

# Quinacrine Hydrochloride Pellets: Preliminary , Data on a Nonsurgical Method of Female Sterilization

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## ABSTRACT

Zipper J, Cole LP, Goldsmith A, Wheeler R, Rivera M (Depts de Fisiología y Biofísica, Escuela de Medicina, Universidad de Chile, Santiago, y Obstetricia y Ginecología, Hospital Sotero del Rio, Puente Alto, Chile, and International Fertility Research Program, Research Triangle Park, NC, USA). Quinacrine hydrochloride pellets: preliminary data on a nonsurgical method of female sterilization.

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The efficacy of transcervical insertions of quinacrine hydrochloride pellets to produce tubal occlusion has been evaluated in a study of 139 women in Santiago, Chile. At one year, the pregnancy rate was 3.1%, an acceptable rate for a nonsurgical method of female sterilization.

## INTRODUCTION

Surgical female sterilization, the most effective method of contraception for women who desire no additional children, requires trained personnel, adequate medical care facilities and the acquisition and maintenance of sophisticated equipment. These requirements can drain expensive and scarce medical resources, especially in the developing world. The demand for female sterilization far exceeds the ability of most countries to provide services; therefore, the development of a rapid, effective, safe, nonsurgical method that can be performed by paramedical personnel remains a high priority.

For over a decade, Zipper and associates evaluated the transcervical instillation of quinacrine hydrochloride for effecting permanent sterilization. His initial animal studies (2) indicated that quinacrine selectively produced significant morphologic changes in the reproductive tract and caused per-

manent tubal fibrosis and occlusion in the rat. In clinical trials, he evaluated various doses, concentrations, solvents for the suspension and instillation schedules of quinacrine (3, 4).

Zipper's quinacrine solution schedule of three instillations of a solution of 1.5 gm of quinacrine powder suspended in 5 ml of 2% xylocaine was unsatisfactory since it resulted in an unacceptably high pregnancy rate and produced occasional transient toxic psychosis (a sudden increase in motor and psychomotor activity; auditory and visual hallucinations, delusions and the occasional presence of ideas of reference; gradual clouding of the sensorium, disorientation, amnesia for recent events and confabulation [1]). The solution method also created intrauterine pressure and involved the preparation of the solution immediately prior to insertion.

## MATERIALS AND METHODS

Quinacrine hydrochloride pellets have been developed to produce a delivery system that would bring the chemical into prolonged contact with the tubal ostia through delayed uterine retention and thus increase the probability of successful occlusion. Because the quinacrine pellet dissolves relatively slowly within the uterine cavity, the risk of rapid intravascular absorption present with the solution may be reduced.

Each quinacrine hydrochloride pellet has a cylindrical shape (Fig. 1) with a diameter of less than 4 mm. The pellets are compacted to contain about 10 mg of quinacrine per mm of length. Insertion is accomplished by placing the pellets in a plastic tube with a push rod positioned behind them. The tube is then passed through the cervical canal until the

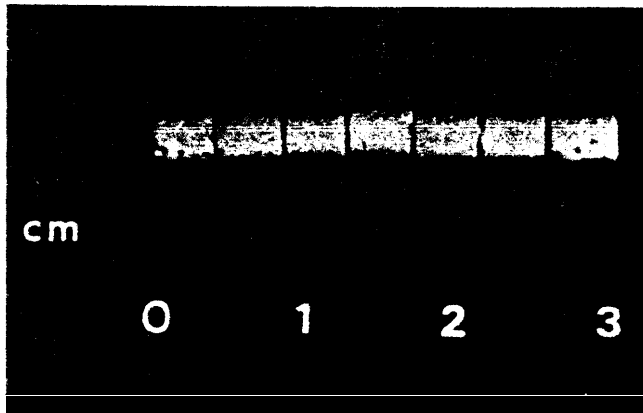


Fig. 1. Quinacrine pellets.

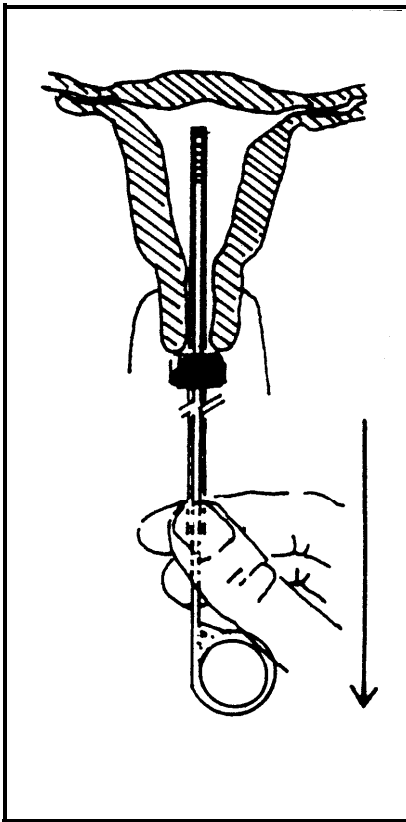


Fig. 2. Technique of quinacrine pellet insertion.

fundus is reached. Dilation is not necessary. The push rod is then held stationary, and the tube is pulled back over it to expel the pellets into the upper segment of the uterine cavity. After the pellets have been discharged, the inserter is removed. The procedure is essentially the same as inserting an IUD (Fig. 2).

From January 1977 through June 1978, 139 women giving informed consent at an outpatient clinic in Santiago, Chile, received three transvaginal insertions of 250 mg of quinacrine pellets preceded by a single pellet of 20 mg of sodium thiopental as their only means of contraception. Sodium thiopental, a hydroscopic agent, was used to increase the viscosity of the uterine fluid in an attempt to improve the intrauterine retention of the quinacrine.

Insertions were performed during the proliferative phase of three consecutive menstrual cycles. Clinical follow-up was scheduled at six and 12 months after the third insertion and at any time when complications or complaints occurred.

Only those women who requested sterilization for family planning reasons and who did not have a history of psychiatric disorders were selected as subjects. If the patient appeared to be unduly nervous or had any pelvic pathologic condition (except cervicitis), she was excluded from the study and either scheduled for a surgical sterilization procedure or provided with another method of contraception.

## RESULTS

The preliminary results obtained from this study indicate that the pellet method of quinacrine insertion is more effective than the quinacrine solution method (Table I). The unacceptably high pregnancy rate associated with the quinacrine solution instillation procedure that occurred in the month between the first and second instillation appears to have been eliminated (Table II). In addition, the pellet method appears to reduce the risk of transient toxic psychosis. No such event has been reported for the pellet patients, compared with 2% of quinacrine solution patients (Table III).

## CONCLUSIONS

Extensive research is being conducted to develop a simple method of nonsurgical female sterilization that can be offered by paramedical personnel in large-scale sterilization programs. Before any such method can be considered satisfactory, the following problems must be solved:

1. Tubal spillage and intravascular injection: Prevention of tubal spillage and intravascular injection is essential with most drugs because agents that cause sufficient tubal trauma to produce occlusion are also likely to cause peritoneal and systemic

Table I. Life-table pregnancy rates per 100 women completing three administrations of quinacrine solution and quinacrine pellets.

Months Since Treatment	Quinacrine Solution (N = 124) <sup>a</sup>			Quinacrine Pellets (N = 124) <sup>b</sup>		
	Woman-Months	Rate	SE	Woman-Months	Rate	SE
6	726	5.7	2.1	681	0.9	0.9
12	1372	9.1	2.6	1124	3.1	1.8
24	2317	10.9	2.9			

<sup>a</sup> Of the 140 patients completing three instillations of quinacrine solution, 124 returned for one or more follow-ups.

<sup>b</sup> Of the 127 patients completing three insertions of quinacrine pellets, 124 returned for one or more follow-ups.

Table II. Reasons women did not complete three administrations of quinacrine solution and quinacrine pellets.

	Quinacrine Solution (N = 200)		Quinacrine Pellets (N = 139)	
	No.	%	No.	%
<b>Reasons for not performing second administration</b>				
Pregnancy	18	9.0	1	0.7
Transient psychosis	4	2.0	0	0.0
Ovarian cyst	1	0.5	1	0.7
Amenorrhea	3	1.5	0	0.0
Adnexitis	1	0.5	0	0.0
Severe headaches	1	0.5	0	0.0
Patient choice	0	0.0	2	1.4
Patient failed to return	4	2.0	1	0.7
<b>Total</b>	<b>32</b>	<b>16.0</b>	<b>5</b>	<b>3.5</b>
<b>Reasons for not performing third administration</b>				
Pregnancy	23	11.5	0	0.0
Cervical synechia	0	0.5	0	0.0
Menorrhagia	1	0.5	1	0.0
Pelvic pain	0	0.0	2	0.7
Headaches	0	0.0	1	1.4
Patient choice	0	0.0	0	0.0
Patient failed to return	1	0.5	3	2.2
<b>Total</b>	<b>28</b>	<b>14.0</b>	<b>7</b>	<b>5.0</b>

reactions. The quinacrine pellet system seems to be an exception. Quinacrine is a noncaustic agent with known toxicology. The solid form of the pellets eliminates the need for forced liquid injection and the risk of rapid intravascular absorption is avoided.

2. Inadequate delivery system: Blind delivery systems are preferable to those requiring direct visualization. A blind delivery system that requires accurate delivery of the chemical agent to the tube is less preferable than one without this requirement.

The quinacrine pellet insertion system does not require localization or cannulation of the tubal ostia.

3. Multiple applications: A problem with all known blind procedures is that more than one application may be necessary. The pellet method of quinacrine hydrochloride requires three insertions. A study of 23 women scheduled for hysterectomies for uterine prolapse who voluntarily accepted the intrauterine insertion of 250-mg quinacrine pellets showed that each insertion occludes only about 63%

Table III. Complications/complaints associated with administrations of quinacrine solution and quinacrine pellets.

Complications/ Complaints <sup>a</sup>	Quinacrine Solution Instillations						Quinacrine Pellet Insertions									
	I (N = 200)		II (N = 168)		III (N = 140)		1 Z-Month Follow-up (N = 103)		I (N = 139)		II (N = 134)		III (N = 127)		12-Month Follow-up (N = 45)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Transient psychosis	5	2.5	1	0.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Menstrual																
Delayed menses	18	9.0	16	9.5	9	6.4	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
Menorrhagia	1	0.5	2	1.2	4	2.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pelvic	2					3.6										
PID	2	1.0	1	0.6	5	3.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Intense vaginitis		1.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
Leukorrhea	0	0.0	0	0.0	1	0.7	2	1.9	0	0.0	0	0.0	0	0.0	0	0.0
Urinary tract infection	1	1.0	1	0.6	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other transient complaints																
Pelvic/abdominal pain	34	17.0	19	11.3	22	15.7	2	1.0	12	8.6	14	10.4	4	3.1	1	2.2
Headaches	13	6.5	6	3.6	2	0.0	1	0.0	0	0.0	0	0.0	0	0.0	1	2.2
Dizziness	7	3.5	0	0.0	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0

<sup>a</sup> Multiple complications/complaints may be reported for each woman.

of the tubes (Bhatt R, Aparicio A, Davidson O et al, unpublished paper, International Fertility Research Program).

The IFRP is currently exploring alternate delivery systems, including the use of an IUD vector to better deliver the quinacrine to the tubal ostia.

### ACKNOWLEDGMENT

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