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Effectiveness of phenol-atabrine-paste (PAP) instillation for female sterilization

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Abstract

Two groups of sterilized women, 3307 by phenol-atabrine-paste (PAP) instillation and 1026 by mini-lap technique, were follow-up interviewed to determine their relative effectiveness. PAP, if successfully performed, was as effective as the mini-lap. The life table pregnancy rates among successful PAP women were 0.21 and 0.28 at I2 and 24 months, respectively. The rates among the unsuccessful PAP women, however, were high: 15.1 and 30.5 at I2 and 24 months, respectively. In spite of its distinctive advantage of being non-surgical, wider promotion of PAP sterilization procedure deserves caution.

Keywoids: Female sterilization; Chemical sterilization; Contraceptive effectiveness; Follow-up study; Phenol-atabrine-paste (PAP).

Introduction

Fear of "operation" by people has been identified as a major deterrent to a wider acceptance of sterilization. Non-surgical methods of sterilization with instillation of phenol-atabrine-paste (PAP) for causing tubal occlusion, therefore, is meeting with increasing acceptance, especially in China.

A number of Chinese investigators have reported the PAP female sterilization technique to be acceptable, safe, and effective [1—4,7—10]. For example, Wu and his associates reported the success rate in locating the tubal orifice and blocking the tube with PAP to be 93% of the total of 1837 cases studied [18]. Wan reported a slightly tower tubal blocking success rate of 90.48% of the total of 2079 tubes studied [15].

The concentration of atabrine in the paste used for sterilization may affect the safety and efficacy of these procedures. Wu and his associates, in a study carried out in Shanghai during 1972-1974, noted that 853 of 1708 women (50%) experienced fever within 10 days after the instillation of PAP with 35 g of atabrine in 100 g of paste. When atabrine was eliminated from the paste, the febrile reaction occurred only in 89 of 1504 women (5.6%), but the failure rate increased from 0.59% when 35 g of atabrine were used to 3.66% when no atabrine was used. With 17.5 g of atabrine in the paste, 34 of 173 women (19.7%) developed fever and only one pregnancy occurred.

In discussing the effectiveness of the PAP procedure, the Chinese investigators frequently ignored the fact that for more than

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10% of the cases, instillation of PAP will not be successful when pregnancy rate is high.

In this article we examine the pregnancy rates among women with both successful and unsuccessful PAP procedure using the life-table technique and discuss the implications.

Methods

A retrospective comparative study was undertaken in 1984 in Beijing, People's Republic of China (PRC). A total of 4000 women sterilized with PAP and 1300 women with the conventional mini-lap procedure were identified for the follow-up study. These women were sterilized by the OEG specialists of two teaching hospitals of the Beijing Medical University — the First Affiliated Hospital and the Renming Hospital — between June 1958 and November 1984.

The procedures were performed either at the clinics of these two teaching hospitals or of two county hospitals located in the suburbs of Beijing, namely, The Chang-ping County Hospital and the Fang-shan County Hospital. The cases were identified from the medical records kept at these hospitals. Most of these women lived in an urban district of Xi-cheng or in the suburban counties of Chang-ping and Fang-shan in the Beijing metropolitan area.

These women were married, 20-49 years old, and had at least one living child when sterilized.

The procedures were performed during the first half of the women's menstrual cycle, either 4 months after delivery, 1 month after first trimester abortion, or 4 months after mid-trimester abortion. Some procedures were performed during lactation, and still some others shortly after removal of an **IUD.**

The PAP used in this study was prepared by the pharmaceutical company in Shanghai and contained'l7.5 g of atabrine, 30 g of phenol, 35 g of biligraphine, 3.5 g of gum tragacanth, and some distilled water in 100 g of paste. An abdominal X-ray was taken immediately after the instillation and a linear tubal shadow of more than 2 cm in length was considered a success. The instillation of PAP followed, in general, the procedures as described by Wu et al. 18]. The minilaparotomy sterilization technique, known as mini-lap, was the most popular method before the PAP technique was introduced.

The women identified for the study were asked to return to the hospitals where sterilizations were performed for gynecological examinations by two OBG doctors and interviews by seven senior female public health students of the Beijing Medical University. All members of the study team, including the OBG doctors and the interviewers, were given 3 days of training. Special attention was paid to improve their interview skills, especially to increase their awareness of various types and sources of bias in interview and the skills and techniques to minimize such bias. The field work started in December 1984 was completed by July 1986.

The questionnaire for the study, designed by Dr. B. Peterson of the Centers for Disease Control in Atlanta, Georgia, was pretested before finalizing. A set of computer diskettes containing the data collected from the study was brought to The Johns Hopkins University for analysis.

Results

Characteristics of study subjects

A total of 3307 PAP and 1026 mini-lap women in the sample were successfully follow-up interviewed. The mini-lap women were slightly older, had somewhat higher levels of education, and more of them lived in urban areas than the PAP group of women. The average age of PAP women was 32.4 years, most of whom (74.8%) had primary education, and 84.9% of whom lived in rural areas. For the mini-lap group, the modal level of education was junior high school (35.5%), and 46.7% of them lived in urban areas.

The mini-lap women had had an average of 3.7 pregnancies and 2.35 live births compared

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Table I. Selected characteristics of study subjects by type of procedures.

	PAP		Mini-lap	
	No.	%	NO.	%
All women	3307	100.0	1026	100.0
Age groups				
20-29	638	19.3	240	23.4
30-34	1799	54.4	442	43.1
35-39	771	23.3	284	27.7
40 +	97	2.9	54	5.3
Unknown	2	0.1	6	0.5
Mean age (SD)	32.4 (3.5)		32.7 (4.2)	
No. of years since procedures				
Less then 1	17	0.5	70	6.8
1 - 2	319	9.6	300	29.3
2 - 3	1254	37.9	9	0.9
3—4	1049	31.7	36	3.5
4 - 5	45	1.4	27	2.6
5 +	623	18.8	583	56.9
Mean (S.D.)	3.3 (1.5)		6.9 (5.7)	
Range	0.4—11.1		0.5—28.1	
No. of pregnancy				
Mean (SD)	3.2 (1.2)		3.7 (1.4)	
No. of live births				
Mean (SD)	2.44 (0.8)		2.35 (1.1)	

with an average of 3.2 pregnancies and 2.44 live births by the PAP women.

Because the PAP technique was introduced relatively recently, the mini-lap group had a longer duration of observation than the PAP group. It averaged 6.89 years for mini-lap and 3.34 years for the PAP group of women (Table I).

Most PAP sterilizations were performed shortly after menstruation (80.8%), with 19.2% of them done during lactation. There was one post-abortion PAP sterilization in

Table II. **Success** or non-success of PAP procedures by the timing of sterilization. Significance between success and **non-success** (sub-total) by the timing of sterilization: $\chi^2 = 117.705$; ***P = 0.0000.***

	Success (%)	Non-success (%)			Total
		< 2 cm	Other	Sub-total	
After menses	2438 (91.3)	39 (1.5)	194 (7.2)	233 (8.7)	2671 (100.0)
Lactation	482 (75.9)	16 (2.5)	137 (21.6)	153 (24.1)	635 (100.0)
After abortion	1	0	0	0	1
Total	2921 (88.3)	55 (1.7)	331 (10.0)	386 (11.7)	3307 (100.0)

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Table III. Pregnancy rates per 100 woman-years by type of procedures. S = success; US = unsuccessful; T = total.

Months since opera ion	No. pregnancy				Woman-years of observation				Pregnancy rate per 100 women years			
	Mini-lap	PAP			Mini-lap	PAP			Mini-lap	PAP		
		S	US	T		S	US	T		S	US	T
0—11	3	6	58	64	12057	35000	4323	39323	0.922	0.206	16.099	1.953
12—23	0	2	58	60	9445	34250	3511	37761	0.000	0.070	19.823	1.907
24—35	0	4	22	26	7803	23320	2079	25399	0.000	0.206	12.698	1.024
36—47	0	0	2	2	7596	11329	733	12062	0.000	0.000	3.274	0.199
48—59	2	0	1	1	7115	7418	297	7715	0.337	0.000	4.040	0.155
60—71	0	1	1	2	6758	6002	221	6223	0.000	0.200	5.430	0.386
72 +	0	0	0	0	22155	2502	88	2590	0.000	0.000	0.000	0.000
Total	5	13	142	55	72929	119821	11252	131073	0.082	0.130	15.144	1.419

the study. However, more mini-iap sterilizations were performed after abortion (43.7%), followed by post-menstrual sterilization (33.7%) and sterilization during lactation (22.6%).

Success or non-success of PAP procedure

For the mini-lap technique, unsuccessful experience is rare; however, PAP is a blind procedure, success of which depends entirely on the experience and skill of the operator. Inability to locate the tubal orifice, or pushing the plastic tube through the uterine or tubal wail may occur. Examination of success rate, therefore, has a significant implication for PAP sterilization. As previously described, an abdominal X-ray taken immediately following PAP instillation showing a linear tubal shadow of longer than 2 cm on both tubes is considered a "success".

Review of the medical records indicated that the PAP procedure had an overall success rate of 88.3 % among the current study subjects. The success rate was significantly higher when the PAP procedure was performed after menstruation (91.3%) than when it was done during lactation (75.9%).

In spite of the fact that the PAP procedure was performed by highly skilled OBG specialists of two teaching hospitals of a medical school, nearly 12% of them were unsuccessful, and this should be a cause for concern. The unsuccessful rate was especially high (24.1 %) when PAP was performed during lactation (Table II).

***The failure rates of* PAP procedure**

Of 3307 women sterilized with PAP procedure, 155 had become pregnant, the "failure rate" being 4.7% . The failures were only 13 out of 2921 (0.4%) among the "successful" PAP, but were 142 out of 386 (36.8%) among the "unsuccessful" cases. The failure rate of 0.4% for "successful PAP" compared favorably with the rate for the mini-lap, which was 5 pregnancies out of 1026, or 0.5 %.

Pregnancy rate per 100 woman-years (Pearl index.)

Table III shows the total woman-years of observation, the number of pregnancies that occurred, and the pregnancy rate per 100 woman-years (Pearl index) with the PAP and the mini-lap procedures by successive observational periods.

Overall, the pregnancy rate was 0.082 for the mini-lap and 1.42 for ail PAP, combining both the "successful" and "unsuccessful" cases. The rates for PAP were especially high during the first (1.95) and the second years (1.91). When the "successful" PAP alone is considered, the pregnancy rate was 0.13 over-

Tnbk IV. **Life table cumulative pregnancy rate per 100 women.**

Months of observation	Cumulative pregnancy rate per 100 women (SE)						
	Mini-lap	All PAP	P*	Successful PAP	P**	Unsuccessful PAP	P***
12	0.3 1(0.2)	1.94(0.2)	< 0.05	0.21(0.1)	> 0.05	15.06(1.8)	< 0.01
24	0.3 1(0.2)	3.79(0.3)	< 0.01	0.28(0.1)	> 0.05	30.47(2.4)	< 0.01
36	0.31(0.2)	4.92(0.4)	< 0.01	0.49(0.1)	> 0.05	38.34(2.6)	< 0.01
48	0.31(0.2)	5.05(0.4)	< 0.01	0.49(0.1)	> 0.0s	39.41(2.7)	< 0.01
60	0.63(0.2)	5.21(0.4)	< 0.01	0.49(0.1)	> 0.05	41.93(3.6)	< 0.01
72	0.63(0.2)	5.53(0.5)	< 0.01	0.67(0.2)	> 0.05	44.57(4.3)	< 0.01

*Significance between mini-lap and all PAP.
● %gnificance between mini-lap and successful PAP.
***Significance between successful PAP and unsuccessful PAP.

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Table V. Life table cumulative pregnancy rate per 100 women by characteristics of women.

	All PAP				Unsuccessful PAP			
	Months of observation				Months of observation			
	12	24	48	72	12	24	48	72
Age (years)								
20-29	2.08(0.5)	3.13(0.6)	4.39(0.7)	4.79(0.9)	17.74(3.9)	27.26(4.6)	36.99(5.5)	41.66(6.8)
30-34	1.84(0.3)	4.12(0.5)	5.11(0.6)	5.78(0.7)	13.99(2.4)	32.27(3.2)	38.95(3.6)	45.05(6.6)
35 +	2.05(0.6)	3.82(0.8)	5.79(1.0)	5.79(1.0)	14.67(4.1)	29.51(5.3)	43.40(6.2)	43.60(4.2)
No. of live birth								
< 2	0.92(0.2)	1.66(0.3)	2.75(0.4)	2.97(0.5)	8.85(2.1)	16.27(2.7)	25.37(3.6)	25.37(3.6)
> 3	0.92(0.3)	1.74(0.4)	3.07(0.6)	3.86(0.8)	6.99(2.5)	15.12(3.6)	25.17(4.8)	35.53(8.0)
Women's education								
< Primary	0.95(0.2)	1.80(0.3)	2.95(0.4)	3.48(0.5)	8.33(1.7)	16.02(2.3)	24.00(2.9)	30.83(5.3)
> Secondary	0.56(0.3)	0.94(0.4)	2.18(0.7)	2.57(0.9)	7.14(4.9)	14.29(6.6)	55.32(17.3)	55.32(17.3)
Women's physiologic status								
After menses	1.54(0.2)*	2.49(0.3)*	3.53(0.4)*	4.12(0.5)*	15.47(2.4)	26.04(2.9)	36.57(3.5)	45.49(6.6)
Lactation period	3.64(0.7)*	9.27(1.2)*	11.42(1.3)*	11.42(1.3)*	14.43(2.8)	37.22(4.0)	43.73(4.3)	43.47(4.3)

*Differences between rates of two categories at specified time point is significant at 5% level ($P < 0.05$). All other categorical differences in this table are not significant.

all, which is slightly higher than the rate for mini-lap (0.082).

Among the "unsuccessful" PAP, however, the pregnancy rate was high, being 15.14 overall. The rate was especially high during the second year, being 19.8. The first year pregnancy rate among those "unsuccessful" PAP was somewhat lower, being 16.1, and this probably was due to some overlap with postpartum amenorrhea and, perhaps, less sexual activity during the first few months after PAP instillation.

It would have been most interesting if it were possible to analyze the pregnancy rates by the length of tubal X-ray,.e.g. longer than 2 cm, l-2 cm, and shorter than 1 cm. Unfortunately, such information was not recorded.

Life table pregnancy rates

The cumulative pregnancy rates calculated with the life table technique are presented in Table IV. Overall, the PAP women became pregnant more rapidly than the mini-lap women. At 12 months the cumulative pregnancy rate was 1.94% for all PAP compared with only 0.31% for the mini-lap group. The difference is statistically significant ($P < 0.05$).

The cumulative pregnancy rates were consistently and significantly higher among all PAP than the mini-lap group of women *($P < 0.01$).*

When the successful PAP alone is considered, the pregnancy rates were 0.21 and 0.28 at 12 and 24 months, respectively. These rates were slightly lower than the corresponding rates for mini-lap. The rates became slightly higher after the third year but the differences, however, are not statistically significant *($P > 0.05$).* PAP is as effective as mini-lap if it is successfully performed. Among the unsuccessful cases the cumulative pregnancy rates were high: 15.06 at 12 months, 30.47 at 24 months, and 44.57% at 72 months.

Pregnancy rates by characteristics of women

The cumulative pregnancy rates among PAP women did not differ significantly by characteristics of women such as age, education, and number of live births. This is true for both the successful and unsuccessful PAP cases. However, the pregnancy rates among all PAP women were significantly higher when the procedure was performed during the lactational period. Among the unsuccessful cases, the differences by these characteristics are generally not significant (Table V).

Outcome of and contraceptive practice follo wing accidental pregnancies

There were a total of 160 accidental pregnancies reported by both groups: 155 from the PAP and 5 from the mini-lap. Of these, 128 or 80% of the-total were aborted but 23 or 14.4% of the total ended in term live births. There were two ectopic pregnancies, one from PAP and one from mini-lap group, one suspected ectopic pregnancy, one still birth, four miscarriages, and one pregnancy of "unknown" outcome.

After the termination of accidental pregnancies, 60 women (37.5%) had IUD inserted, 53 (33.1 %) started using oral contraceptives, and 18 (11.3 %) repeated the sterilization procedures — 17 PAP and 1 mini-lap. Husbands of seven women (4.4%) used condoms, and 14 (8.7%) women were not using any method. The contraceptive status of the remainder was "unknown".

Discussion

Although current surgical female sterilization procedures are relatively simple and safe, they are still viewed as a form of "operation". The fear of operation by women, especially those less educated in the developing countries, is considered a major deterrant to wider acceptance of sterilization. Non-surgical methods of sterilization, therefore seem to offer much promise for wider acceptance and could have a significant impact on the global family planning programs [11].

The attempt to block the tubes with chemicals for the purpose of sterilization dates back

to as early as 1949 [6]. However, wider clinical application of non-surgical procedures for sterilization owes its advocacy to the pioneering work of Zipper and associates who used quinacrine hydrochloride for effecting permanent blocking of the tubes [19]. At the present time the effectiveness and safety of three chemical agents are being more actively pursued in clinical trials: quinarcine, phenol, and methyl cyanoacrylate [18].

Wu and associates in Shanghai, People's Republic of China, have studied the pharmacological actions of some 11 chemicals on the mucosa of the tubes of animals and humans since 1979 and, as a result, have determined phenol-atabrine-paste (PAP) to be the most promising for the purpose of non-surgical sterilization. They have conducted clinical trials to determine the effectiveness of PAP procedure since 1972 and reported generally favorable results [18].

Various Chinese investigators have also reported their experience with the use of the PAP technique of female sterilization. Their reported "success rates" vary from some 72.7% [1] to 96.2% [3]. The rather large difference in "success rates" is partly due to the different criteria used to determine "success." Generally speaking, a successful PAP procedure means correctly identifying the orifice of the tube and instillating the prescribed quantity of PAP into the tube to cause blockage of a certain length of the tube, as evidenced by an X-ray shadow. Some investigators considered_ the length of tubal shadow of longer than 2 cm to be a "success" while some others were satisfied with a length of 1 cm. The denominator for calculating the success rates also varies: either success rate per number of women (blocking both tubes), or per number of tubes instillated.

Most investigators now consider a tubal shadow of longer than 2 cm of both tubes with one single PAP instillation as a "success" and these are the criteria adopted by this study. It would have been most interesting if it were possible to analyze the pregnancy rates by different "success" criteria, e.g., the length of tubal X-ray shadow of longer than 2 cm, 1-2 cm, and shorter than 1 cm. Unfortunately, such information was not available on the medical records. Future investigators should make certain to enter such information on the medical records.

Few Chinese investigators have reported the effectiveness of PAP as measured by the Pearl pregnancy rate and still fewer have used the life table technique to study its effectiveness. Moreover, most of the studies on PAP female sterilization in China were conducted by the clinicians following up their own clients and often at their own clinics. Non-response rates in such studies were usually high and there is a possibility of investigator's bias [9].

The results of this study indicated that the PAP procedure is as effective as the mini-lap method if it is successfully performed. The Pearl index of 0.13 per 100 woman-years with PAP compared nearly equally with the rate of 0.085 per 100 woman-years for the mini-Iap.

Unfortunately, for nearly 1 out of every 8 cases (11.7%) the PAP procedure will not be successfully performed. The failure rate was especially high when PAP was performed during lactation: nearly 1 out of every 4 cases (24.1%) failed. The life table cumulative pregnancy rate among those unsuccessful PAP women was high: 15.1 at I2 months, 30.5 at 24 months, and 44.6 at 72 months, all per 100 women. The fertility rate of married women 30-34 years old in the study areas during 1982-1983 was about 40 per 1000 (or 4 per 100) [17]. The pregnancy rate of 15.1 at 12 months is extremely high, suggesting that unsuccessful PAP procedure gave women a false sense of security. This raises an important ethical question of sending these "unsuccessful" PAP women home to get pregnant. They should have been sterilized with the conventional mini-lap technique, or if they refuse, should be warned of the risk of accidental pregnancy, then be given appropriate protection such as IUD insertion or use of oral and other effective contraceptive methods to prevent unwanted pregnancies.

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Including both the successful and unsuccessful cases, the overall pregnancy rates of PAP women were 1.94 at 12 months and 3.79 at 24 months, compared with 0.31 at 12 and 24 months for the mini-lap women. The pregnancy rates of PAP appear to be somewhat higher than those of the improved IUDs such as TCu-380Ag [12].

Reversal of PAP sterilization will be more difficult than the surgical sterilization procedures because of severe tissue damage on a longer portion of tube.

There are significant advantages of the PAP method over the surgical techniques of female sterilization. Nevertheless, based on the above findings, wider promotion of the PAP procedure deserves careful consideration.

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