



## A comparison of quinacrine sterilization (QS) and surgical sterilization (TL) in 600 women in Guizhou Province, China

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### Abstract

**Objectives:** Compare the safety and efficacy of quinacrine sterilization (QS) and surgical sterilization, also known as tubal ligation (TL). **Methods:** 300 women accepted QS in Guiyang, China during the period from July 1995 to September 1997. Each patient was scheduled for follow-up at 3, 6, 12 and 24 months. In March 1998, a comparison group of 300 women electing TL during the same time period was systematically chosen. Researchers visited the village of every woman and conducted a structured interview. Each candidate was given a general health and pelvic exam at a clinic in her village. All interviews and exams were completed in August 1998. **Results:** Of the 289 QS patients interviewed (a follow-up rate of 96.3%), 265 had had 2 insertions. There were 3 pregnancy failures for a cumulative life table failure rate of 1.2 per 100 women at 24 months. The 299 TL patients (a follow-up rate of 99.7%) had a similar rate of 0.7. There were no life-threatening side effects or deaths in either group. QS was less disruptive, more easily tolerated, required fewer resources and was viewed more favorably than TL by women and their spouses. **Conclusions:** Both methods were found safe and very effective. However, QS was considered to be more acceptable than TL.

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**Keywords:** quinacrine sterilization, nonsurgical sterilization, tubal ligation

### 1. Introduction

Guizhou is a province of more than 36 million people. It has the second-lowest per capita income in China. As in most countries, there is a great demand for simple, safe, effective and inexpensive sterilization services. When the leadership in Guizhou Province learned of quinacrine sterilization (QS) in 1993, tens of thousands of cases had already been performed in Vietnam and elsewhere [1]. Reports on QS in China were limited to a single 18-month follow-up study of 100 cases by Dr. Ding Juhong in Nanjing, Jiangsu

Province [2]. In 1993, QS was adopted by the Guizhou Provincial Science Commission (GPSC) as one of its Eight Five-Year Key Research Projects. That same year, the Guizhou Provincial Research Institute for Family Planning was chosen to conduct research on this new method. During the course of our information gathering process, we received assistance from the Center for Research on Population and Security (CRPS) in the United States. With the approval and support of the Guizhou Provincial Family Planning Commission and the GPSC, we conducted a clinical trial of 300 cases between July 1995 and September 1997. In March 1998, the State Family Planning Commission of China in Beijing requested that a retrospective study be undertaken that would compare the experiences of the

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QS patients to those of 300 women who had chosen surgical sterilization at a similar time. This report focuses on that comparison.

## 2. Materials and methods

The QS protocol for this trial used quinacrine hydrochloride in the form of pellets. Each pellet is 3.5 mm in diameter and 5 mm in length and contains 36 mg of quinacrine. All pellets were provided by CRPS. Seven pellets (252 mg) were deposited using a modified CuT intrauterine device (IUD) inserter from 3 to 7 days after menstruation ended and/or 6 weeks after the last delivery or abortion. A second insertion was performed 4 weeks later. This group included 300 women of child-bearing age who meet the following criteria: volunteer to receive this permanent sterilization and to participate in post-procedure follow-up scheduled at 3, 6, 12 and 24 months. Those who have post-procedure amenorrhea would submit to pregnancy tests as well as pelvic and ultrasound exams. Excluded from the study were women with a history of ectopic pregnancy, psychosis, other serious systemic diseases and reproductive system diseases. For inclusion in the study, her uterine cavity should measure between 5–8 cm in length. Three study sites were chosen in suburban Guiyang. These were the family planning stations in the districts of Huaxi, Baiyun and Wudeng. All women were asked to remain in a supine position for 2 hours immediately after each insertion before leaving the clinic. Each patient was instructed to use a temporary method of contraception for 3 months from the time of the first insertion.

The comparison or control group consisted of 300 women who had undergone tubal ligation (TL). The protocol consisted of a tubectomy procedure involving a small abdominal incision and removal of approximately 1.5 cm of the fallopian tube. These patients had been sterilized in a routine service program and had not agreed in advance to any long-term study protocol. Only women who volunteered to participate were included. Each of the 3 clinics chosen for the QS study also maintained a registry of all TL cases performed at that clinic. Focusing on the portion of the registry for the period from July 1995 to September 1997, a systematic sample was taken from each clinic, to approximate the number of QS procedures performed

there. There were about 3 times as many TL cases as QS procedures at each clinic. Therefore, every third TL case on the registry was selected in each clinic until the requisite number for the study had been identified.

Both groups of women had a general health exam, including a battery of liver and kidney function tests, and a pelvic exam, including a cervical smear. Also, subsets of QS patients underwent an endometrial biopsy and/or a battery of reproductive hormone tests. This battery included: follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E<sub>2</sub>) and a prolactin (PRL) measurement. Twenty-five women who were relying on condoms for contraception were systematically selected from 2 of the clinics (Huaxi – 13 women and Baiyun – 12 women) to serve as a control group. The women in the condom group were registered in each clinic. Then, for the purpose of identifying a representative sample, every third woman on the list was chosen until the appropriate number was reached. The QS study group was similarly chosen from these same 2 clinics by selecting every third woman on the list of QS patients in each clinic until 15 women were chosen from each clinic. Blood samples were collected from both cases and controls for the hormone study during days 3 to 7 after menstruation. The subset of QS patients who underwent an endometrial biopsy was limited to those women who agreed to this invasive procedure when asked during the interviews for the retrospective study.

Between March and August 1998, researchers visited the villages of the QS patients and the TL controls. The structured questionnaire was administered and the general health and pelvic examinations were performed at a clinic in their village.

## 3. Results

A total of 289 QS patients of the 300 were located, interviewed and examined for a follow-up rate of 96.3%. A biopsy had not been mentioned at the time of recruitment for the QS study. When asked to do so as a part of this retrospective study, 58 women agreed to an endometrial biopsy. Similarly, they had not been informed beforehand about the battery of reproductive hormone tests and only 30 subjects were randomly chosen to participate in this testing.

All 300 TL patients of the sample were contacted;

Table 1

Cumulative life-table failure rates for 100 women for 2 insertions of quinacrine ( $N=265$ ) versus tubal ligation ( $N=299$ ) in Guizhou Province, China, 1998

Months	Failures	At risk	Rate	SE
<b>Quinacrine sterilization (QS)</b>				
3	1	265	0.4	0.38
6	0	264	0.4	0.38
9	1	264	0.8	0.54
12	1	252	1.2	0.69
15	0	194	1.2	0.69
18	0	165	1.2	0.69
21	0	147	1.2	0.69
24	0	105	1.2	0.69
<b>Tubal ligation (TL)</b>				
3	2	298	0.7	0.47
6	0	297	0.7	0.47
9	0	294	0.7	0.47
12	0	281	0.7	0.47
15	0	256	0.7	0.47
18	0	241	0.7	0.47
21	0	219.5	0.7	0.47
24	0	161.5	0.7	0.7

299 were interviewed and examined for a follow-up rate of 99.7%. One woman refused to participate in this retrospective study.

One of the more important ways in which these two groups differed was the mean length of time between their sterilization procedure and the follow-up visit. The mean length of follow-up for QS patients was 20.8 months while it was 25.8 months for TL patients, a full 5 months' difference. This had much to do with the way the TL sample was taken.

Women receiving 2 insertions numbered 265, and 3 of them became pregnant. Table 1 shows the cumulative life-table failure rates of the two groups through 24 months. The rate at 2 years was 1.2 per 100 women for QS users who had 2 insertions and 0.7 for TL patients. There were 2 pregnancies among the 24 women who had a single insertion for a gross pregnancy rate of 8.3%. Table 2 compares QS users to TL users with respect to demographic and physiological characteristics. QS patients were 1.7 years older

Table 2

A comparison of demographic and physiological characteristics of women who chose QS ( $N=289$ ) versus TL ( $N=299$ )

Parameter	QS (mean)	TL (mean)
Age (years)	30.7	29.0
Husband's age (years)	32.6	30.8
Living children (no.)	2.06	2.08
Births (no.)	2.10	2.12
Pregnancies (no.)	2.8	2.4
Induced abortions (no.)	0.6	0.3
Age of youngest child (years)	2.5	2.7
Weight (kg)	49.6	49.1
Height (cm)	155.7	156.5
Systolic pressure (mmHg)	100.7	99.4
Diastolic pressure (mmHg)	70.4	67.7
Menstrual cycle length (days)	29.0	28.7
Menstrual period length (days)	4.5	4.8

QS: quinacrine sterilization; TL: tubal ligation

than women who had obtained a TL and their husbands were likewise older. This age difference is significant and may account for other small differences seen between the 2 groups. Child loss was exceedingly low, a mean of 0.04 children for both groups. "Child loss" is defined as the death of a child from birth until the mother came to the clinic to be sterilized.

The number of TL users was similar to the QS users at each of the three clinics (Table 3). QS patients had a little more schooling on the average but they were far more likely to have used a temporary contraceptive method (47% compared to 20%). However, the majority in both groups had never used such a method. Discussion of sterilization with their husbands was all but universal (99% for QS users and 100% for TL users). Husbands were much more supportive of QS. The greatest difference found between the two groups was in the counseling before the procedure. In the QS group, one woman had not been counseled by her clinician prior to the procedure, while 89.3% of the TL cases reported that they had received no counseling.

Before discussing side effects, it should be noted that women who have a TL usually are not hospitalized, but return home for a few days of complete bed rest. Then they are given light duty for 30 days. Women who have QS usually return to work immediately. None of

Table 3  
QS ( $N=289$ ) versus TL ( $N=299$ ): a comparison of environmental factors, Guizhou Province, 1998

Parameter	QS (%)	TL (%)
<b>Clinic site</b>		
Baiyun	47.8	42.5
Huaxi	41.5	47.2
Wudeng	10.7	10.4
<b>Education</b>		
No school	3.5	6.4
Elementary school	34.3	38.5
Middle school or above	62.3	55.2
<b>Ever used contraception before sterilization</b>		
Yes	47	20
No	53	80
<b>Discussed sterilization with husband</b>		
Yes	99	100
No	1	0
<b>Husband's attitude</b>		
Supportive	91.0	60.9
Wife should make the decision	8.3	39.1
Disagree	0.3	0.0
Unknown	0.3	0.0
<b>Counseled by clinician prior to procedure</b>		
Yes	99.7	10.7
No	0.3	89.3

QS: quinacrine sterilization; TL: tubal ligation.

these women experienced complications or side effects during either the QS or TL procedures. Furthermore, Table 4 shows that 73.7% of the QS cases and 49.8% of the TL cases experienced no side effects during the first week after the procedure. A similar proportion complained of lower abdominal pain. Women who had chosen TL were much more likely to report that their general health status had deteriorated during the period since the procedure (48.5% as opposed to 22.5% among QS users). As can be seen in Table 4, TL users reported more frequently that they now lack energy (21.0% and 2.8%, respectively) and got feverish easily far more often than QS users (13.0% vs. 0.3%). None

Table 4  
Side effects following QS ( $N=289$ ) and TL ( $N=299$ ) procedures, Guizhou Province, 1998

Side effect	QS (%)	TL (%)
<b>Discomfort within first week of procedure</b>		
None	73.7	49.8
Lower abdominal pain	18.7	19.4
Yellow discharge	1.4	1.0
Headache	0.3	1.0
Pruritis	4.2	10.7
Fatigue	1.4	18.1
Lumbago	0.3	0.0
<b>Post-procedure assessment of health status</b>		
Unchanged	77.5	51.5
Worse than before	22.5	48.5
<b>In what way is health worse</b>		
Weight increased	2.1	0.0
Weight decreased	0.7	0.7
Headache and dizziness	5.2	6.0
Pelvic pain	3.5	10.0
Infection	0.3	0.7
Gets feverish easily	0.3	13.0
Lack of energy and weakness	2.8	21.0
Lower back pain	6.2	0.0
Other	1.4	0.0
<b>Post-procedure working ability</b>		
Same as before	92.0	48.8
Easily fatigued	8.0	51.2
<b>Post-procedure menstrual cycle</b>		
Same as before	72.7	65.5
Shorter than before	18.3	18.7
Longer than before	8.3	15.7
Ammenorrhea	0.7	0.0
<b>Post-procedure menstrual flow</b>		
Same as before	63.7	60.2
Scantier than before	29.1	24.1
More than before	6.6	15.7
-	0.7	0.0
<b>Pap smear results</b>		
No specific abnormal cells	69.2	83.6
Atypical cell, no cancerous signs	30.4	16.4
Abnormal growth	0.3	0.0
<b>Liver function tests normal</b>		
	100.0	100.0
<b>Kidney function tests normal</b>		
	100.0	100.0

QS: quinacrine sterilization; TL: tubal ligation.

of the side effects experienced by either group of women required treatment.

QS patients overwhelmingly (92%) confirm that working ability is unchanged since the procedure, while 51.2% of TL patients reported that they are now easily fatigued. Although both groups (nearly two-thirds) informed us that their menstrual cycles are largely unchanged (see Table 4), more QS patients experienced less flow and more TL patients reported a greater flow. One woman using QS reported continuous amenorrhea at follow-up 2 years after the procedure. Pap smears revealed no specific abnormal cells in most women but the proportion showing atypical cells was higher among QS cases (see Table 4). This came as no surprise since quinacrine does cause temporary inflammation of the endometrium. The findings of the liver and kidney function tests were normal in all women.

A total of 58 QS patients agreed to have an endometrial biopsy. None showed any abnormal findings. No differences were observed between the QS patients and the unmarried women controls in levels of FSH, LH, E<sub>2</sub> and PRL [3].

As noted above, there were 5 pregnancies in this QS series. Two women became pregnant after obtaining but a single insertion and both decided to carry that pregnancy to term. Three women became pregnant after obtaining 2 insertions of quinacrine pellets and one of them chose to carry that pregnancy to term. All 3 of these women gave birth to sons. Two of them had never used a temporary contraceptive. The third had used both the IUD and the Pill and she had previously become pregnant while on the Pill. During follow-up visits in 2002, when the three boys were 4, 4 and 6 years of age, all three were found to be happy and healthy, both mentally and physically. The boy whose mother became pregnant after one insertion, is shown at age 4 with his mother in Fig. 1. These 3 women reported that their quinacrine insertions were uneventful; that their health and sex life remained unchanged after QS. During these follow-up visits, protocol violations other than having but a single insertion were identified. Of these 3 patients who became pregnant, none had remained in a supine position for the required 2 hours or used contraception for 3 months following the first insertion. Furthermore, one woman had her only insertion on the 15th day following menses rather than during the 3 to 7 days

following the end of menstruation as recommended in our protocol.

There was one attempt at reversal of QS in this series. This woman gave birth to twins in February 1997 at age 23. Four months later she obtained her first insertion of quinacrine. Before she was due for the second, one of the twins died of hydrocephalus. She did not pursue another QS procedure. On 6 April 2000, she came to the Guizhou Research Institute for Family Planning to meet with the first author, and requested that an attempt be made to reverse her QS. She explained that she had not had any problems, except infertility, and that her menses had been normal since QS. She had completed her menstrual period 2 days before. A hysteroscopic examination was performed. First, the doctor inserted a number 7 Hegar's bougie under hysteroscopic guidance into her uterine cavity with a camera attached. At the same time, distention liquid (10% glucose) flowed slowly into the uterine cavity from the bougie. The uterine cavity appeared as a cylinder and the tunica intima of the uterine cavity was smooth and both yellow and white in color. Most of the endometrium was red and smooth. There were some tunica intima adhesions which were not serious. They were dissected by the flowing distention liquid. The scar tissue filling the orifices or ostia of the fallopian tubes was white (see Fig. 2). Then the doctor moved the number 7 Hegar's bougie into both orifices of the fallopian tubes and infused distention liquid (10% glucose) with methylene blue added. This was difficult, as resistance was encountered (Fig. 3). The doctor felt that the pressure was high when he tried to infuse distention liquid into the fallopian tube. If the tube was patent, the methylene blue would flow freely into the fallopian tube and out through the fimbria. However, in this case, the methylene blue did not seem to flow into the tube at all. But the bougie pressed through the scar tissue at the ostia. When the bougie was withdrawn, the opening to the tube was filled with methylene blue distention liquid (Fig. 4). After completing the hysteroscopy, ultrasonography seemed to show a little methylene blue in the Pouch of Douglas but the finding was not pronounced. This suggested that the pressure from the distention liquid alone may have been sufficient to open a tube.

On 8 May 2000 she was diagnosed as pregnant in a local hospital. Unfortunately, she had a spontaneous



Fig. 1. A healthy boy conceived after QS.

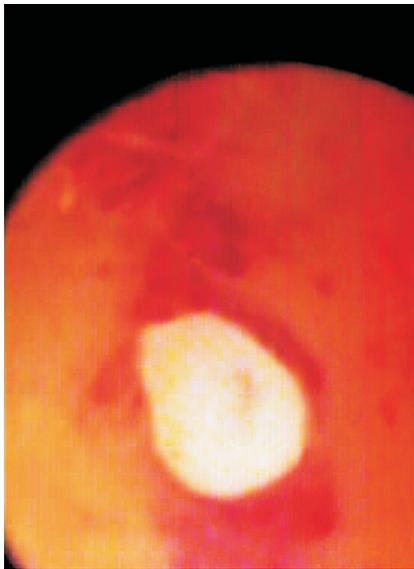


Fig. 2. Scar tissue fills the tubal ostia.

abortion on 13 July 2000. She became pregnant again on 30 May 2001. But on 2 August 2001, an ectopic pregnancy was diagnosed in the left fallopian tube. She was operated on the next day in the Guizhou Provincial Hospital. The ectopic pregnancy was removed from the left tube and the tube repaired. The surgeon found that the right tube was completely blocked. A TL was performed on the right tube to insure that she would not later be faced with another ectopic pregnancy in the right tube. This patient wants to have another child but



Fig. 3. Bougie filled with methylene blue pressing through scar tissue at ostia.



Fig. 4. Backflow of methylene blue from tube.

has continued to use the Pill because she fears another ectopic pregnancy.

#### 4. Discussion

The two groups of women differed in length of follow-up: a mean of 20.8 months for the QS group and

25.8 months for the TL group. This difference is largely due to the essentially stable numbers seeking TL during the study period while requests for QS were increasing throughout the patient intake period. Thus, a greater proportion of QS cases were performed later in the July 1995–September 1997 study enrollment period, as can easily be seen in Table 1. However, this difference in length of follow-up does not appear to have had any effect on the outcomes of the monitoring. If there are any, they are not apparent.

There is a significant difference in ages between the 2 groups. The QS group was on the average 1.7 years older. It is not possible to say with certainty why this difference in age exists. However, given the preference for QS found in this study, a plausible explanation is that some of the women had considered TL for a time and then rejected it, even though they wanted to be sterilized. When this new option for sterilization came along, they acted, seeking out QS – at a slightly older age. That 47% of QS users had at some time used a temporary method of contraception compared to only 20% of TL users supports this explanation. It is possible that this increase in age accounts for the higher blood pressure and weight and the slightly greater number of pregnancies and abortions. However, on the whole this significant difference in age did not change the outcome of this study in any substantive way.

The exceedingly low rate of child loss prior to seeking sterilization is remarkable. Only 1 in 25 couples in both groups had lost a child. This reassurance of child survival makes sterilization a more attractive option.

A total of 24 women had received but a single insertion. The gross pregnancy rate was 8.3%, much higher than the rate with 2 insertions. The majority of these single insertions occurred when there was a single logistics breakdown. The supply of quinacrine pellets to clinics was temporarily disrupted and this can be avoided in the future. In the case of the one child loss in this series (discussed above), the woman chose not to have her second insertion because she wanted to have another child. It is possible that a few of the women were simply not sufficiently self-motivated to seek the second insertion. However, there may have been some among them who did not fully understand that they needed to return for a second insertion or recognize its importance, or they were misinformed by a friend or relative who had chosen to have a single

insertion. Aside from always placing the pellets at the fundus, nothing has more effect on the failure rate than insuring that the woman has 2 insertions of pellets. Good counseling and visiting the woman if she fails to return for her appointment for her second insertion will help lower the failure rate with this method.

There were other protocol violations and they too may have contributed to a higher failure rate. Performing the insertion at or just after the time of ovulation is known to increase the risk of pregnancy. Also, there are many documented cases in other countries of pregnancies occurring during the period between the first and second insertion. In our province this is particularly important because such a high proportion of women never used any temporary contraceptive method prior to seeking sterilization. Only 47% of QS users and 20% of TL users had done so. This is particularly challenging for the counselor.

Both QS and TL had excellent results in this series. There were no deaths, serious complications or side effects of great consequence in either group. While deaths with TL are occasionally reported, no deaths have been reported with QS anywhere. Although none were found in this series, there are occasionally serious complications reported with TL. Usually 3–7 days of hospitalization are needed with TL, followed by light duty for 30 days. After QS women can return to work immediately. Compared to TL, only a fraction of medical resources are needed with QS. Thus its cost is commensurately much lower than for TL. Most important, this study showed that there is a preference for QS over TL. Women sought QS after having delayed requesting surgical sterilization. They were 50% more likely to report a side effect following TL. Two years after the procedure, those who chose QS were much more apt to have a positive assessment of their health status (77.5% versus 51.5% respectively). Two years later, among women who had undergone QS, only 8% felt that their ability to work had changed for the worse compared to 51% among TL users. Also, husbands showed a preference for QS, although not necessarily for the most altruistic of reasons. QS was found to inconvenience husbands considerably less because the procedure does not affect its users' routine work and life, including her normal sexual activities.

We found, during the course of the interviews, that many recipients are willing to promote QS and had recommended this procedure to their relatives and

friends. These recipients were responsible for its rapid acceptance in Guizhou Province. The good counseling they had received was evidently critical (99.7% of them reported that they were well informed by their clinician before the procedure as compared to only 10.7% of TL users). Our counseling also no doubt, in part, accounted for our low failure rate in this series even though these were the very first 300 cases of QS in this province.

This study has shown that QS has many advantages over surgical sterilization. It is safe, reliable, simple to perform, does not use anesthesia. Health providers who perform IUD insertions can carry out this procedure. It is well suited for our frontier and underdeveloped

areas. In short, QS helps implement the family planning policies set by our government.

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