

NONSURGICAL FEMALE STERILIZATION WITH QUINACRINE PELLETS : MALAYSIAN EXPERIENCE*

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Introduction

Transcervical delivery of various chemical compounds have been studied as a means of nonsurgical female sterilization. Such a method is needed, especially for developing country programs where safety and effectiveness should be coupled with ease of delivery of the method. Chemicals that have been and are still being tested include silver nitrate, ethanol, formalin, phenolmucilage, methylcynoacrylate, quinacrine and tetracyaline.

In 1980, Zipper and co-workers demonstrated the effectiveness of transcervical quinacrine pellet method for nonsurgical female sterilization (1). The method utilizes an intrauterine device inserter to deposit 250mg of quinacrine hydrochloride as pellets in the uterine cavity. The quinacrine produces inflammation and fibrosis that is confined primarily to the intramural portion of the fallopian tube.

Some 5 years later, in a review on the safety and efficacy of Quinacrine nonsurgical female sterilization, Kessel et. al. (2) concluded that the quinacrine pellet method is quite safe and no complications or side-effects, other than temporary pain and oligomenorrhoea have been reported. However they called for greater experience to ensure that rare, serious complications do not occur.

In 1985, the National Population and Family Development Board (NPFDB), Malaysia, initiated a small study to evaluate this method of female sterilization. The study was contracted through the International Federation of Family Health (IFFH) with funding by the International Development Research Center (IDRC). Indonesia also participated in a **similar** study.

The overall objectives of the study were to evaluate the effectiveness of intrauterine quinacrine pellet application as a method of female sterilization on the basis of one year follow-up; and to evaluate the safety, cost, acceptability and ease of administration of this procedure. One hundred women were to be recruited for the study.

Subjects and methods

Women requesting female sterilization were selected for the study after appropriate screening and counseling according to the study protocol. Only those with regular menstrual cycles (28-35 days) and normal Papanicolaou smears were included. Three insertions at monthly intervals were administered during the proliferative phase of the women's, menstrual cycle. At each insertion 7 pellets of quinacrine hydrochloride or in total 250mg quinacrine hydrochloride were delivered transcervically using the standard

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Copper T inserter. After the 3rd insertion, follow-up visits were scheduled at 1, 3, 6 and 12 months.

Data was recorded in the data reporting form for all cases at each visit; including unscheduled visits for complaints and follow-up.

Three centers in Peninsular Malaysia were chosen to participate in this study, Kuala Lumpur in the Central region, Ipoh for the Northern region and Johor Bahru in the Southern region.

The study commenced in July 1985 following a two-day training program. The physicians and other research team staff discussed in detail various aspects of the study with 2 consultants appointed by IFFH for the study.

Results

Number of cases recruited

Up to September 1986 (14 months recruitment period), 25 cases were

recruited for the study from the Kuala Lumpur center. Two-thirds of the cases were recruited in the last 6 months of this period. Efforts to intensify recruitment via increased motivation activities at all family planning clinics in the Klang Valley serving Kuala Lumpur and publicity in the news media were unsuccessful.

The centers in Ipoh and Johor Bahru did not start the study for varying (administrative) reasons.

Profile of acceptors

Of the 25 acceptors, 60% were from urban residence.

There was a preponderance of Indian women (48%) compared to the Chinese and Malay women (28% and 20% respectively) as can be seen in Table I.

TABLE I
DISTRIBUTION OF ACCEPTORS BY ETHNIC GROUP
(N = 25)

CHARACTERISTIC	FREQUENCY	PERCENTAGE
Ethnic Group		
Malay	5	20
Chinese	7	28
Indian	12	48
Others	1	4
Total	25	100

Only one-fifth of the women were breastfeeding their children at the time **they were** recruited for the study.

The age of acceptors ranged from 25 to 41 years with a mean age of 33.4 years. More than one-third of the acceptors were between 36 —40 years of age. The number of livebirths recorded from the acceptors range from 2 to 9 children with a mean of 4.4 children (Table II).

Insertion procedure

Insertion was easy in all except 2 cases. In the first case insertion was difficult due to a tight cervical os and a small posterior fibroid. The second woman had giddiness, probably due to vaso-vagal reflex. Both cases nevertheless completed their 3 insertions.

Follow-up rate

The follow-up rate was good with on-

TABLE II
DISTRIBUTION OF ACCEPTORS BY AGE AND TOTAL
LIVEBIRTHS (N = 25)

AGE (YEARS)	TOTAL LIVEBIRTHS								TOTAL	
	2-3		4-5		6-7		8+		N	%
	N	%	N	%	N	%	N	%	N	%
21-25	-	-	-	-	1	4	-	-	1	4
26-30	1	4	5	20	1	4	-	-	1	28
31-35	4	16	3	12	-	-	-	-	1	20
36-40	4	16	1	4	2	8	2	8	9	36
41-45	-	-	1	4	-	-	-	-	1	4
TOTAL	9	36	10	40	4	16	2	8	25	100

With regard to education level (Table III), most acceptors had an average of 6 years of schooling and none have had tertiary education. The husbands of these acceptors however attained slightly higher educational standards (mean 7.8 years) while one-third had completed higher secondary (7 — 9 years).

An examination of the last main method of contraception used showed an even percentage of 24% having used the condoms, oral pills and intrauterine devices. 20% had not used any method at all, whereas the injectable and rhythm method were used by one acceptor (4%) each.

ly one case defaulting the scheduled visits. She defaulted after the first insertion, recalled back 8 months later through home-visiting but subsequently defaulted again after the 3rd insertion.

Fifteen cases completed the one-year follow-up visits at the time of this **report**.

Terminations

There were 2 cases of terminations. Both occurred while still in the insertion phase of the study. One acceptor was removed from the study after the 2nd insertion because of complaints of persistent low pelvic pain. No obvious

Quinacrine nonsurgical female sterilization

TABLE III
DISTRIBUTION OF ACCEPTORS BY EDUCATION OF
WIFE AND HUSBAND (N = 25)

EDUCATION (YEARS)	WIFE		HUSBAND	
	N	%	N	%
0	3	12	2	8
1- 6	11	44	8	32
7- 9	8	32	6	24
10-12	3	12	8	32
13-16			1	4
TOTAL	25	100	25	100

abnormality however was detected even at laparoscopy which was carried out after vaginal and intracervical cultures were shown to be negative. The other subject was excluded from the study due to pregnancy.

Pregnancy

There was one pregnancy (intrauterine) which occurred between

the first and second insertion of the quinacrine pellets. This was in a 32-year old Indian lady who had had 5 livebirths. The pregnancy was terminated by dilatation and curettage and laparoscopic tubal ligation was performed during the same procedure.

Side-Effects and complications

For the purpose of this study, Amenorrhea is defined as no menstrual period on the expected date. Amenorrhea was reported in 20% of cases after the first insertion and increased to 25% at 1st follow-up at 1 month. Thereafter the incidence declined and did not become a problem from the 3rd follow-up visit (Table V).

Complaints of *scanty menstrual periods* which was not frequent between insertions of the quinacrine pellets became progressively more common in the follow-up period (Table VI).

On the other hand excessive amount of menstrual flow was reported in the

TABLE IV
DISTRIBUTION OF ACCEPTORS BY
PREVIOUS CONTRACEPTION USED
(N = 25)

METHOD	N	%
Condoms	6	24
Oral Pills	6	24
Intrauterine Device	6	24
Injectables	1	4
Rhythm	1	4
Nil	5	20
Total	25	100

TABLE V
AMENORRHEA ASSOCIATED WITH INSERTION OF QUINACRINE
PELLET

TIMING	INCIDENCE OF AMENORRHEA	
	N	%
At insertion I (N = 25)		
At insertion II (N = 25)	5	20.0
At insertion III (N = 25)	6	25.0
At follow-up :		
1 month (N = 20)	5	25.0
3 months (N = 20)	2	10.0
6 months (N = 20)	0	0
12 months (N = 15)	0	0

TABLE VI
SCANTY MENSTRUAL PERIOD ASSOCIATED
WITH INSERTION OF QUINACRINE PELLET

TIMING	INCIDENCE	
	N	%
At insertion I (N = 25)	3	12.0
At insertion II (N = 25)	2	8.0
At insertion III (N = 24)	1	4.2
At follow-up :		
1 month (N = 20)	1	5.0
3 months (N = 20)	3	15.0
6 months (N = 20)	3	15.0
12 months (N = 15)	4	26.7

period **between insertions but did not** become a problem subsequently. Two of these cases required treatment.

Intermenstrual bleeding was not a problem in this study.

The mean duration of 'flow **at admission** was 49 days and this became

shorter **by almost half a day over the** next one year period. The difference was not statistically significant (Table VII).

Menstrual cycle length did not vary significantly throughout the study (Table VIII).

TABLE VII
MEAN DURATION OF MENSTRUAL ROW AFTER
QUINACRINE PELLETT INSERTION (N = 25)

QUINACRINE	MEAN DURATION OF FLOW (DAYS)		
1st Insertion	4.9	±	1.5
2nd Insertion	4.6	f	1.4
3rd Insertion	4.4	f	1.2
Follow-up :			
1 month	4.2	±	0.9
3 months	4.4	±	1.5
6 months	4.1	±	1.4
12 months	4.5	±	1.8

TABLE VIII
MEAN LENGTH OF MENSTRUAL CYCLE AFTER
QUINACRINE PELLETT INSERTIONS (N = 25)

QUINACRINE	MEAN LENGTH OF CYCLE (DAYS)		
- Insertion I	29.9	±	2.8
- Insertion II	31.6	±	4.1
- Insertion III	30.6	±	3.4
Follow-up :			
- 1 month	31.3	f	2.3
- 3 months	29.7	±	3.2
- 6 months	30.8	f	4.2
- 12 months	30.2	f	4.0

Complaints of genito-urinary nature was found more frequently in the period between insertions than at the follow-ups (Tables IX). However these complaints were transient in nature and most subsided with conservative treatment. Intensive counseling played an important role during this period. However one patient was diagnosed as having pelvic inflammatory disease 5 months after completing 3 quinacrine insertions. She responded well to antibiotic treatment.

Other general complaints included headaches, chills, fever, pain in the limbs, especially the left leg, and abdominal cramp in 4 to 12% of the acceptors in the period between insertions. One subject complained of occasional headaches in the follow-up visits up to the one-year period. Treatment was usually symptomatic if at all any was given. Subjects were otherwise counseled.

Two cases complained of tinnitus during the study period. One acceptor had the problem some 5 months after insertion. An ENT (Ear, Nose, Throat)

assessment demonstrated hyperacusis an hearing defect. However the symptoms and signs resolved spontaneously 3 months later. The other subject was thought by the ENT specialist to have a deviated nasal septum resulting in her tinnitus. In both cases the expert opinion was that the complaints were unlikely to be due to or associated with the quinacrine administered.

Discussion

In this Malaysian study acceptability appeared to be the main problem towards establishing quinacrine insertion as a nonsurgical female sterilization method for contraception. A number of eligible clients declined to be included in the study when informed that the effectiveness is lower than the other (surgical) method currently available. Also another sterilization study being conducted at the same center was drawing away some of the women seeking permanent contraception. Nevertheless the acceptors included those women with lower education, older age and high parity who therefore would benefit most from this method of sterilization.

TABLE IX A
GENITO-URINARY COMPLAINTS IN THE PERIODS
BETWEEN QUINACRINE PELLET INSERTION

COMPLAINTS	INSERTION I		INSERTION II		INSERTION III	
	N	%	N	%	N	%
Pain in vaginal area			2	8.0	-	-
Vaginal pruritus				-	1	4.1
Leucorrhoea •					3	12.3
Non-specific vaginitis			1	4.0		
Painful micturition			3	1-2.0		-

• Note : Two patients complained of vaginal discharge and mild vaginal itching.

TABLE IX B
GENITO-URINARY COMPLAINTS IN THE FOLLOW UP
PERIOD AFTER QUINACRINE PELLETT INSERTION

COMPLAINTS	FOLLOW UP •					
	1st		2nd		3rd	
	N	%	N	%	N	%
Trichomonas vaginitis	1	5.0				
Non-specific vaginitis	-	-	1	5.0		
Non-specific cervicitis	-	-	1	5.0		
Leucorrhea			1	5.0		
Pruritus vulvae			1	5.0		
Pelvic Inflammatory Disease					1	5.0

• Note : No complaints were noted at the 4th Follow-up visit.

Only one failure was noted in the insertion period. This event could have been prevented if study cases were allowed to use a conventional method like the condoms to protect them during the intervening period up till after the third insertion. No pregnancies were reported in the one-year follow-up period. However continual follow-up is mandatory considering that pregnancies may occur years later. The study by Zipper et. al. (1) showed a pregnancy rate at 1 year after the 3rd insertion to be 3.1 while Guzman — Serani (3) reported a pregnancy rate of 1.5 to 2 per 100 women per year in a 3-year follow-up study. In a four-year follow-up study on Quinacrine Sterilization, Bhatt and Waszak (4) found a cumulative life-table pregnancy rate of 3.7 at 48 months. While menstrual complaints were common in the period between insertions and thereafter, most of the complaints were transient and well tolerated. The slight decrease in the

amount of menstrual flow may actually be beneficial to these women.

On the whole morbidity is low and no life-threatening conditions occur although one case underwent a full work-up including laparoscopy to exclude chemical peritonitis. Tubal spillage is unlikely with the pellet method.

Conclusion

Due to the small sample size of only 25 subjects it is difficult to conclude at the present moment on the effectiveness and safety of this method of sterilization. A larger study is needed to test the acceptability of this method among Malaysian women. The method offers certain advantages over the current surgical methods in being easy to administer and can be delivered in a clinic setting. We may benefit from a simplified system for delivery of the quinacrine pellets requiring no more than one procedure and an improvement in the efficacy of new formula-

tions of the quinacrine compound. It was observed **that subjects are** reluctant to undergo this method of sterilization. This is probably due to the fact that this method is new and potential subjects refuse to accept this method as **they** are not familiar with it and that effectiveness of the method is uncertain.

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