

Quinacrine sterilization in Tripura, India*

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Abstract

A 611-case clinical trial of quinacrine sterilization (QS) was conducted at Agartala, Tripura State, India, using a unique protocol. No pregnancy failures were reported after a mean of 45.8 months of follow-up. Three trans-cervical insertions of 324 mg, 288 mg, and 252 mg quinacrine pellets were used in the first, second, and third insertions, respectively. Insertions were done on Days 6-10 of the menstrual cycle with the women remaining in a slight Trendelenberg position for 2 h post insertion. Antibiotics were prescribed after each insertion, and 3 months' supply of an additional contraception provided from first insertion. A unique inducement to report pregnancy failures was employed. Each woman was offered the equivalent of 5 months' family income to report any pregnancy following QS and a free menstrual regulation procedure. No pregnancies were reported. An independent follow-up visit to a systematic sample of 40 women found no pregnancies. © 2001 Elsevier Science Inc. All rights reserved.

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1. Introduction

Sterilization, especially for women, comprises 75% of India's contraceptive prevalence [1]. In the 1980s, laparoscopic sterilization became popular in camps in Tripura State. Several serious complications from these camp procedures came to my private practice in Agartala. In early 1979, the quinacrine sterilization (QS) method was introduced in Calcutta by the Indian Rural Medical Association (IRMA). This information was taken back to the Tripura Branch of IRMA, and its Executive Committee sanctioned a trial of QS in my private practice. After training in QS in Calcutta in 1990, the QS trial was initiated on 1 June 1990.

2. Materials and methods

In 1990 a standard protocol for QS had not yet been developed [2]. To satisfy concerns of the Tripura Branch of IRMA, a very cautious protocol was decided on as follows:

1. Three monthly insertions of quinacrine pellets were given on Days 6-10 of the menstrual cycle during no bleeding.
2. The Copper T intrauterine device (IUD) insertion technique was used in which the quinacrine pellets-loaded inserter, with aseptic precautions, was advanced to the fundus, and the sheath first withdrawn to release the pellets and then the inserter and plunger were withdrawn.
3. The first insertion was with nine pellets of 36 mg each (324 mg), the second insertion with eight pellets, and the third insertion with seven pellets.
4. The woman remained in the supine position, slightly Trendelenberg, for 2 h after each insertion.
5. Oral contraceptives were prescribed for three cycles starting with the first insertion. In addition, condom use was advised for three months.
6. After each insertion, ampicillin 250 mg plus cloxacillin 250 mg was prescribed three times a day for 5 days.
7. Follow-up was not set at specific times, but the woman was encouraged to return to the clinic when experiencing any difficulty.
8. At the time of the first insertion, each woman was offered the equivalent of 5 months' family income to report any pregnancy following the procedure. She was also told that a free menstrual regulation proce-

* The International Federation for Family Health provided quinacrine pellets and funded the independent follow-up visit of the systematic sample Of 40 women.

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sure would be provided if she experienced a pregnancy. There was no charge for follow-up contacts.

All women participating in this trial were made aware of the fact that this was a new method under investigation. A consent form recommended by IRMA was signed by each subject.

Quinacrine insertions were performed during two periods: 507 between June 1, 1990 and June 29, 1993, and 104 between January 3, 1996 and June 18, 1997. The cut-off date for analysis was January 31, 2001.

3. Results

Careful records, including date of last menstrual period, insertion dates, and date of last clinic contact, were kept on each case and were sent to IRMA for processing. No serious complications were noted in this trial.

The lack of any failures prompted a request by the International Federation for Family Health for a prospective home visit on a 10% systematic sample of the 611 cases. This was arranged by the IRMA Calcutta office, which hired a female social worker to do the home visits. The home visits were conducted in June 1999. In addition, the secretary general of IRMA visited four participants living near Agartala. Of the 62 cases in the sample, 40 were located and were found to not have experienced a pregnancy since the QS procedure. For the 22 cases not contacted, 12 women had given incorrect addresses, perhaps for privacy reasons. The remaining 10 women had moved from the area.

All 611 cases returned to the clinic for one or more follow-up visits after the QS procedures. These women were private patients in the clinic. I am their doctor and see them for routine medical checkups and a variety of illnesses. Follow-up was usually not related to QS, but follow-up notes were recorded in their QS record. This resulted in 28,012 months of follow-up without a single pregnancy reported. This was an average of 45.8 months of follow-up for the 611 women. After 6 years, a life table analysis found that 60 cases remained at risk (see Table 1).

4. Discussion

This is the first reported QS trial with 6 years of follow-up using the Copper T IUD insertion technique without a pregnancy failure. Two other trials that used the Hieu insertion technique [3], which deposits all pellets (seven pellets in these trials) at the fundus, have reported zero pregnancy failures [4,5]. The Hieu technique is performed as follows: the modified Copper T IUD inserter, loaded with pellets, is advanced to 1/2 cm from the top of the uterus (the fundus), and then the push rod is advanced until all pellets are placed at the fundus.

There are several features of the protocol that may ex-

Table 1

Cases still at risk in 6-month segments of life table analysis after 611 quinacrine sterilization procedures

Months	Number at risk
6	609.0
12	573.0
18	551.0
24	542.5
30	474.0
36	409.0
42	342.5
48	260.0
54	180.5
60	136.0
66	90.0
72	60.0

plain our improved efficacy. First, it is known that multiple insertions improve efficacy [6]. But, even with three insertions of seven pellets, a 3% failure rate was reported [7] when using the Copper T IUD insertion technique. With this insertion technique, the loaded inserter is advanced to 1/2 cm from the fundus and then, holding the push rod steady, the cannula is slowly withdrawn. When all pellets have been placed in the uterus, the inserter is withdrawn. This technique results in a straight line of pellets along the midline of the uterus. Second, the higher dose of nine pellets and eight pellets on the first and second insertions, respectively, could be a factor. Merchant et al., in a pre-hysterectomy study [8], showed that a nine-pellet insertion gave 100% tubal closures. Third, the use of oral contraceptives plus condoms is an innovation for which there is no comparable data. Fourth, the use of broad-spectrum antibiotics post insertion is another innovation without comparative data. Fifth, the slightly Trendelenberg position for 2 h post insertion might be a factor. Ferreira et al. [9] have shown by vaginal ultrasound that the dissolved "lake of quinacrine" remains at the fundus for at least 1 h while the woman is in the supine position. Ferreira's trial, still in progress, shows no pregnancy failures after two insertions of seven pellets by using the Hieu insertion technique.

Each of these protocol innovations would require randomized comparative trials to accurately determine their role in efficacy of QS. Evidence from nonrandomized studies can also provide useful evidence. For example, the most important advance in reducing the failure rate of QS was the discovery by Hieu of the importance of placing all pellets at the fundus.

The lack of scheduled follow-up visits is an acknowledged deficiency in this study. However, another trial in Eastern India with a similar strategy of encouraging additional visits without charge and first trimester abortion without charge did report pregnancy failure consistent with protocols undertaken [10]. The sample survey and large accumulated months of follow-up provided evidence of absence of pregnancy failure in the current trial.

Benagiano recently reviewed the controversy concerning the use of quinacrine for nonsurgical female sterilization [11]. The results of this study provide further evidence that QS can be used safely and effectively.

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