



Quinacrine sterilization (QS) in Iran and the use of HSG as a measure of success

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Abstract

Objectives: To establish the safety, effectiveness and acceptability of quinacrine sterilization (QS) in Iran. To determine whether the hysterosalpingogram (HSG) performed under low pressure can be used to demonstrate success of the QS procedure rather than waiting for a pregnancy to occur in order to demonstrate failure. **Methods:** This study was initiated in September 1990 in a private family planning clinic in Tehran, Iran. Patient intake for this analysis was completed 31 December 1998 and the cut-off date for follow-up data to be included in this analysis was 30 July 2002. During this period, 268 women received QS. From inception until April 1994, 160 women entered the study. The first 62 women received 3 insertions and the remainder received 2. Short-term side effects were closely followed in these 160 women. From 18 February 1994 until the patient intake cut-off date, 131 women entered the study and 46 of them received an HSG. **Results:** With 4 to 12 years of follow-up there have been 7 pregnancies for a gross pregnancy rate of 2.6%. However, the use of the HSG tripled the risk of pregnancy for women who underwent the procedure. Furthermore, HSG, even when performed under minimal pressure, indicated failure of the QS procedure about 6% of the time when in fact both tubes would have closed had there been no intervention. Side effects were minor when compared to the complications of surgical sterilization. **Conclusions:** QS was found to be safe, effective and preferred over surgical sterilization by Iranian women. HSG understated the number of patients with bilateral tubal closure, or with tubes that would have closed given a little more time.

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1. Introduction

In 1986, the population growth rate in Iran was 3.8%, one of the highest in the world [1]. In 1994, in response to social and economic pressures, the government became very concerned with this situation. As a consequence, the Ministry of Health has taken various steps to promote family planning. Encouraging messages to limit the size of families are evident everywhere and modern contraceptives, including surgical sterilization and vasectomy, are available throughout the country [2].

There is undoubtedly a great demand for tubal occlusion. But the risks associated with surgical sterilization, its inaccessibility to a large proportion of the population, the fear of surgery generally and the fact that many women are poor candidates for any surgery prevent us from meeting the demand. The pressing need for the development of a non-surgical procedure has been apparent for some time. In 1990, the only method ready for clinical trials was one using quinacrine pellets (QS), the creation of Dr. Jaime Zipper and his colleagues [3]. In response to our own requirements, a clinical trial of QS was initiated in my private family planning practice in Tehran.

As one explains QS to patients and other clinicians,

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the method appears remarkably simple. The response to its description has all too often been, "What sounds too good to be true usually is." By 1994, this reaction was proving to be a great hindrance to the acceptance of this method in Iran. In a preliminary report on the early experience with QS, anecdotal evidence supporting this position is cited [4]. A test for an endpoint other than pregnancy had to be found. In this way we would be able to document the success of the procedure before exposure to the risk of pregnancy became apparent. Because abortion is illegal in Iran, such a test would be important to the acceptance of QS by both physicians and patients.

In 1993, El Kady and his colleagues in Egypt published their results on the use of the hysterosalpingogram (HSG) as such an endpoint in 159 women [5]. He reported that HSG showed open tubes in 27% of them after 2 insertions and 6% after 3. These findings were inconsistent with the failure rates seen in Tehran, but the idea of using the HSG as an endpoint was very attractive. In some women, the pressure it creates in the tubes could have dislodged the plug of scar tissue and reopened a tube. Perhaps El Kady was using a pressure during the HSG that was higher than needed. El Kady had observed that no failures were reported during the 2 years of follow-up after the HSG showed closure.

In 1994, Alpizar reported on 694 cases in Costa Rica. He had performed HSG on 129 of these women but bilateral obstruction was found in only 89% of them. Again these results were inconsistent with pregnancy rates in Tehran. Alpizar also noted that this rate was increased in women receiving HSG (4.3% as compared to Tehran 2.0%) [6]. Alpizar found fewer than half as many open tubes compared to El Kady (11% vs. 27%). Differences in pressure could account for the difference in rates. In both cases, just how much pressure was used and whether it was consistent was unknown.

The use of HSG in QS had considerable potential value in Iran and elsewhere. The decision was made to undertake a trial to test HSG as an endpoint using a minimal amount of pressure.

2. Methods

Only women who could continue follow-up for a long period were selected for this study. A total of 268 QS procedures were performed. To ensure

informed consent, all prospective acceptors and their husbands were counseled prior to the procedure. This preparation included a detailed description of the method and its administration, possible complications and side effects and the risk of failure. The permanent and irreversible nature of the procedure was explained. Both members of the couple signed an informed consent form.

The International Federation for Family Health (IFFH) QS protocol [7] based on the work of Zipper and his colleagues, was applied throughout the study. Originally, Zipper had recommended that quinacrine be administered in three doses of 252 mg (seven pellets of 36 mg each) at one-month intervals [7]. But after the first 62 procedures a second regimen was followed. Zipper had changed his recommendation to two monthly doses plus 50 mg of an antiprostaglandin to lessen spasm and thereby reduce the failure rate and pain. These changes were adopted for the last 98 procedures of that study, using 55.5 mg of ibuprofen in the form of three 18.5 mg pellets. Use of this protocol continued until the patient intake cut-off date for this report. Side effects were carefully recorded in these 160 women.

On February 18, 1994, a third protocol was adopted. Many women were requesting HSG because they or their family physicians wanted reassurance that the procedure was successful in closing the tubes before they terminated other contraceptive methods. Patients who requested an HSG were offered this service. However, they were referred to a single radiologist, a colleague sympathetic to QS who agreed to use minimal pressure. No attempt was made to assign patients to the two groups. It depended entirely on the woman's preference. This protocol was continued until December 31, 1998, the case intake cut-off date for this report. Follow-up of all cases continued until 31 December 2002.

In our investigations, a modified Copper-T IUD inserter was used to administer the quinacrine pellets, as follows: after preparing the cervix and sounding the uterus, the clinician set the flange on the inserter sleeve, and advanced the inserter to the fundus. She then withdrew the inserter 0.5 cm, fixed the inserter sleeve and slowly advanced the plunger to expel all pellets at the fundus. The inserter was then withdrawn. Fundal placement was used from the very beginning in 1990, although it was not described in the literature

until 1993 [8]. After each insertion, the woman was given a five-day course of antibiotics.

Women returned to the clinic for follow-up one, two and 15 days after each insertion; one, two, three and six months after the last insertion; and then annually. There was no charge for these visits. A cycle of oral contraceptives was provided at the time of the last insertion and at the one- and two-month follow-up visits. Every woman was followed until the cut-off date for this report. There is considerable confidence that every pregnancy and serious complication would have been reported (Table 1).

Table 1

Additional follow-up of the 160 patients in the series reported in *International Family Planning Perspectives* [Ref. 4], after 5.9 years of follow-up (case intake from September 1990 to April 1994), Tehran, Iran

Number of cases	Pregnancies	
	N	%
First 62 (3 insertions)	2	3.2
Last 98 (2 insertions)	1	1.0
Total 160	3	1.9

3. Results

A total of 46 women had an HSG, while 85 QS patients undergoing the procedure during the same time period did not.

Complications and side effects following QS for the first 160 patients have been documented elsewhere [9]. These are summarized in Table 2 in addition to the prescribed treatment. The type and frequency of these adverse events (AE) did not change during the remainder of this series. All have been minor and easily treated. There have been no allergic reactions except possibly for local pruritis.

Failures from the first two protocols are reported in Table 3. These patients have been followed for 8 to 12 years each. Pregnancies experienced with the third protocol are shown in Table 3. Follow-up has ranged from 4 to 9 years for this group. Pregnancy among women receiving an HSG was twice as high as it was among non-HSG patients (4.3% vs. 2.4%). There were 7 pregnancies in this series of 268 cases for a gross rate of 2.6% with 4 to 12 years of follow-up. The seventh

Table 2

Complications and side effects reported following nonsurgical female sterilization with quinacrine pellets, and prescribed treatment, Tehran, Iran 1990–1994 (N = 160)

Complication	N	Treatment
Lower abdominal pain	18	analgesic
Itching (local)	16	cortisone cream
Fever \geq 5 days	14	antibiotic (4 days)
Backache	8	analgesic (2–3 days)
Vaginal discharge	8	anti-fungal, antibiotic vaginal suppository (6 days)
Spotting	8	none
Decreased menses	7	none
Cervical adhesion	1	surgical correction
Bleeding	1	vasoconstrictor

Table 3

Pregnancy following QS during period (February 18, 1994 to December 31, 1998) when 46 of 131 patients requested HSG 2–4 months post second insertion, with 6 months to 5 years follow-up, Tehran, Iran

HSG	Cases (N)	Pregnancy	
		N	%
Performed	46	2	4.3
Not performed	85	2	2.4
Total	131	4	3.1

Table 4

HSG vs. pregnancy as an endpoint among QS patients, September 1990 to December 1998, Tehran, Iran (N = 268)

	Endpoint	
	HSG (N)	Pregnancy (N)
Cases (N)	46	222
Positive (N)	4	5
Failure (%)	8.7	2.3

pregnancy was a blighted ovum occurring 12 months after QS and resulted in a spontaneous abortion after 2 months. This patient had not had an HSG. There have been no ectopic pregnancies.

Table 4 reveals that HSG grossly overstates failure of

tubal closure. This experience with HSG suggests that 8.7% of women did not have tubal closure. But among patients who did not have an HSG, only 2.3% went on to become pregnant.

4. Discussion

HSG is probably not very useful even if the technique did not cause pregnancies. The failure or pregnancy rate using HSG as the endpoint was 3.8 times higher than that for pregnancy (8.7% vs. 2.3%). This was an improvement over the findings of El Kady and Alpizar, perhaps due to the use of a lower pressure. Nevertheless, this rate, in our opinion, is not acceptable.

In the four cases where the HSG was positive for an open tube (Table 4), the two-insertion QS procedure was repeated without difficulty. In three cases, the HSG was repeated after the second procedure. In the other case, the clinician declined to repeat the HSG. Because of false positives, and because HSG may blow out a plug of scar tissue with resulting pregnancies, we would not recommend HSG as an endpoint for QS.

QS was found to be both safe and effective in Iranian women. This experience is consistent with the assumptions of researchers everywhere. After 12 years of performing this procedure and an enormous amount of feedback from patients, this investigator highly recommends this method. In Iran, the greatest obstacle

to its widespread adoption is simply the lack of awareness among our physicians of the extensive scientific evidence already documented internationally confirming QS to be safe, effective and acceptable to women.

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