

CHEMICALLY INDUCED TUBAL OCCLUSION IN THE
HUMAN FEMALE FOLLOWING A SINGLE
INSTILLATION OF QUINACRINE

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ABSTRACT

In a case study of ten fertile women receiving a single intrauterine instillation of a suspension of Quinacrine, the six patients who did not have a hysterectomy 5 to 6 days later were found to have non-patent tubes when tested at least three weeks post-instillation. Five of these patients were using oral contraception prior to, during, and after treatment. Of the remaining four patients who underwent surgery within one week of instillation, three were found to have lesions suggesting tubal inflammation; none of these patients were using any-kind of contraception.

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INTRODUCTION

A simple method of sterilization has concerned physicians for many years. In particular, methods have been sought that could be used by paramedical personnel in developing countries. The intrauterine instillation of tubal occluding agents is a possible solution to this problem. Zipper has observed that Quinacrine has an occlusive effect on the intramural portion of the human fallopian tubes and that this effect appears to be permanent. However, he found it necessary to use two instillations of Quinacrine to obtain an occlusion rate of 84.3 percent as tested by tubal insufflation and pregnancy exposure (1). In this report we have studied tubal changes following a single instillation of Quinacrine as determined by tubal insufflation, hysterosalpingography and/or surgical pathology.

METHODS

All patients included in this study were volunteers who had requested sterilization. In three of these, bilateral vaginal tubal ligation was attempted but could not be completed for technical reasons. In the remaining seven patients vaginal tubal ligation was contraindicated, thus (see Table I) vaginal hysterectomies were indicated and the patients agreed to participate in this study in the interim. When possible, tubal patency was proved prior to instillation either by tubal insufflation or hysterosalpingogram (see Table I). Quinacrine was instilled in early or mid-cycle and was given in the out-patient department. One gram of Quinacrine (Ataric; Winthrop) was suspended in 6 ml of sterile water for injection and instilled into the uterine cavity via a flexible polyethylene cannula inserted through the cervix. In patients with a large cervical os, a perforated rubber stopper was fitted 1-1/2 inches behind the tip of the cannula to prevent reflux of the suspension. Since the capacity of the cannula is about 2 ml, only 4 ml (approximately 680 milligrams) of Quinacrine entered the uterus. Injection time was approximately one minute and the cannula was held in place for one or two minutes following injection to prevent reflux. However upon removal of the cannula, in most cases, some suspension was seen to reflux into the vagina.

Patients were kept under observation for at least an hour following the procedure. Follow-up was scheduled for the next month although some patients underwent surgery earlier (see Table III). In four patients, only pathological studies were done, two had clinical and pathological studies and the remainder

have been under clinical follow-up to the present time (Table II). Methods of interim contraception can be seen in Tables II and III.

TABLE I

CASES INCLUDED IN THIS STUDY

CASE #	AGE	PARITY	REASON FOR INCLUSION	PATENCY PROVED PRIOR TO INSTILLATION
1. (LB)	39	3013	failed vaginal tubal ligation	not done
2. (BC)	30	5025	obesity	not done
3. (SC)	32	2112	only right tube vaginally ligated	Rubin-pos.
4. (DC)	23	5006	vaginal hysterectomy	not done
5. (VP)	34	1132	vaginal hysterectomy	not done
6. (Rr)	34	4024	only right tube vaginally ligated	Rubin-pos.
7. (DR)	29	3023	vaginal hysterectomy	not done
8. (EB)	42	4004	obesity	Rubin-pos.
9. (ME)	37	4014	obesity	HSG-pos.
10. (MK)	21	3033	obesity	HSG-pos.

TABLE II

PATIENTS RECEIVING CLINICAL, FOLLOW-UP

CASE	OCCLUSION PROVED BY	TIME FROM INSTILLATION
2. (BC)*	Rubin -neg Pathology (see Table III)	5 months 6 months
3. (SG)	Rubin -neg Rubin -neg HSG -neg	1 month 3 months 7 months
6. (RR)	HSG -neg	7 months
8. (EB)	Rubin -neg HSG -neg	1 month 1 month
9. (ME)*	Rubin -neg Pathology (see Table III)	3 weeks 10 weeks
0. (MK)	Rubin -neg	3 months

All patients except #6 were taking oral contraceptives prior to, during and after treatment with Quinacrine.

*These patients underwent vaginal hysterectomies at 6 and 2-1/2 months post-instillation.

TABLE III

PATHOLOGICAL FINDINGS

CASE #	BIRTH CONTROL	TIME INTERVAL FROM INSTILLATION	PATHOLOGY OF FALLOPIAN TUBES
1. (LB)	none	5 days	L-no pathological changes R-focal obliteration of the lumen
2. (BC)*	O.C.	6 months	L-mild peritubal chronic inflammatory reaction R-narrowing with focal denudation of the mucosa
(DG)	none	6 days	L and R-focal acute exudative inflammatory isthmic portions
5. (VP)	none	6 days	L and R- no pathological changes
7. (DR)**	none	5 days	L-mild perisalpin-gitis R-no pathological changes
9. (ME)*	O.C.	10 weeks	L and R-segmental inflammatory stenosis of isthmic portions

*See footnote in Table II.

O.C. = combination oral contraceptives

**Received only 200 mg Quinacrine.

RÉSULTS

All 6 women followed clinically showed tubal occlusion following a single instillation of Quinacrine (Table II). Of the four women who were operated within one week of instillation; histological examination showed one with pathological changes in both tubes, two had changes in one tube **only** and one showed no changes (see Table III). Two other patients who had hysterectomy 2.5 and 6 months after instillation, upon histological examination were **found** to have gross pathological changes confirming their previous clinical findings of tubal occlusion. Pathological changes were confined to the intramural portion of the tube up to date no side effects or pregnancies have been observed in this group of ten patients. **There were** no changes in the menstrual pattern after treatment. There was no **intermenstrual** bleeding or menorrhagia.

DISCUSSION

The outstanding finding in this study was that the tubes of the patients who were examined at least three weeks following a single Quinacrine instillation were found to be occluded. Most of these women were using oral contraceptives prior to, during and after treatment. Of the patients examined within one week of instillation (none of them were using oral contraceptives), the tubal lesions varied from none to marked pathological changes. Zipper (1) used an endometrial cannula for instillation which did not occlude the cervix. We used a polyethylene cannula and made certain that no reflux occurred during instillation. Thus, higher intrauterine pressure was probably accomplished during the procedure and probably the Quinacrine suspension went through both fallopian tube openings.

It is also possible to speculate on the role of combination oral contraceptives as a potentiating agent in the action of Quinacrine. It was observed by Mahgoub et al. (3) that injected progestins cause a "stasis and supression" of the epithelial cells in the epithelium of the fallopian tube. Also, a decrease in tubal motility in vitro was obtained by the use of oral contraceptives by Jakobovits et al. (4). Both these observations suggest that oral contraceptives may have some **potentiating effect** by allowing a longer contact between the super-saturated solution of Quinacrine and the tubal epithelium. Since it is thought that the mechanism of action of Quinacrine as an **occlusive** agent is dependent upon its binding with DNA, we may speculate that the action of oral contraceptives may

allow a longer contact with this epithelium, thus increasing chances of penetration into the cell and subsequent binding to DNA. It has also been stated that this **binding** can be inhibited by an increase in zinc concentration (2). It is not known at the present time whether oral contraceptives have any effect on the zinc concentration in the epithelium of the human fallopian tube. In conclusion, our observations differ slightly from Zipper on the following points: (a) all patients with an interval longer than three weeks between a single instillation and testing had evidence of tubal occlusion; (b) most of our patients were using oral contraceptives at the time of instillation* (c) while Zipper used an endometrial cannula for instillation which does not completely occlude the cervix, we believe our technique of preventing cervical reflux during the procedure results in a higher intrauterine pressure which allows Quinacrine to enter both utero-tubal junctions in a single instillation. It must be realized that these preliminary findings are limited to a small number of women. The results obtained, however, justify further clinical investigation.

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