



Quinacrine nonsurgical female sterilization in Baroda, India: 23 years of follow-up of 84 women

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Abstract

Objectives: Evaluate the long-term effectiveness and safety of transcervical insertion of quinacrine hydrochloride pellets for nonsurgical female sterilization (QS). **Methods:** During the period June 1979 through January 1980, 84 women were admitted to a study at the Baroda Medical College and Hospital, Baroda, India. Our protocol called for three transcervical insertions of 252 mg of quinacrine hydrochloride to be deposited in the uterus of each patient. Follow-up was scheduled at 6, 12 and 48 months after the last administration. **Results:** These women were 25 to 39 years of age at the time of the QS procedure and now, 23 years later, have completed their reproductive years. There were 4 pregnancies subsequent to the completion of QS, all prior to their 4-year follow-up. Thus, the life-time failure rate for these women was 3.7%. Complaints were minor, especially when compared to surgical sterilization. There were no long-term effects suspected of being attributable to QS. **Conclusions:** QS appears to be a reasonably effective method that is much safer than surgical sterilization.

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1. Introduction

For decades, surgical sterilization has been the most effective and the most popular method for limiting family size. It has also been the most widely used. Surgical methods are difficult to provide, thus limiting access. Furthermore, there are life-threatening and other serious complications associated with surgical sterilization and many women fear surgery. Consequently, experimentation with a nonsurgical modality has been considered vitally important for decades. Zipper, of Santiago Chile, who has led the effort to produce such a method from the beginning, designed one that uses quinacrine in the form of pellets. From January 1977 to June 1978, 139 women, under Zipper's

direction, gave informed consent at an outpatient clinic in Santiago. They received three transcervical intrauterine insertions of 250 mg of quinacrine pellets [1]. By late 1978, results of this study were found to be promising.

Zipper's first trial of quinacrine pellets had been partially funded by Family Health International (FHI), earlier called the International Fertility Research Program (IFRP), then led by Elton Kessel, and supported by the United States Agency for International Development. In the Fall of 1978, FHI decided to expand this research by undertaking a larger clinical trial that would include centers around the world. With approval from its Human Subjects Committee, FHI chose 4 collaborators, among them the Indian Fertility Research Programme, which appointed the author to conduct this study on its behalf.

Research of the quinacrine pellet method (QS) continued in India until August 14, 1998. It is estimated

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that nearly 30,000 cases were carried out in that country. Indian researchers contributed significantly to the development of the currently recommended protocol for performing QS. But on that date, the government banned QS, criminalizing the procedure. This decision was made without any input from Indian obstetrician-gynecologists or other scientists involved in contraceptive technology. With this in mind, the author decided that, since the patients in his original study would have nearly all entered menopause after 23 years, this would be an appropriate time to do an additional follow-up.

2. Materials and methods

This study was conducted at Baroda Medical College in Baroda, India. The subjects were 84 women who gave informed consent from June 1979 through January 1980. The criteria for admission were that they requested sterilization for family planning reasons and had no history of medical or psychiatric problems. Women who had pathologic pelvic conditions (except mild cervicitis) were excluded. A 252 mg dose of quinacrine hydrochloride, in the form of seven cylindrical pellets, 3.3 mm in diameter, each 4 mm in length, was deposited in the uterus of each patient with the use of a modified Cu-T-200 IUD inserter using a technique similar to the one for CuT placement. Three insertions were made, 4 weeks apart.

The insertions were done on an out-patient basis, without any premedication, during the proliferative phase of the menstrual cycle in interval women (who were not pregnant within the last 42 days). They were observed for 2–3 hours before allowing them to go home. All were sexually active and they were not permitted to use any contraception after the first insertion. Follow-up was scheduled at 6, 12 and 48 months after the last insertion. These patients were also asked to return at any time there were complications or complaints.

In October of 2002 another follow-up visit was requested. This monitoring was completed in March, 2003. Out of 84 women who had QS, 74 were available for follow-up. These patients were asked about any medical problems they might have experienced since QS. Complete physical and gynecological examinations were performed at clinic visits. A Papanicolaou smear

was taken on all the subjects who appeared for this follow-up. Ultrasound examinations were performed in 20 cases. Nine other women, with whom we corresponded but did not see at the clinic, were asked to report any pregnancy or illness since QS and whether they had had any physical examination elsewhere since undergoing QS.

3. Results

Results of the study through the 4-year follow-up have been previously reported in detail [2,3]. The mean age of the women admitted was 31.3 years, ranging from 25 to 39. The median number of years of education was 4.4 years and 77.4% were from urban areas. The number of live births was 3.9, with a range of 2 to 6. The last pregnancy outcome before sterilization for over 80% of the women was a live birth, and the mean time interval between the end of their last pregnancy termination and first insertion was 18.5 months. A majority of patients reported that either they or their husbands were the most important person involved in their decision to request sterilization. Over half cited the undesirable side effects of other contraceptive methods as the reason for choosing sterilization.

Three women became pregnant before their third insertion. Their pregnancies were terminated by suction evacuation and they were then excluded from the study. The remaining 81 patients completed all three insertions, with only one requiring analgesia during the procedure. Mild pain was experienced by 10 subjects (11.9%) during the first insertion. Five (6.1%) complained of mild or moderate pain during the second insertion, while 4 women (4.9%) reported pain during the third one.

Follow-up in this study was excellent. All 81 women were seen at a four year follow-up visit. Three pregnancies were diagnosed at 23, 25 and 26 months after the completion of the last insertion. The cumulative life-table pregnancy rate at 48 months was 3.7/100 women.

The most serious complication reported during the first four years was a case of menorrhagia in a 37-year-old patient. An abdominal hysterectomy was performed 3 years after the sterilization procedure. Two women who complained of abdominal pain were examined at

48 months. In one there was a thickening in the right fornix, and in the other tenderness was elicited in the left fornix but no mass was felt. Other follow-up complaints included leukorrhoea, backache, hypertension, and amenorrhoea – one to four cases each. None of these complications or complaints appeared to be related to the sterilization procedure itself. A comparison of the menstrual cycle length and the duration of menstrual flow between pre and poststerilization data indicated no significant differences.

The follow-up rate after 23 years was even more remarkable – 88% (74 of 84 women). Sixty-five women were examined and 9 were followed-up through correspondence.

No further pregnancies occurred after the four-year follow up. Therefore, the life-time pregnancy rate is 3.7/100 women. Their ages at the time of follow-up ranged from 43 to 60. Except for three women, the rest had entered menopause. Three more had undergone hysterectomy – two for uterine prolapse and one for dysfunctional uterine bleeding. The histology of the specimen did not show any cancer. Two women died due to causes unrelated to QS – one was bitten by a snake and the other was in a motor accident. Six years after QS insertion, one patient suffered from hepatitis Type A. She is now in good health. Four subjects complained of leucorrhoea and six had symptoms suggestive of a urinary tract infection. Three women sustained fractures due to accidental falls. Menopausal symptoms were seen in 9 of the group. Ten had blood pressures greater than 140/90 mm mercury. Breasts were atrophic in 24 cases and looked normal in the rest. No breast lump or any abnormality was noted. Abdominal palpation did not reveal any abnormality. Four women needed hysterectomies; one was recorded at the 4 year follow-up and three more since then. Indications for hysterectomy were uterine prolapse and menorrhagia. Senile vaginitis was seen in 6 women. Two subjects had a monilial vaginal infection. Ultrasound examination was performed in 20 cases. Two patients had small fibroids of 1 cm size on the anterior uterine wall, which did not cause any symptoms.

A Papanicolaou smear was taken in every examined woman. It showed inflammatory changes in 8 of them. Malignant cells were not seen in any smear. Genital malignancy was not seen in any woman.

The patients who came for follow-up were asked if they were satisfied with QS. All except those who conceived were satisfied with the method. They liked its simplicity and reputation for no morbidity or mortality associated with QS. They had heard of complications and even death after surgical sterilization.

4. Conclusions

The long term follow-up of the QS technique shows that it is a simple, inexpensive and effective method of female sterilization. The pregnancy rate is within acceptable limits. Women are largely satisfied with the procedure. There were minimal initial side effects and long-term follow-up does not show any serious adverse effect. The method is simple, cost-effective and is acceptable to women. We strongly feel that QS is a good alternative to surgical sterilization. We do not have data on chances of success for reversing fertility when pregnancy is desired. At present QS should be considered for women who desire no more children.

We feel it is now necessary to review the ban of the QS method in India by the Drug Controller. It would be appropriate for the Drug Controller of India to consult gynecologists in India who have some experience with the method. The US FDA has given permission for a QS trial and it should not happen that India is the last country in the world to recognize the value of this simple, inexpensive and reasonably effective method.

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