	Death by years			Total
	1985	1986	1987	
Muang	2	3	1	6
Ban Phai	3	1	0	4
Pol	0	1	0	1
Chumpae	1	1	0	2
Nam Pong	1	2	2	5
Kranuan	0	0	0	0
Puvieng	1	0	0	1
Nong Rua	1	1	3	5
Chonnabot	1	0	0	1
Munjakiri	2	1	0	3
Nong Song Hong	2	0	0	2
Wang Noi	0	0	0	0
Sri Chompu	2	0	0	2
Ubolratana	0	0	0	0
Ban Phang	0	0	0	0
Kao Saun Kwang	0	0	0	0
Pra Yuen	1	0	0	1
Wang Yai	0	0	0	0
Puey Noi	0	0	0	0
Puphaman	0	0	0	0

Table 12. Crude incidence rate of cervical cancer in Khon Kaen Province 1985-1987. Geographical distributions

Districts	Years		
	1985	1986	1987
Muang	15.72	21.63	14.61
Ban Phai	12.40	15.01	5.41
Pol	7.22	26.70	12.04
Chumpae	13.88	8.53	18.35
Nam Pong	6.17	18.52	12.10
Kranuan	4.91	0.00	11.81
Puvieng	7.86	7.87	7.79
Nong Rua	9.83	7.40	16.98
Chonnabot	16.59	29.31	0.00
Manjakiri	4.37	8.73	4.30
Nong Song Hong	8.88	11.43	6.21
Wang Noi	10.00	5.10	5.11
Sri Chompu	8.47	11.34	13.99
Ubolratana	5.26	10.69	10.53
Ban Phang	4.19	25.23	12.41
Kao Suan Kwang	0.00	0.00	6.44
Pra Yuen	6.43	13.03	13.10
Wang Yai	14.98	22.23	7.62
Puey Noi	0.00	10.61	20.53
Puphaman	11.17	0.00	21.86
Overall	11.09	14.27	11.23

Table 14. Crude mortality rate of cervical cancer in Khon Kaen Province 1985-1987. Geographical distributions

Districts	Years		
	1985	1986	1987
Muang	1.37	2.03	0.66
Ban Phai	4.13	1.36	0.00
Pol	0.00	2.43	0.00
Chumpae	2.31	1.71	0.00
Nam Pong	2.06	4.12	4.03
Kranuan	0.00	0.00	0.00
Puvieng	1.97	0.00	0.00
Nong Rua	2.46	2.47	7.28
Chonnabot	4.15	0.00	0.00
Munjakiri	4.37	2.18	0.00
Nong Song Hong	5.92	0.00	0.00
Wang Noi	0.00	0.00	0.00
Sri chompu	5.68	0.00	0.00
Ubolratana	0.00	0.00	0.00
Ban Phang	0.00	0.00	0.00
Kao Saun Kwang	0.00	0.00	0.00
Pra Yuen	6.43	0.00	0.00
Wang Yai	0.00	0.00	0.00
Puey Noi	0.00	0.00	0.00
Puphaman	0.00	0.00	0.00

Table 15. Races of cervical cancer patients in Khon Kaen province 1985-1987. From population-based cancer registry

Race	Number of cases	Percent
Thai	256	94.81
Chinese	3	1.11
Others	1	0.37
Missing data	10	3.71

Table 16. Religions of cervical cancer patients in Khon Kaen Province 1985-1987. From population-based cancer registry

Religions	Number of cases	Pergent
Buddhism	258	95.56
Christian	1	0.37
Muslim	1	0.37
Missing data	12	3.70

Table 17. Marital status of cervical cancer patients in Khon Kaen Province 1985-1987. From population-based cancer registry

Marital status	Number of cases	Percent
Single	4	1.48
Married	266	98.52

Table 18. Stages distribution of cervical cancer patients in Khon Kaen Province 1985-1987. From population-based cancer registry

Stages	Number of cases	Percent
Stage I	38	13.97
Stage II&III	133	48.90
Stage IV	11	4.04
Unknown	88	33.09

common were squamous cell,large cell non-keratinized type (47.41 %).

Discussion

Most of statistics concerning cervical cancer in Thailand were the relative frequencies of tumors. The data were obtained from cases diagnosed and treated at certain hospitals or institutes. This was the first report of which data were obtained from population-based collection. The interpretation of this data should be done cautiously because this preliminary report was done retrospectively. Underestimation might have occurred because of who had cancer and died at home without notifying the underlying cancer diseases at death certificates. Those who had cancer and went for diagnosis and treatment in Bangkok without referring back to Khon Kaen might also have been lost from the investigation.

Table 19. Pathology of cervical cancer in Khon Kaen Province 1985-1987. From population-based cancer registry.

Pathology	Cases	Percent
SCC,K,NOS	16	5.93
SCC,Large Cell,NK	128	47.41
SCC,Small Cell,NK	10	3.70
SCC Grade I	2	0.74
SCC Grade II	1	0.37
SCC Grade III	2	0.74
SCC,NOS	44	16.30
Adeno CA Grade I	4	1.48
Adeno CA Grade III	1	0.37
Adeno CA,NOS	15	5.56
Adenosquamous CA.	2	0.74
Papillary Adeno CA, NOS	1	0.37
Mucin-Producing Adeno CA	1	0.37
Undiff CA, NOS	2	0.74
No Microscopic Confirmation	41	15.19
Total	270	100.00

The age-standardized incidence rates obtained from this study were comparable to those of other countries[3] (Table 20). The incidence and mortality rates of Khon Kaen were in the middle of those. Eventhough the incidence rates fluctuated during the three year period, mortality rates were observed to be de-

Table 20. Incidence of cervical cancer in Khon Kaen province compared with selected countries in the world

Country	Registry*	ASR**
Brazil	Sao Paulo	35.1
Canada	Ontario	9.9
China	Shanghai	8.5
Hong Kong	Hong Kong	23.7
India	Bombay	20.6
India	Bangalore	40.2
Israel	Israel	4.0 (All Jews)
		5.1 (Born Israel)
		3.0 (Non-Jews)
Japan	Osaka	16.0
Japan	Hiroshima	22.0
Philippines	Rizal	16.6
Poland	Warsaw	14.7
Singapore	Singapore	17.0 (Malay)
		9.9 (Indian)
		28.0 (Indian)
United Kingdom	Birmingham	12.3
U.S.A.	Atlanta	8.5 (White)
		18.9 (Black)
Thailand	Khon Kaen	17.2

*Approved By International Agency For Research On Cancer (WHO).
ASR** = Age-Standardized Incidence Rate.

creasing. This may be due to the mass screening for cervical cancer in Khon Kaen during the period from October 13 to October 17, 1986[4] and the continuous screening program since 1976.

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Risk Factors for Recurrences of Cervical Cancer After Radical Hysterectomy and Pelvic Lymphadenectomy at Srinagarind Hospital

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Abstract: *The study of risk factors for recurrence of carcinoma of cervix after radical hysterectomy and pelvic lymphadenectomy for stage I and IIA was carried out among patients operated upon at Srinagarind Hospital from 1976 to June 30, 1988. There was no recurrence among patients with stage IA. The recurrent rates were 8.40 and 19.40% for stage IB and IIA respectively. The recurrent rates among patients with pelvic nodes involvement and without nodes involvement were 15.20 and 8.10% respectively. Again, with endometrial involvement the recurrent rate among these patients was 40.40% while only 7.70% recurrent rate encountered in those without endometrial involvement. The dilference was significant statistically .The age of the patients and extent of lesions were the important risk factors. Microscopic findings, type of lesions, surgeons and surgical techniques played no important role in recurrence of the cancer. (Thai J Obstet Gynaecol 1989;1:47-55)*

Keywords: cervical cancer, surgery, recurrence, risk factors

Recurrence of cancer is defined as a tumor found after 3 to 6 months following therapy, while disease found within that time period is often termed persistent disease.[1] It also includes those that later become evident after a period of complete clinical remission. Disease discovered after primary surgical approach should be termed persistent if margins or nodes were involved. Some authors define recurrence wthin any time period as tumor regrowth in cases in which no tumor was knowingly left behind.[2] Recurrences after radical hysterectomy with pelvic lymphadenectomy for stage IB and IIA vary from 10% to 20% in most institutes, for patients with negative nodes at the time of radical hysterectomy, about 10% recurrent rate.[2] Despite postoperative whole pelvis radiation therapy for 88% of all patients, 34.2% developed recurrence in Burke's series.[3] Also Burke and coworkers[4] reviewed 31 cases with FIGO

stage IB cervical carcinoma who developed recurrent disease after radical hysterectomy and pelvic lymphadenectomy. The over all incidence of recurrence was 11.3%. Sites of recurrence were central pelvis in 35%, pelvic side wall, 39%, and distant 26%. Patients treated with postoperative pelvic radiotherapy for positive pelvic nodes or surgical margin involvement were more likely to develop distant recurrence. High-risk factors are apparent in these patients. If tumor is present in vascular spaces, the endometrial cavity, the deep endocervical stroma or the paracervical (cardinal ligament) tissue are invaded, or if a tumor is undifferentiated or 3 cm or larger in size, one may predict a high recurrent rate.[3] The disease-free interval depends on different factors including the adequacy of initial treatment, host resistance, the original stage, volume of tumor and adequacy of follow-up.[1]

This study was to review risk factors for recurrence after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital during 12 year period and to explore suitable treatment for the future and selection of patients.

Materials and Methods

During 1976 to June 30, 1988, 218 cases of cervical cancer stage IA, IB and IIA were operated on. The data from 1976 to 1983 were retrospectively collected from records of the operative room, the Department of Pathology and the medical record unit. Since 1984, all records were collected prospectively and kept by the Division of Gynaecologic Oncology, Department of Obstetrics and Gynaecology. The follow-up data were obtained from the Gynaecologic Oncology tumor clinic and the hospital-based cancer registration of the cancer unit, Faculty of Medicine. The operative technique performed in this hospital was class III extended hysterectomy due to Piver's classification[5] and the modified Okabayashi technique as mentioned by Sekiba.[6] Postoperative care was closely observed for any complications and prophylactic antibiotics were routinely given.

Follow-up for patients began at the tumor clinic with the first examination 4 weeks postoperatively, then every 3 months for the first year and every 6 months for the rest of their lives. Complete physical and pelvic examinations with Pap smear were done every time.

All recurrence cases were given radiotherapy with or without chemotherapy. Questionnaires would be sent to those who did not attend the tumor follow-up clinic.

The analysis of data was performed using descriptive statistics and contingency tables with chi-square test, and analysis of disease-free interval, using Cutler-Ederer life table analysis with log-rank tests. The censor date was June 30, 1988. Those who missed two appointments were labelled as lost in the analysis.

Results

Incidence of Recurrence and FIGO Stages

From 1976 to June 30, 1988, 218 cases of cervical cancer stage IA, IB and

IIA were operated upon at Srinagarind Hospital. Twenty recurrences(9.10%) were diagnosed, 16 cases of stage IB (8.40%), 4 cases of IIA(19.40%) and there were no cases of stage IA which recurred at the time of censoring with no statistical significant. Fig.1 shows the disease-free curve in different stages with statistical significance.

Nodal Status

Fifteen out of 185 cases of those who had negative lymph nodes had recurrence, while five out of 33 cases of positive lymph nodes recurred without statistical significance(Table 1). The disease-free curve is shown in Fig.2 and no statistical significance is observed.

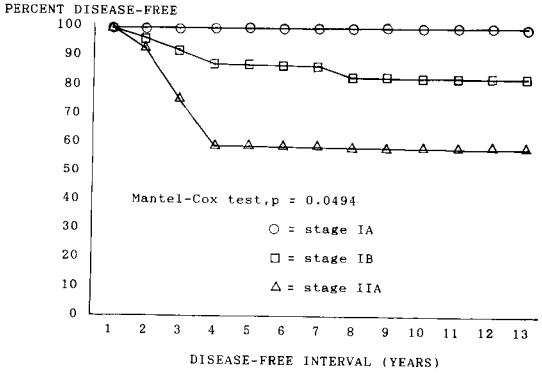

Fig. 1 Disease - free curve after radical hysterectomy at Srinagarind Hospital 1976-1988

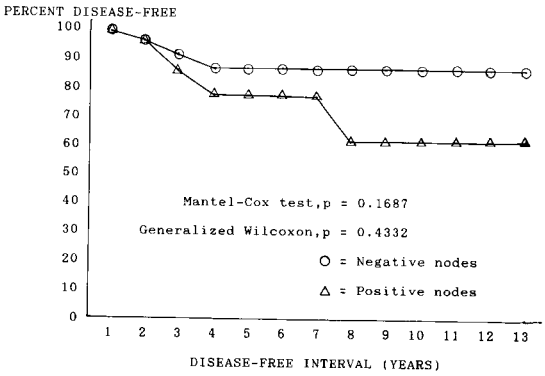

Fig. 2 Disease - free curve after radical hysterectomy at Srinagarind Hospital 1976-1988

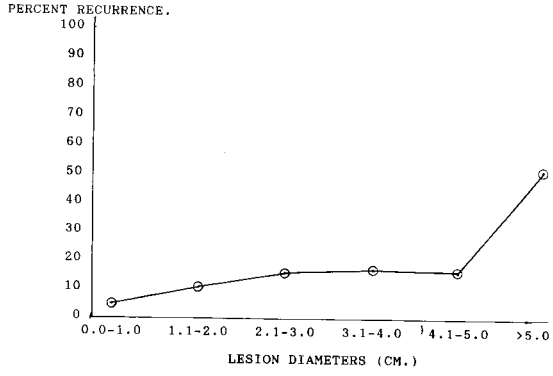

Fig. 3 Radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Stratified by lesion sizes

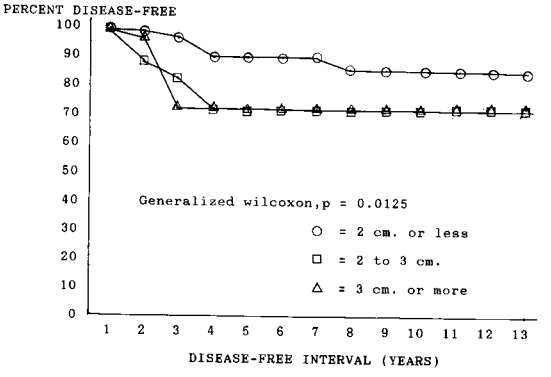

Fig. 4 Disease free - curve after radical hysterectomy at Srinagarind Hospital 1976-1988 : Lesion diameters

Lesion Sizes

Table 1 and Fig.3 show the increased percentage of recurrence with the increase in size of tumors with statistical significance. The percentage increased mostly after the tumor diameter became greater than 4 cm. Fig.4 shows the disease-free curve of those who had 2 cm or less, 2 to 3 cm and 3 cm or more. The curve significantly changed when size became greater than 2 cm.

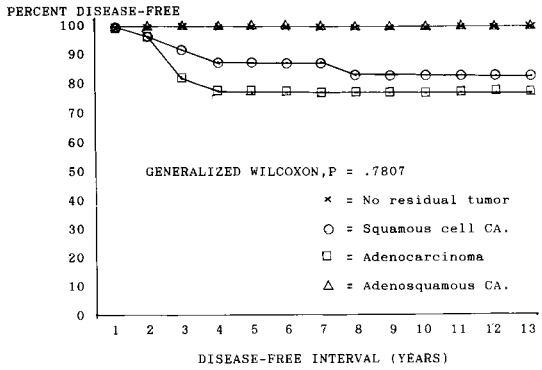

Fig. 5 Disease free curve after radical hysterectomy at Srinagarind Hospital 1976-1988 : Cell types

Table 1 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital

FIGO Stages	Total cases	Recurrence	Percent	p-value
IA	6	0	0.00	
IB	191	16	8.40	
IIA	21	4	19.40	0.201
Nodal Status				
Negative nodes	185	15	8.10	
Positive nodes	33	5	15.20	0.3351
Lesion Diameters (cm)				
0.0-1.0	93	4	4.30	
1.1-2.0	64	6	9.40	
2.1-3.0	33	5	15.20	
3.1-4.0	19	3	15.80	
4.1-5.0	7	1	14.30	
5.1 or more	2	1	50.00	0.0035
Histology				
Squamous cell	180	15	9.09	
Adenocarcinoma	36	5	16.13	
Adenosquamous	2	0	0.00	0.072
Lesion Types				
No lesion*	18	1	5.56	
Ulcerative	75	5	6.70	
Polypoid	35	1	2.90	
Cauliflower	7	11	14.10	
Infiltrative	12	2	16.17	0.3264

* Including postconization and occult IB.

Histology

No statistical significance was observed by histology in recurrent paterns in Table 1 and Fig.5.

Lesion Types

There was no different recurrent rates by lesion types (Table 1).

Surgical Factors

There was no relationship between surgeons, surgical techniques and recurrence (Table 2).

Extent of Tumor

Table 3 shows the correlation of tumor extent and involved different

Table 2 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenecomy at Srinagarind Hospital : Surgical factors

Surgeons	Total cases	Recurrence	Percent	p-value
Surgeon 1	135	12	8.89	
Surgeon 2	33	6	18.20	
Surgeon 3	23	1	4.30	
Surgeon 4	21	0	0.00	
Surgeon 5	6	1	16.70	0.2614
Surgical techniques				
Wertheim-Meigs	113	12	10.60	
Okabayashi	105	8	7.60	0.5947

Table 3 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Tumor extent

Tumor extents	Total cases	Recurrence	Percent	p-value
Vagina				
Involved	9	2	22.20	
Not involved	209	18	8.60	0.426
Left cardinal ligament				
Involved	7	1	14.30	
Not involved	211	19	9.00	1.0000
Right cardinal ligament				
Involved	7	1	14.30	
Not involved	211	19	9.00	1.0000
Endometrium				
Involved	9	4	44.40	
Not involved	209	16	7.70	0.0016

structures with the rate of recurrence. Only endometrial involvement is observed to be a great risk factor for recurrence in this study.

Age

Table 4 shows the percentage of recurrence for different age intervals. When ages were grouped into 35 years or less and above 35, there was statistical significance in recurrent rates. Fig.6 shows the disease-free curve for those aged below and above 35 years with statistical significance.

Discussion

Radical hysterectomy and pelvic lymphadenectomy is considered to be the treatment of choice for cervical cancer stage IB and IIA in this hospital. Failure rate of treatment of cervical cancer stage IB and IIA has varied from 10 to 20% in most series with primary surgery or radiation therapy.[1,2] At Srinagarind Hospital, the recurrence of stage IA,IB and IIA altogether is 9.10%, 8.40% for stage IB and 19.40% for stage IIA, which are in the acceptable range. FIGO stage was found to be one of significant risk factor for recurrence. From this study, the significance was found from the disease -free curve. With increasing stages, the rate of nodal involvement increased, 15.5% for stage IB and 50.0% for stage

Table 4 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Age factor

Age	Total cases	Recurrence	Percent	p-value
30 or less	12	3	25.00	
31-35	30	5	16.70	
36-40	45	4	8.90	
41-45	46	3	6.50	
46-50	36	2	5.60	
51-55	28	1	3.60	
56-60	16	2	12.50	
60 or more	5	0	0.00	
Cutpoint at age 35				
35 or less	42	8	19.00	
Above 35	176	12	6.80	0.0300

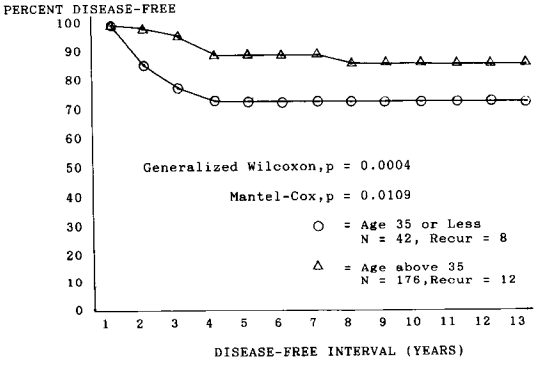

Fig. 6 Disease-free curve after radical hysterectomy at Srinagarind Hospital 1976-1988 : By ages 35 and cutpoint

IIA in O'Brien's report.[7] Increase in rate of lymphatic involvement should increase the rate of recurrence.[2,4,8-17] In this study, the recurrent rate for negative nodes group was 8.10% and for positive nodes group 15.20%, without statistical significance. This is because of the administration of radiotherapy to all cases of positive nodes, vaginal cuffs and parametrium but not endometrial involvement.

It is clearly seen from Table 1, Fig.3 and Fig.4 that lesion size is the important risk factor for recurrence with statistical significance, which corresponds to previous reports.[2,4,7,9,12,18] Many authors[2,4,18-20] have mentioned about histology as risk factor for recurrence. Patients with adenocarcinoma or adenosquamous carcinoma had higher risk of recurrence than those who had squamous cell carcinoma. From this study, patients with adenocarcinoma had higher rate of recurrence than patients with squamous cell carcinoma but without statistical significance. Lesion types had no significant relationship to recurrent rate in this study, but in advanced stages, the endocervical infiltrative types had higher recurrent rate than other types.[21] It was also seen from Table 2 that surgeons and surgical techniques had no influence on recurrence as far as the standard procedure practiced.

Parametrial extension and vaginal involvement was mentioned to be a risk factor for recurrence.[14,22-23] Due to radiotherapy given to all of those patients with parametrial and vaginal edge involvement, there was no difference in recurrent rate. It was clearly seen from this study that endometial involvement was a significant risk factor for recurrence. This finding does agree with previous reports.[24-29] Those with endometrial invasion should administer adjuvant chemotherapy incombination with routine radiotherapy.

There have been some reports about younger ages, especially those 35 years or less, having higher risk of recurrence than older people[30-36]. Table 4 and Fig.6, show total agreement with previous reports.

The above mentioned risk factors, should be used as guidelines for selecting patients for the surgery in order to decrease recurence and increase survival rates in treatment of cervical cancer in this hospital.

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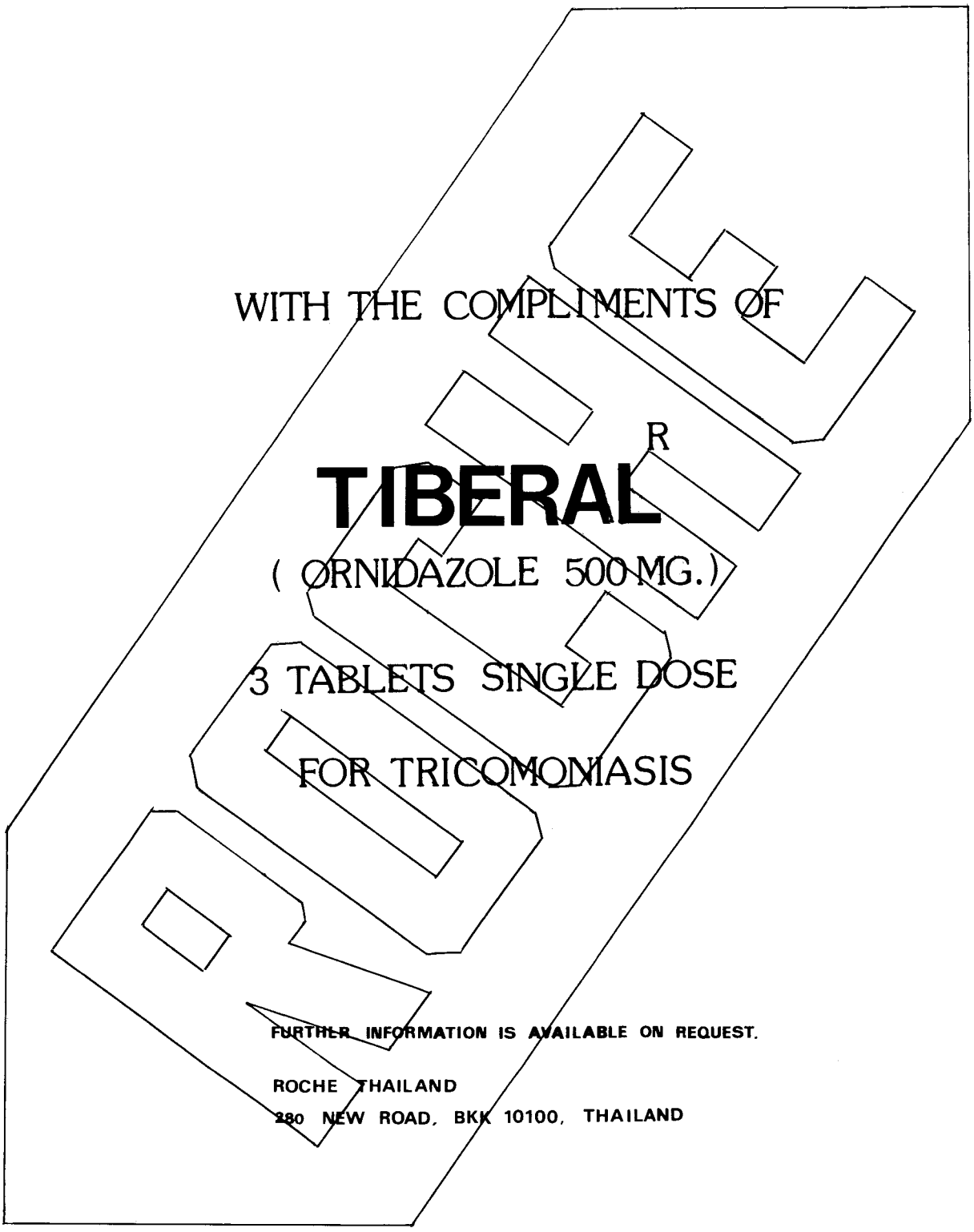
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Ovarian Carcinoma and Serum Lactic Dehydrogenase Levels

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Abstract: *Preoperative and postopertive levels of serum lactic dehydrogenase (LDH) were measured in 218 patients with various gynaecologic diseases. Among 119 patients with benign gynaecologic diseases, the LDH levels were in normal limit, except for two patients of endometriosis and benign cystic teratoma who showed silght elevated LDH values. The LDH levels were elevated in 36/51 patients (70.6 per cent) with ovarian carcinoma. All 8 patients with malignant germ cell tumors showed abnormal LDH levels, especially the average LDH value of dysgerminoma was about three times higher than the maximum normal value. The incidence of abnormal LDH in patients with advanced ovarian carcinoma was higher than in patients with stage I and II ovarian carcinoma (78.4 to 50.0 per cent). There were no elevations of LDH levels in patients with CIN, cervical and endometrial carcinoma. The results from this study suggest that in the presence of a pelvic mass together with an elevated LDH level, diagnosis of ovarian malignancy should be considered. (Thai J Obstet Gynaecol 1989 ; 1 : 57-62)*

Key words: ovarian carcinoma, serum lactic dehydrogenase

Several biochemical substances have been used as tumor markers in patients with gynaecologic cancers. The best known and most widely used markers were human chorionic gonadotropin , alpha-fetoprotein, and carcinoembryonic antigen[1]. Recently, radioimmunoassay using a monoclonal antibody to detect ovarian carcinoma has also been used[2,3].

Lactic dehydrogenase (LDH) is a glycolytic enzyme which is present in various normal tissues and nepolasms of the human body. There have been some reports of elevation of this enzyme in the patients with ovarian carcinoma[4-6].

The purposes of this paper are: 1) to compare the LDH levels in patients with benign and malignant gynaecologic diseases, 2) to study the LDH levels in

patients with various histologic types and stages of ovarian carcinoma.

Materials and Methods

Subjects for this study included 218 patients with various gynaecologic diseases who were admitted for operations in the gynaecologic ward, Siriraj Hospital between April 1987 and June 1988. All patients were free from myocardial infarction, breast disease, liver disease, leukemia, and lymphoma. Preoperative and postoperative serum lactic dehydrogenase determinations were performed in each patient. The LDH levels of 10 patients with normal intrauterine pregnancies were also studied for comparison. The LDH levels were determined by the method of Wroblewski and La Due with the normal value of 120-280 U/L. A histopathologic study was done postoperatively on the surgical specimen obtained from each patient. The Fisher exact probability test was used for statistical comparison.

Results

The ages of the patients, the diagnoses, and the levels of serum lactic dehydregenase before and after operation

Table 1. Serum LDH in 218 patients with various gynaecologic diseases and 10 normal pregnant women

Diagnosis	No. of patients	Age mean ± SD	LDH before operation (U/L) mean ± SD	LDH before operation (U/L) abnormal cases (%)	LDH after operation (U/L) mean ± SD	LDH after operation (U/L) abnormal cases (%)
Ectopic pregnancy	5	29.4 ± 4.9	173.8 ± 55.0	0	194.8 ± 21.9	0
Pelvic infection	7	32.4 ± 5.9	180.7 ± 40.6	0	224.8 ± 31.4	0
Genital prolapse	21	54.7 ± 10.8	192.4 ± 42.9	0	191.1 ± 25.1	0
Myoma uteri	25	40.4 ± 6.3	204.2 ± 26.0	0	224.5 ± 36.5	0
Adenomyosis	9	41.3 ± 5.4	183.7 ± 25.6	0	206.8 ± 30.2	0
Endometriosis	17	32.6 ± 8.5	198.8 ± 48.5	1 (5.9)	212.2 ± 40.2	1 (5.9)
Benign ovarian tumor	35	34.3 ± 13.4	191.6 ± 37.9	1 (2.9)	221.7 ± 31.9	1 (2.9)
Ovarian carinoma	51	46.5 ± 15.4	439.2 ± 393.8	36(70.6)	419.4 ± 407.5	31 (60.8)
Cervical intra-epithelial neoplasia	23	37.2 ± 9.5	190.7 ± 30.7	0	183.2 ± 40.2	0
Cervical carcinoma	19	43.7 ± 11.0	184.9 ± 42.4	0	207.7 ± 35.8	0
Endometrial carcinoma	6	42.5 ± 17.1	197.0 ± 40.9	0	226.0 ± 31.9	0
Intrauterine pregnancy	10	25.9 ± 2.9	242.7 ± 29.2	0	-	-

are shown in Table 1. Among 119 patients with benign gynaecologic diseases, there were only 2 patients with elevated LDH; one of endometriosis and the other of benign cystic teratoma. However, both patients had levels below 300 U/L (284 U/L and 294 U/L respectively). Of 51 patients with ovarian carcinoma, the levels before operation elevated in 36 patients (70.6 per cent) with a maximum value of 2,721 U/L. After their operations, the levels decreased to normal in only 5 patients. There were no elevated LDH levels in patients with cervical intraepithelial neoplasia, cervical and endometrial carcinoma, nor in normal pregnant women.

Table 2 shows the levels of LDH before and after operation relating to the histopathologic diagnoses of ovarian carcinoma. Of 9 patients with mucinous cystadenocarcinoma, the mean value of LDH was in the normal range, with abnormal levels in 4 patients (44.4 per cent) before operation and 1 patient (11.1 per cent) after operation. All 8 patients with malignant germ cell tumors showed abnormal levels, which is quite significant when compared to the abnormal levels of 26/39 patients (66.7 per cent)

Table 2. Serum LDH in 51 patients with ovarian carcinoma

Tumor cell types	No. of patients	Age	LDH before operation (U/L)		LDH after operation (U/L)	
		mean ± SD	mean ± SD	abnormal cases (%)	mean ± SD	abnormal cases (%)
Serous cystadenocarcinoma	19	49.5 ± 12.4	481.2 ± 550.9	14 (73.7)	453.1 ± 479.3	12 (63.2)
Mucinous cystadeno carcinoma	9	55.4 ± 8.5	260.1 ± 69.4	4 (44.4)	246.6 ± 37.9	1 (11.12)
Adenocarcinoma	3	47.3 ± 10.8	439.3 ± 108.9	3 (100)	366.7 ± 91.7	3 (100)
Clear cell carcinoma	3	38.7 ± 8.9	558.0 ± 280.6	3 (100)	292.0 ± 62.6	2 (66.7)
Endometrioid carcinoma	5	41.6 ± 14.8	367.2 ± 226.7	2 (40)	578.8 ± 682.4	2 (40)
Immature teratoma	1	44	306	1 (100)	397	1 (100)
Endodermal sinus tumor	3	19 ± 2.2	482.0 ± 246.8	3 (100)	659.3 ± 513.2	3 (100)
Dysgerminoma	3	36.0 ± 17.0	887.3 ± 288.4	3 (100)	516.7 ± 263.6	3 (100)
Malignant mixed germ cell tumor	1	16	367	1 (100)	316	1 (100)
Granulosa cell tumor	1	74	365	1 (100)	408	1 (100)
Metastatic tumor	3	55.0 ± 7.8	314.7 ± 149.2	1 (33.3)	346.0 ± 94.0	1 (33.3)

with malignant epithelial tumors ($p = 0.057$). The 3 patients with dysgerminoma showed markedly elevated LDH, with an average value about three times higher than the maximum normal value. For metastatic ovarian carcinoma, only 1 patient (33.3 per cent) showed abnormal level.

The stages of the ovarian carcinoma according to the International Federation of Gynecology and Obstetrics (FIGO), and the levels of LDH before and after operation are shown in Table 3. Before operation, the abnormal levels were found in 7/14 (50 per cent) of the patients with stage I and II diseases. It was significantly less than those found in 29/37 (78.4 per cent) of the patients with stage III and IV diseases ($p < 0.05$).

Discussion

Serum lactic dehydrogenase levels have been reported to be elevated in patients with lymphoma, granulocytic leukemia, carcinoma of the pancreas and gall bladder, metastatic carcinoma of the breast and metastatic carcinoma of the liver. Such findings have also been noted in cases of myocardial infarction, infectious mononucleosis, thrombocytopenia, obstructive jaundice, and acute hepatitis[7-9].

LDH is major enzyme in glycolysis and reversible catalyzes pyruvate to lactic acid. Malignant tissue has high glycolytic activity as Cori and Cori[10] and Warburg[11] reported many years ago. Thus, one would expect that patients with increased glycolytic activity will consequently have an elevation of LDH level. The ovary is a multipotential and totipotential organ. During malignant change, it may show high glycolytic activity resulting in an increased LDH level which can be measured in the circulating plasma. So the LDH test may be useful in the diagnosis of ovarian carcinoma.

Previous reports have shown that LDH was elevated in the presence of

Table 3. Serum LDH in patients with various stages of ovarian carcinoma

Stages	No. of patients	Age	LDH before operation (U/L)		LDH after operation (U/L)	
		mean ± SD	mean ± SD	abnormal cases (%)	mean ± SD	abnormal cases (%)
I	10	30.6 ± 11.3	354.7 ± 317.6	5 (50)	319.7 ± 200.4	4 (40)
II	4	55.0 ± 9.2	465.3 ± 310.5	2 (50)	248.3 ± 55.5	1 (25)
III	30	49.9 ± 13.8	466.8 ± 452.1	23(76.7)	452.6 ± 469.7	22(73.3)
IV	7	49.4 ± 14.5	427.0 ± 202.8	6(85.7)	517.1 ± 400.2	4(57.1)

ovarian carcinoma but not in benign tumors of the ovary, leiomyoma of the uterus, carcinoma of the endometrium, carcinoma of the cervix, or carcinoma of the sigmoid colon[4,5]. In this study, LDH levels were elevated in about two-thirds (70.6 per cent) of the patients with ovarian carcinoma. In other benign gynaecologic diseases, cervical and endometrial carcinoma, and pregnancy, the LDH levels were still within normal limits. There were abnormal levels in each case of endometriosis and benign cystic teratoma, but the values were only slightly elevated to 284 and 294 U/L respectively.

LDH levels were found to be elevated in all cases of malignant germ cell tumors, with striking elevation in patients with dysgerminoma. The marked elevation of LDH in dysgerminoma was also reported by several authors[5,6,12,13]. In patients with ovarian carcinoma of common epithelial cell types, LDH levels were found to be elevated in two-third of the cases. It should be noted that the mucinous type of ovarian carcinoma showed an average levels approaching the upper limit of normal value. Burrows[14] reportd serum LDH levels of 61 patients with ovarian malignancies which were approaching the upper limit of normal value, and there was considerable overlap with the normal range.

The present study shows that there are higher incidence of abnormal LDH levels in advanced ovarian carcinoma (FIGO stage III and IV). It is assumed that more tumor cell volumes will have more glycolytic activity, resulting in enzyme LDH elevation.

Awais[4,5,13] reported that after effective treatment of carcinoma of ovaries, LDH levels decreased to normal range and remained normal as long as the carcinoma was under control. In this study, the LDH levels, after treatment, did not decrease satisfactorily to normal range. Therefore, they can not be used as a monitoring parameter for an assessment of the effectiveness of therapy.

Although the results of the present study show that serum lactic dehydrogenase seem to be helpful in the diagnosis of carcinoma of ovary, no decisive or unequivocal claim is made. Any woman with a pelvic mass together with an elevated serum lactic dehydrogenase level could be considered having carcinoma of ovary, and diagnosis of ovarian carcinoma should be included until proved otherwise.

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Postpartum Insertion of Modified Intrauterine Devices

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Abstract: *This study has been conducted to investigate and compare three postpartum IUDs insertion within 5 days after delivery, viz:1) Mod.LLD with LLD, 2) Mod. T Cu 380 A with T Cu 380 A and 3) Mod.LLD with Mod. T Cu 380 A. It showed that the expulsion rate of Mod.LLD was significantly lower than LLD; no statistical difference in the expulsion rate between Mod. T Cu 380 A and T Cu 380 A, and the expulsion rate of Mod.LLD was significantly higher than Mod. T Cu 380 A. Medical complications of either modified IUD were not increased. No pregnancy or perforation occurred in any of the group 12-months of use for any of these IUDs.(Thai J Obstet Gynaecol 1989;1:63-70)*

Key words: postpartum insertion, modified intrauterine devices

Postpartum insertion of intrauterine devices (IUDs) is easy insertion and convenient for mothers who have normal delivery in hospital. Expulsion rates are expected to be high, but the IUDs insertions are safe from infection and perforation.[1-3]

In 1977, Family Health International modified the standard Lippes Loop D and Copper T 220 C for postpartum use. The simplest design was the addition of chromic catgut sutured material to the upper arms of the two standard devices. The new devices were named the Delta Loop and Delta T. It was hoped that the free ends of the sutures (each 0.5 cm long) projected into the endometrium and secured the position of IUD. The suture projections biodegrate within six weeks of insertion, as the postpartum uterus is involuted. Its expulsion rate is then reduced to a minimal level.[4-6]

The purposes of this trial were to find out the expulsion rate of new modified Lippes Loop D and modified T Cu 380 A and to study complications of both modified IUDs.

Materials

Two modified IUDs were used in this study. The first was a Modified Lippes Loop D (Mod. LLD) (Fig.1) with chromic catgut materials No. 2 sutured on the upper three curves of the standard

Lippes Loop D (LLD). Each free end of the suture is 0.5 cm long, the length between each point to suture being more distant than its Delta Loop and at different levels. It is expected that Mod.LLD is better held in proper position of the uterine cavity than Delta Loop. The second was a Modified T Cu 380 A with chromic catgut materials No. 2 added to the upper arm of the standard T Cu 380 A. The T Cu 380 A can be used up to 5 years.

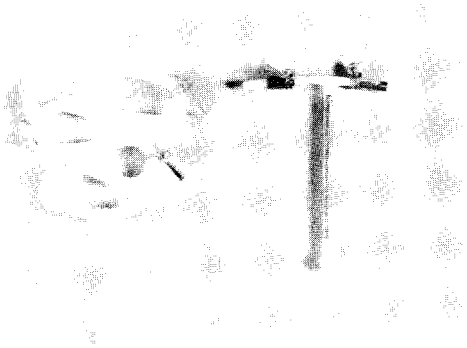

Fig 1. Modified Lippes Loop D and T Cu 380 A

Patients and Methods

The postpartum patients had no contraindication for this method of contraception. All had normal deliveries and postpartum status in the Rajavithi Hospital. They could be reached easily during 12 months of follow-up.

The first study comparing Mod. LLD and LLD had 110 postpartum women assigned to use each device. The second study comparing Mod. T Cu 380 A and T Cu 380 A had 200 postpartum women assigned use each device.

Time of insertion

In both studies, IUDs were inserted 6 hours to 5 days after delivery and all acceptors were observed 24-48 hours before discharge.

Insertion Technique

In the first study, Mod.LLD and LLD were grasped with Randall Kidney Stone forceps and placed at the uterine fundus by replacement technique (Fig 2).

Fig 2. Modified LLD, grasped with forceps

In the second study, Mod. T Cu 380 A and T Cu 380 A were put in a plastic tube and inserted at the uterine fundus by withdrawal technique (Fig.3).

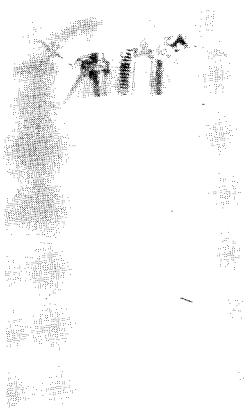

Fig 3. T Cu 380 A, put in the plastic tube

Follow-up

All acceptors were examined one month after delivery. Subsequent follow-up visits were scheduled at 3,6 and 12 months after insertion. The acceptors who did not come for routine check-up were visited at home.

Results

Mod. LLD vs LLD

Women in both groups were not significantly different with respect of age and parity ($p > .05$) (Table 1,2)

Table 1 Age distribution

Age	Mod. LLD		LLD		Mod. T Cu 380 A		T Cu 380 A	
	No	%	No	%	No	%	No	%
15 - 19	15	13.6	23	20.9	37	18.5	36	18.0
20 - 24	45	40.9	47	42.7	91	45.5	105	52.5
25 - 29	24	21.8	19	17.3	48	24.0	47	23.5
30 - 34	18	16.4	16	14.6	19	9.5	9	4.5
35 - 39	8	7.3	5	4.5	5	2.5	3	1.5
Total	110	100.0	110	100.0	200	100.0	200	100.0
Mean ± SD	25.1 ± 5.6		24.0 ± 5.5		23.0 ± 4.2		23.6 ± 4.8	

Table 2 Parity

Parity	Mod. LLD		LLD		Mod. T Cu 380 A		T Cu 380 A	
	No	%	No	%	No	%	No	%
1	36	32.7	47	42.7	111	55.5	109	54.5
2	41	37.3	42	38.2	61	30.5	65	32.5
3	24	21.8	10	9.1	21	10.5	20	10.0
4	7	6.4	7	6.4	5	2.5	5	2.5
5	2	1.8	4	3.6	2	1.0	1	0.5
Total	110	100.0	110	100.0	200	100.0	200	100.0
Mean ± SD	2.1 ± 1.0		1.9 ± 1.0		1.6 ± 0.8		1.6 ± 0.8	

At the Cumulative six month, Gross Life Table, the expulsion rate were 15.6 for Mod. LLD and 21.1 for LLD, the difference was significant for comparison ($P < 0.05$). After insertion during 7 - 12 months the expulsion rates of both groups were not different (Table 3).

There were relationships of the expulsion rates during 8 weeks after insertion and the time of insertion (Table 4). The expulsion rates of both IUDs insertion within 24 hours of delivery were higher than those after 24 hours of delivery.The expulsion rates of both groups were not related to parity, as shown in Table 5.

Table 3 Gross Cumulative Life Table Rates per 100 women : Expulsion

Month	Mod. LLD	LLD	Mod. T Cu 380 A	T Cu 380 A
1	11.4 ± 3.1	8.5 ± 2.7	4.1 ± 1.4	4.7 ± 1.5
2	12.4 ± 3.2	15.6 ± 3.5	7.2 ± 1.9	6.3 ± 1.8
3	13.5 ± 3.4	17.7 ± 3.7	8.3 ± 2.0	7.4 ± 1.9
6	15.6 ± 3.5*	21.1 ± 3.9*	8.8 ± 2.0	8.5 ± 2.0
12	17.9 ± 3.7	23.5 ± 4.2	9.4 ± 2.1	9.1 ± 2.1

*P < .05

Table 4 Relationship of expulsion rate (percentage) during 8 weeks after insertion with time of insertion

Time of insertion (hrs)	Mod. LLD n = 110	LLD n = 110	Mod. T Cu 380 A n = 200	T Cu 380 A n = 200
< 24	13.9	23.9	8.9	8.8
25 - 48	10.0	11.8	7.5	3.1
> 49	12.5	3.3	3.7	5.4

Table 5 Relationship of expulsion rate (percentage) and parity

Parity	Mod.LLD n = 110	LLD n = 110	Mod. T Cu 380 A n = 200	T Cu 380 A n = 200
1	16.7	23.4	9.5	7.5
2	17.1	19.0	9.4	10.1
≥ 3	18.2	23.8	7.3	7.9

Bleeding and/or pain at two months after insertion were encountered more frequent in the Mod.LLD than in the LLD groups (Table 6). However, at the six and twelve-months the Gross Cumulative Life Table bleeding and/or pain rates among both groups were not significant different.

Gross Cumulative Life Table of PID rates are shown in Table 6. At one month, PID rates were 1.0 per 100 women, equally for both IUDs, and no significant difference encountered between either device at six and twelve months.

Termination event rate of Mod.LLD was lower than LLD at 12 months (Table 7).

Table 6 Gross Cumulative Life Table Rates per 100 women : Medical complication

Month	Mod.LLD	LLD	Mod. T Cu 380 A	T Cu 380 A
Bleeding and/or pain				
1	2.0	0.0	0.5	0.5
2	4.3	2.3	2.7	2.2
3	4.3	2.3	3.3	4.5
6	6.6	6.1	4.4	5.1
12	10.4	10.5	6.7	8.4
Infection or PID				
1	1.0	1.0	0.5	1.6
2	1.0	1.0	1.1	1.6
3	1.0	1.0	1.1	1.6
6	2.2	2.4	1.1	1.6
12	2.2	2.4	2.3	1.6

Table 7 Net Cumulative Life Table Rates per 100 women at 12 months of use

Event	Mod.LLD	LLD	Mod. T Cu 380 A	T Cu 380 A
Pregnancy	0.0	0.0	0.0	0.0
Expulsion	18.0	22.7	9.2	8.7
Removal :				
Medical	7.5	9.5	4.6	4.1
Planning pregnancy	0.0	1.9	0.0	0.5
Personal	6.6	8.5	4.6	6.2
Termination	32.1	42.6	18.4	19.5
Continuation	67.9	57.4	81.6	80.5
Women - months	939.5	878.5	2023.5	1919.5

Mod. T Cu 380 A vs T Cu 380 A

Age and parity of women inserted with Mod. T Cu 380 A and T Cu 380 A were similar in both groups (Tables 1 and 2).

At six months, the expulsion rates of Mod.T Cu 380 A and T Cu 380 A were 8.8 and 8.5 per 100 women respectively, and there was no significant difference in the expulsion rates between two devices. After insertion during 7 - 12 months, the expulsion rates of both IUDs showed no difference(Table 3). A relationship was noted in the expulsion rates at 8 weeks after insertion to the time immediately after insertion (Table 4). The expulsion of both IUDs insertions within 24 hours of delivery were higher than after 24 hours of delivery. The expulsion rates of both IUDs insertion were not related to parity (Table 5).

Bleeding and/or pain rates from Mod. T Cu 380 A and T Cu 380 A at two months after insertion were equal (Table 6). At six and twelve months, bleeding and/or pain rates of both IUDs did not show significant difference in comparison. At the one month, PID rates of Mod.T Cu 380 A and T Cu 380 A were 0.5 and 1.6 per 100 women respectively (Table 6), and at six and twelve months, PID rates of both groups did not show significant difference in comparison.

Termination event rates of Mod. T Cu 380 A and T Cu 380 A were not different (Table 7).

Mod. LLD vs Mod. T Cu 380 A

At twelve months, the expulsion rate of Mod. LLD was significantly higher than Mod. T Cu 380 A ($P < .05$) (Table 3). Bleeding and/or pain rate of Mod. LLD was higher than Mod. T Cu 380 A, but it was not statistically significant (Table 6), and there were no significant difference in PID rates of either IUD.

Termination event rate of Mod. LLD was higher than Mod. T Cu 380 A at twelve months (Table 7).

Neither pregnancy nor perforation of the uterus occurred in any of the 4 groups during the 12-month period.

Dicussion

At six months, the various expulsion rates of Deltal Loop inserted within ten minutes after placental delivery ranged from 3.1 to 27.2 per 100 women [6-10]. In this study, the expulsion rate of Mod. LLD, inserted after delivery 6 hours to 5 days, was 15.6 per 100 women, and the expulsion rate in the previous study of Delta Loop with the same technique and time of insertion was 19.7 per 100. [11]

The expulsion rate of Mod. LLD was in the low rate of expulsions reported and the expulsion rate of Mod. LLD is significantly lower than LLD.

At six months, the various expulsion rates of Delta T Cu 220 C inserted within ten minutes after placental delivery ranged from 8.0 to 14.2 per 100 women. In this study, the expulsion rate of Mod. T Cu 380 A, inserted 6 hours to 5 days after delivery was 8.8, which is in the low range of other reports, and there was no significant difference between the Mod. T Cu 380 A and T Cu

380 A expulsion rates.

The expulsion rate of Mod. LLD was significantly higher than Mod. T Cu 380 A. This might be because they are different types of IUDs.

In developing countries, some patients do not attend antenatal clinics. Most patients would be highly motivated to accept IUD insertion after completing delivery and being admitted to a postpartum ward. Thus, the optimal time of postpartum IUD insertion would be within 2 - 3 days after delivery. During this time it is easy to perform insertion and convenient.

Factors which caused high expulsion rate of postpartum IUD insertion were related to the insertor's experience, the method of insertion, the type of devices and the time of insertion. Other factors of modified IUDs which may be important in causing expulsion are the film of blood clot covering the endometrial cavity which may be a barrier of projection for the free end of suture into the endometrium, the length between each point of suture being too close, and each point of suture being in the same level such as Mod. T Cu 380 A. The latters might cause the IUD not to be held firmly in the proper position in the uterine cavity.

The complication rates (bleeding and/or pain and PID) were not higher when compared with other reports. [7-10]

This study has shown that immediate postpartum IUD insertion is a perfectly safe procedure, and it may be useful for future research efforts for new types of IUDs and modified IUDs.

In summary, a comparison for each group of postpartum IUDs insertion within 5 days after delivery, the expulsion rate of Mod. LLD was significanlty lower than LLD, Mod. T Cu 380 A and T Cu 380 A showed no significant difference, and Mod. LLD was significantly higher than Mod. T Cu 380 A. The medical complications with either modified IUD were not increased. Neither pregnancy nor perforation of uterus occurred during 12 months of use.

Acknowledgments

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First Year's Experience with Norplant

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Abstract:*Health Promotion Center Region I introduced Norplant for family planning clinics in June 1, 1986, and a clinical study of Norplant was carried out. Characteristics of most acceptors were aged between 18-40 years, lived in Bangkok, two parities, low monthly incomes and primary educational levels. Most previously used oral contraceptive methods. Health personnel were the most important source of information on Norplant. During 1 year follow up, the most found side effect and menstrual pattern was irregular bleeding. The follow up rate was high in the first week, 96.9%, and then declined respectively. The rate after one year follow up was only 54.32%. The continuation rate was high, 99.38% during the one year, and no pregnancy occurred among acceptors. Therefore, Norplant is a good contraceptive method which can be used effectively in family planning programmes. (Thai J Obstet Gynaecol 1989;1:71-75)*

Key words: first year experience, Norplant

Health Promotion Center Region 1 introduced *Norplant* for family planning in June 1, 1986. The author had studied all acceptors clinically from June 1, 1986 to May 31, 1987, a follow-up period of one year. During that period, observations were made on the characteristics of the acceptors, their incomes, their educational levels, their previous contraceptive methods, their sources of information on *Norplant*, it's complications and side effects, the follow-up rate, the acceptor's menstrual patterns, their continuation rate on the use of it, as well as their pregnancy rate. This study should be considered as a guideline for introducing *Norplant* in family planning and as a comparison to other previous studies.

Materials and Methods

The *Norplant* system consists of six silastic tubes/capsules. Each tube is 34 mm long, 2.41 mm in diameter and contains 36 mg of levonorgestrel. Both ends of the tube are sealed. The implantation area is the inner surface of upper arm. The insertion of those 6 tubes, in fan shape, is approximately 6 - 8 cm above the elbow.

The criteria for the selected acceptors of this study were between 18 - 40

years of age, no contraindication for progestin-only contraception, having at least one child, no lactation, no pregnancy, and accepting the subdermal implantation.

Each acceptor was given a full explanation on the pros and cons of the method. Their physical and pelvic examination were normal.

The follow-up visits after the implantation were scheduled for the first seven days, first month, third month, and sixth month. After that, it was then every six months.

Results

The characteristics of the acceptors are shown in Table1-4.

The oral combined pill was the most used of their previous contraceptive methods, 55.6%, while the condom was the least used, about 1.8%, as shown in Table 5.

As shown in Table 6, health personnel were the most important source of information on *Norplant* as they made 42% of the acceptors aware of the

Table 1 Age distribution of the acceptors

Age	Number	Percent
below 20	11	6.8
21 - 25	40	24.7
26 - 30	75	46.3
31 - 35	21	12.9
above 35	15	9.3
Total	162	100

Table 2 Parity

Parity	Number	Percent
1	62	38.3
2	74	45.7
3	22	13.6
4	2	1.2
5	2	1.2

Table 3 Incomes of acceptors, in Baht

Income	Number	Percent
Below 1000	5	3.1
1001 - 3000	68	42.0
3001 - 5000	47	29.0
5001 - 7000	20	12.3
7001 - 9000	9	5.6
Above 9000	13	8.0
Total	162	100

Table 4 Education

Level of education	Number	Percent
Illiteracy	13	8.0
Primary school	94	58.0
Secondary school	28	17.3
College	18	11.1
University	9	5.6
Total	162	100

Table 5 Previous contraceptive method

Contraceptive methods	Numbers	Percents
Oral pill	90	55.6
Injection	36	22.2
Intrauterine device	23	14.2
Condom	3	1.8
Nil	10	6.2
Total	162	100

Table 6 Sources of information on *Norplant*

Sources	Number	Percent
Health personnel	68	42.0
Cousins and friends	45	27.8
Mass media	31	19.1
Norplant acceptors	18	11.1
Total	162	100

system. On the other hand, 27.8% became informed through cousins or friends and 19.1% through mass media.

The complications and side effects of *Norplant* are shown in Table 7, 66.7% of the acceptors had no complications or

Table 7 Complications and side effects from norplant

Complications and side effects	Numbers	Percents
Nil	108	66.7
Irregular bleeding	36	22.2
Ecchymosis	9	5.5
Nausea/vomiting	4	2.5
Headache	3	1.9
Anorexia	1	0.6
Acne/chloasma	1	0.6
Total	162	100

side effects of *Norplant*. The most significant effect found was irregular bleeding(22.2%) while the least were acne and chloasma(0.6%).

It is obvious that 96.9% of the acceptors had followed-ups at seven days, then the rate declined. As a matter of fact, the rate at one year follow-up was only 54.32%(Table 8).

After being followed-up a period of one year, most acceptors had irregular bleeding (40.90%). The cyclic bleeding was found only 19.32% while the remainders were amenorrhea(Table 9).

Table 8 Follow-up rate

Time	Number	Rate (%)
First week	157	96.9
First month	114	70.4
Third month	98	60.5
Sixth month	82	50.6
Twelveth month	88	54.32

The continuation rate in the first year was high, as 99.38% continuing to use *Norplant*. There was only one case that removed it because her husband was vasectomized. No pregnancy was found during this one year period.

Table 9 Menstrual pattern

Menstrual pattern	Number	Percent
Irregular bleeding	36	40.90
Amenorrhea*	35	39.77
Cyclic bleeding	17	19.32

*> 3 months amenorrhea

Discussion

From this study, most acceptors were young, rather low socioeconomic level, and had 1 - 3 children. These acceptors are good candidates for *Norplant* since it could prolong the spacing, benefit the health of acceptors as well as remove a burden on their families and society. Moreover, it can last for five years.[1,2]

In considering previous contraceptive methods, this study found that oral combined pill was the most used and condom the least. Health personnel were the most important source of information

on *Norplant* as also found in other study.[1] In fact, they played an effective role in *Norplant* information and family planning.

There were no serious complications or side effects from *Norplant*. Irregular bleeding was the most found side effect which the same as other studies.[1-7] The complications and side effects, however, could be treated and explained to the acceptors.

Follow-up rate was high (96.9%) at the first seven days and then the rate declined. At six months, the follow-up rate was 50.6%, and only 54.32% at the end of the first year. Some reasons for the decline in follow-up rate were, firstly, some of the acceptors lived up-country, secondly, some of them had no complications or side effects, and lastly, some changed their addresses.

As for the study on menstrual pattern during one year follow-up, irregular bleeding was the first indication, followed by amenorrhea and cyclic bleeding. The result of this study was different from others. They found that regular bleeding was the pattern of menstruation for most.[2,8]

From the continuation rate, it was found that all acceptors, who were followed-up to the sixth month, continued to use it. As previously informed, at the end of the first year, there was just one case that removed it as her husband was vasectomized,thus, resulting in 99.38% continuation after one year from insertion. This was similar to the other study which found that the continuation rate within the first year was as high as 95.5%.[8] In comparison to other methods, the continuation rate within the first year was 68.2% for IUD and 60% for injection.[8] After one year follow-up, no pregnancy was found. This result was the same as the other studies.[1,2,8]

This study shows that *Norplant* is highly accepted and is suitable for the low socioeconomic acceptors who want to prolong spacing between children in 3-5 year intervals. It is highly effective with low complications and side effects, has a higher continuation rate than other methods, and low pregnancy rate.

From other studies, *Norplant* does not have an effect on liver function, lipid mtabolism and glucose metabolism.[9-11] Therefore, *Norplant* is one very good contraceptive method which can be used effectively in family planning programmes and should be distributed for use nationwide.

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AN INVITATION TO THE 13th ASIAN & OCEANIC CONGRESS OF OBSTETRICS & GYNAECOLOGY MEDICAL EXHIBITION

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Spontaneous Rupture of a Short Gastric Artery Following Low Forceps Delivery : Case Report

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Abstract: *A 29 years old primigravida at term with normal antenatal records was delivered of a baby by forceps extraction. Soon after delivery, she began intraabdominal hemorrhage. Exploratory laparotomy revealed rupture of a short gastric artery. The operation was complicated with blood clotting defects, hepatic subcapsular hematoma, pneumonia, and subacute bowel obstruction. She eventually recovered and was discharged on day 15 post delivery. Postpartum check including cardiovascular examination and oesophago-gastro-duodenoscopy revealed no abnormalities. (Thai J Obstet Gynaecol 1989;1:77-79)*

Key words: spontaneous rupture, short gastric artery, forceps delivery

Spontaneous intraabdominal hemorrhage during pregnancy is a life threatening complication with significant maternal morbidity and mortality. It requires prompt diagnosis and treatment. This report is an exremely unusual case of intraabdominal hemorrhage caused by rupture of the short gastric artery after low forceps delivery.

Case report

A 29 years old (Mrs. P.T.) primigravida at term was admitted to delivery suite with early signs of labour. Blood pressure was 130/80 mmHg. Pulse rate was 80/min regular. There was no history of high blood pressure, proteinuria or edema throughout the antenatal period. The baby was in a cephalic presentation and was engaged. The fetal heart sound was regular. Labour was augmented by artificial rupture of the membranes followed by a syntocinon infusion via a pump. She was given epidural analgesia. After $1\frac{1}{2}$ hours of second stage she required Neville-Barnes forceps delivery because of maternal exhaustion. At this stage the blood pressure was noted to be 140/90 mmHg.

Three hours later she was found to be shocked with symptoms and signs of

intraabdominal hemorrhage. Emergency exploratory laparotomy was performed. There was approximately 1500 ml of blood in the peritoneal cavity. The pelvic organs appeared normal. There was no evidence of bleeding from the uterus, tubes, ovaries and broad ligament. The liver, gall blaedder, spleen, bowels and omentum also appeared normal. A small arterial bleeder was finally found at the fundus of the stomach. This was suture ligated. No pathological lesion was detected macroscopically apart from the bleeding artery. A redivac drain was inserted. The abdomen was then closed.

She was given 14 units of blood, 7 units of plasma and 6 units of platelets. Her condition during the operation was satisfactory.

Unfortunately,4 hours later, she developed shortness of breath and hypoxemia. There was also further evidence of intraperitoneal hemorrhage. Blood coagulation profile showed normal platelets but slighty prolonged APTT and prothrombin ratio.

A second exploratory laparotomy was performed. There was a moderate quantity of blood within the peritoneal cavity with some pooling in the left upper quadrant. There was a large hematoma adherent to the anterior surface of the left lobe of liver and to the left of the falciform ligament. This was representing a subcapsular hematoma with capsular disruption and subsequent bleeding. This area was initially left undisturbed while the region of previous blood loss high on gastric fundus was inspected and found to be secure. There was a small amount of venous bleeding from a small vein in relation to the tail of the pancreas which was controlled by oversewing. There was no significant bleeding from this region. The slpeen and other abdominal organs were again noted to be normal. The hematoma was cleared from the left lobe of the liver and there was a considerable ooze from its raw surface. This was controlled by moist packing and subsequently by onlay application of SURGICEL soaked in topical thrombin and supplemented by an omental wrap.

Hemostasis appeared satisfactory. The abdomen was thoroughly lavaged. A sump-drain was left in the left upper quandrant. The abdomen was then closed. During the operation the blood pressure had risen to 190/115 mmHg. This was controlled with hydralazine intravenously.

Postoperative recovery was complicated with pneumonia and subacute bowel obstruction which eventually settled. Her coagulation profile subsequently returned to normal.

She was given captopril to control blood pressure and was discharged home on day 15 post deivery. She was asked to continue captopril for 10 days.

At 6 weeks postpartum check-up her cardiovascular exmination was unremarkable. Her blood pressure was 115/80 mmHg standing and 120/70 mmHg lying, and her fundi showed no signs of hypertension. The surgical wound was satisfactory. Pelvic examination was normal. She was on the minipill for contraception.

Oesophago-gastro-duodenoscopy revealed no abnormality either in mucosa

or vascular pattern.

Discussion

Intraabdominal hemorrhage in pregnancy, particularly in association with labour and delivery, is usually caused by rupture of the uterus. Nevertheless, there are a few reports of ruptured aneurysms of the splenic, renal and middle colic arteries[1-4]. Spontaneous bleeding from utero-ovarian veins[5-6] and hepatic subcapsular hemorrhage have also been described[7].

During pregnancy the arterial walls are altered in biochemical composition and morphological structure which, in some way, affect the dynamics of circulation[8]. This patient had gestational hypertension which is likely to worsen the above condition.

Splenic artery aneurysm is the second most common aneurysm next to abdominal aortic aneurysm. Anatomically, the blood supply at fundus of the stomach comes from short gastric arteries which are branches of the splenic artery. Therefore, it is possible that the ruptured short gastric artery may have contained a microaneurysm although the main splenic artery did appear normal. Unfortunately we do not have proven histology. Hepatic subcapsular hemorrhage in this patient is probably secondary to blood clotting defects after a massive blood transfusion from the first operation.

In summary, gestational alterations in the arterial wall due to hormonal and local hemodynamic events in combination with stress and strain in labour may be the cause of ruptured short gastric artery in this patient.

To the best of our knowledge, this is the first case of ruptured short gastric artery in pregnancy.

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