

Quinacrine pellet nonsurgical female sterilization in Wonosobo, Indonesia*

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Objective: To evaluate the efficacy, safety, and acceptability of two monthly transcervical applications of quinacrine, 252 mg, and ibuprofen, 55.5 mg, as pellets for sterilization.

Design: Prospective clinical study.

Setting: Family planning clinic of a referral hospital.

Patient(s): Two hundred normal women who requested sterilization and volunteered for this method.

Intervention(s): Each woman received quinacrine, 252 mg, and ibuprofen, 55.5 mg, transcervically as pellets in the proliferative phase of two consecutive menstrual cycles from August 1992 to October 1993.

Main Outcome Measure(s): Life-table pregnancy failure rates and incidence of complications and side effects.

Result(s): The pregnancy failure rate was 2.0 per 100 women at 24 months. There were no serious complications, and side effects were transient.

Conclusion(s): Intrauterine insertion of quinacrine pellets is a safe and acceptably effective method of nonsurgical female sterilization. (Fertil Steril® 1997;67:966-8. © 1997 by American Society for Reproductive Medicine.)

Key Words: Quinacrine pellet sterilization, nonsurgical female sterilization, female sterilization

Surgical female sterilization, the most prevalent and effective method of contraception for women who desire no more children, requires trained personnel, adequate medical care facilities, and acquisition and maintenance of sophisticated equipment. For three decades investigators have been trying to develop a safe, effective nonsurgical method to satisfy the unmet need for voluntary sterilization. It is projected that some 328 million women will avail themselves of such services in the next 10 years if they become available (1). Transcervical insertion of quinacrine pellets using a modified intrauterine

device (IUD) inserter, as developed by Zipper and co-workers (2), is the leading candidate to accomplish this goal. Clinical experience with the method has been reviewed recently (3), including some evidence that addition of an antiprostaglandin may improve its efficacy and relieve mild side effects. Quinacrine promotes inflammation and fibrosis in contact with certain tissues, including the fallopian tube.

This method is of particular interest to a developing country such as Indonesia, which has a very low prevalence of female sterilization (2.9%) and an unacceptably high maternal mortality of 390 per 100,000 live births. The method could raise contraceptive prevalence, thereby slowing population growth and reducing maternal mortality by prevention of unwanted pregnancies, especially for high parity women.

The aim of this study was to evaluate the efficacy, safety, and acceptability of two transcervical applications of 252 mg quinacrine and 55.5 mg ibuprofen as pellets for nonsurgical female sterilization. The study was approved by the National Family Plan-

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ning Coordination Board of Wonosobo Regency, Central Java Province, which served as the institutional review board.

MATERIALS AND METHODS

A prospective clinical study of quinacrine nonsurgical female sterilization was conducted at the Wonosobo Regency Hospital, Central Java Province, Indonesia. From August 1992 through October 1993, 200 women, who gave informed consent, received 252 mg of quinacrine hydrochloride in the form of seven cylindrical pellets (Sipharm, Sissein, Switzerland) followed by 55.5 mg ibuprofen in three pellets transcervically during the proliferative phase of the menstrual cycle. All insertions were made by the senior author (A.S.). The pellets were inserted again in the next menstrual cycle. Dilatation was required in <5% of cases. The procedure is essentially the same as inserting a Copper T IUD (Kimia Farma, Bandung, Indonesia).

Follow-up was scheduled at 6, 12, 24, and 48 months after the last insertion and at any time when complications or complaints occurred. Women were admitted to the study if they requested sterilization for family planning reasons and preferred this method over surgical sterilization. Excluded were women (<2%) who had pathologic pelvic conditions (except cervicitis), such as upper tract infection, or gross distortion of the uterine cavity or who appeared unusually nervous. Those women who had to be excluded were offered a choice of surgical sterilization or other methods of contraception.

Data were collected on standardized forms developed by the International Federation for Family Health. Life-table analysis was used to calculate efficacy.

RESULTS

All 200 women completed the first insertion but 3 declined the second and were offered an alternative method; 2 additional women were lost to follow-up during the second year because they moved from the area.

Most of the women (178, 89.0%) came from rural areas; they were provided transportation to the hospital in small groups. There were 22 (11.0%) urban dwellers. The mean age was 33.2 ± 9.75 (SD) years, and age ranged from 24 to 40 years. The mean number of live births for the population was 3.5 ± 0.50 , with a range of two to eight live births. Contraceptive use reported for the 3 months before the first insertion approximated the pattern for Indonesia as a whole. A total of 43% of the subjects had used an effective contraceptive method compared with 47% for all of Indonesia.

Complications and complaints reported between insertions and up to 1 year and 2 years after the second insertion are shown in Table 1. The main side effect after the first insertion was lower abdominal pain (116 cases, 60.1%). Two women reported severe abdominal pain and required antibiotic and analgesic treatment. Fever occurred in 26 cases (13.5%) and leukorrhea in 15 (7.8%) up to 1 month after first insertion. These symptoms lasted from a few hours to a few days. Symptoms were generally milder after the second insertion. In two women, temporary amenorrhea that occurred (1.0%) during the first year lasted up to 4 months but required no treatment.

Four women became pregnant after the second insertion during the 2-year follow-up period. Pregnancies occurred 4, 5, 14, and 18 months after the second insertion. The pregnancy rates are shown in Table 2. The diagnosis of pregnancy was made by pelvic examination and confirmed by pregnancy test. One of the pregnancies was terminated by vacuum aspiration. The other three ended in spontaneous delivery of a term infant, and no major malformation was noted, although one delivery was complicated by postpartum bleeding because of retained placenta.

DISCUSSION

Our results in terms of complications and pregnancy failures are consistent with those reported by others (3). In more than 100,000 quinacrine sterilizations to date, there has been no reported case fatality and serious complications are rare (3).

Hieu and coworkers (4) suspect that the insertion technique may affect efficacy and recommend a revised technique to ensure that all pellets are placed at the fundus. We used the traditional technique, as with a Copper T IUD (Kimia Farma) insertion, resulting in a vertical column of pellets starting at

Table 1 Complications and Complaints Reported Within 1 Month of First Insertion and Within First and Second Years After Second Insertion (Wonosobo, Indonesia, 1992 to 1994)*

Complication/ complaint*	One month after first insertion (n = 200)	One year after second insertion (n = 197)	Two years after second insertion (n = 193)
Amenorrhea	2 (1.0)	2 (1.0)	4 (2.1)
Menorrhagia	7 (3.5)	3 (1.5)	3 (1.6)
Leukorrhea	15 (7.5)	4 (2.0)	3 (1.6)
Lower abdominal pain	116 (58.0)	1 (0.5)	1 (0.5)
Fever	26 (13.5)	4 (2.0)	—

* Values are number of subjects with percentage in parentheses.

† Women could have multiple complications or complaints.

Table 2 Cumulative Pregnancy Rate per 100 Women After Second Insertion of 252 mg **Quinacrine** and 55.5 mg Ibuprofen as Pellets (**Wonosobo**, Indonesia, 1992 to 1994)

Months after insertion	No. at risk	No. of pregnancies	No. of withdrawals	Pregnancy rate	Cumulative pregnancy rate
				%	%
				1.0	
0 to 6	197	2	0	0.0	1.00
6 to 12	195	0	0		1.00
12 to 24	195	2	2	1.0	2.00

the **fundus**. It could be that if we had used the technique of Hieu et al. (4), our pregnancy failure rate might have been lower, as suggested by Bairagi et al. (5). Only a randomized study of these insertion techniques will provide an answer.

There is considerable evidence that at least a second insertion is needed for high efficacy (3). However, Mullick and colleagues (6) have achieved efficacy rates of >99% at 18 months by providing medroxyprogesterone, 150 mg IM, at the time of a single insertion of quinacrine. We await a confirming report.

Concerns have been expressed regarding possible carcinogenicity of intrauterine administration of quinacrine because it is a known mutagen. However, there are no reports of cancer with use of quinacrine for treatment or prophylaxis for malaria at much higher doses orally (36,000 to 52,000 mg/y) than needed for sterilization by intrauterine application. Also, a recent 2- to 14-year follow-up study in Chile (3) showed no evidence of increased risk of cancer by intrauterine administration of quinacrine.

From present knowledge of this method of nonsurgical sterilization we believe that the benefits of the method outweigh known risks for a developing nation such as Indonesia. There also may be some advantages for an industrialized country.

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