

CHEMICALLY INDUCED TUBAL OCCLUSION
IN THE HUMAN FEMALE USING
INTRAUTERINE INSTILLATION OF QUINACRINE

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H1N 120

ABSTRACT

Thirty healthy volunteers, 30 years-and older, received one or more intrauterine instillations of quinacrine (1 gm) in order to obtain a chemically induced occlusion of the Fallopian tubes. Prior patency of the latter was checked either by the Rubin test or by hysterosalpingography (in 8 patients). **Bilateral occlusion** occurred in 12 patients after the first instillation; this was shown by the Rubin test, done for all subjects 4 to 6 weeks after the procedure, and by hysterosalpingography in 11 out of the 12 patients with a negative Rubin test. ~~From~~ the remaining 17 volunteers (one opted out), 11 cases of occlusion were obtained after a second instillation. Three patients received a third instillation, with positive results in two. Thus bilateral occlusion was produced in **25 out of the 30** referred patients. So far 11 patients were seen in follow-up 6 to 8 months after the last instillation; in all cases hysterosalpingography confirmed the **long** lasting state of occlusion.

Accepted for publication May 23, 1975

INTRODUCTION

Zipper, Stachetti and Medel were the first to report on the occlusive effect of quinacrine on the Fallopian tube (1). They found it necessary to use two instillations to obtain a high yield of bilateral occlusion (84.3%). More recently, Davidson and Wilkins published ten cases treated by a single instillation of quinacrine; the proportion of complete occlusion is difficult to assess because of short follow-up (2). They speculated that two factors might be important to obtain successful results. The first is related to the use of a technique permitting the complete occlusion of the cervix from within the opening, so that no reflux should occur during instillation. As a second factor, they thought that the preceding administration of contraceptive medication would yield a higher percentage of occlusion because of the drug-decreasing effect on the motility of the tubes.

In this study, a new technique was devised for a better occlusion of the cervix in order to prevent any reflux of quinacrine. The sample of subjects included patients using and patients not using contraceptive medication. It was then possible to estimate the contribution of this factor on the final outcome. More than one instillation were performed when indicated; the results reflect the effects of one up to three quinacrine instillations.

METHODS

Patients

This paper reports on the first 30 patients who underwent our procedure. They were included in the study according to the following criteria: married female, between 30 and 45 years of age; asking for a voluntary sterilization because of medical or socioeconomical reasons: bilateral patency of Fallopian tubes as proven by a Rubin test (24 patients) or by hysterosalpingography (6 patients); good physical and mental health as determined by a complete medical history and physical examination; written consent from both spouses after a detailed explanation of the procedure by one of the authors. Excluded from the experiment were patients with cervicitis, those who had a previous caesarean section and pregnant subjects as checked by an immunological test.

The most often stated medical reason for the patients' request of a voluntary sterilization was their intolerance to contraceptive medication or to the use of an intrauterine device.

The first six subjects received particular attention. They were given their first instillation under fluoroscopic control in the department of radiology immediately after an phstersosalpingography. They were also submitted to routine pharmacological and biochemical tests. The results of the latter were normal both prior to and 4 to 6 weeks after the procedure. The other 24 patients were treated in the office.

Medication

For each instillation, one gm of sterile quinacrine chlorhydrate (Atabrine[®]) was suspended in 6 ml of water (35 ml would be needed to completely dissolve this amount of quinacrine), Atropine sulfate, at the dose of 0.4 mg per os, was added to the protocol after the observation of a vaginal reaction suffered by our first patient during the procedure. The reaction might have been secondary to the overflow of the irritant solution into the peritoneal cavity. The accessory administration of atropine was also thought to prevent an eventual muscular spasm at the utero-tubal junction which would hinder the active substance flow into the tubes. No special medication was needed for pain and only one patient received diazepam (5 mg) 30 minutes before the procedure because of her anxiety.

Procedure

After vaginal disinfection with Petadine[®] 1%, a sterile vaginal speculum was inserted. A local cervical anesthesia with carbocaine 3% (without ephedrine) was made and then a sterile pediatric indwelling catheter (no. 8) was inserted in the uterus. The balloon of the catheter inside the uterus was then inflated with 2 ml of sterile water. The catheter was pulled to check the total obstruction of the cervix from within. The solution (6 ml) of quinacrine was then instilled slowly over a period of five minutes and the pressure on the syringe was kept for an additional five minutes. Some reflux occurred after the catheter was removed ~~and~~ sanitary roll of paper was left in the vagina. The patient was kept under observation for another hour following the procedure.

Four to six weeks after the first procedure, the patient was seen again. A Rubin test was done and also an hysterosalpingography if the Rubin test was negative. If there was no occlusion proven, the instillation was repeated, using again 1 gm of quinacrine. The patient was scheduled again 4 to 6 weeks later and the procedure was repeated a third time if no occlusion was found.

When bilateral occlusion was shown, the patient was scheduled for follow-up 6 to 8 months later. Each time, a gynaecological examination was done and the patient had to answer a questionnaire for possible side effects regarding general health and gynaecological symptoms if any.

Occlusion of the Fallopian tubes on hysterosalpingography was graded from 0 to 4.

Grade 0: no occlusion at all; contrast medium found in uterus, tubes and abdominal cavity.

Grade 1: contrast medium found in the uterus and also in the abdominal cavity, but none in the tubes.

Grade 2: contrast medium found in the uterus and also in the tubes for some distance, but none in the abdominal cavity.

Grade 3: contrast medium found in the uterus and for a very short distance (1 cm or less) in the proximal portion of the tubes.

Grade 4: contrast medium found only in the uterus, none in the tubes.

RESULTS

The Table shows the results on the 30 patients; they are numbered in chronological order. Twenty-five patients had clinical evidence of tubal occlusion either by a Rubin test alone (4 cases) or by an hysterosalpingography (21 cases). Twelve patients needed only one instillation, 11 needed two and two needed three. Among the five patients found with no occlusion one received only one instillation (she refused further treatment) three received two instillations and one had three. So far, 3 patients are still waiting for their third instillation according to the protocol. Thus from a possible total of 30, 11 occlusions

TABLE.

TABULATION OF RESULTS

CASE #	AGE	PARITY Gr. Para AB	Prior Tubal Patency Proved by	Occlusion after 4 to 6 weeks	2nd Instil.	Occlusion after 8 to 12 weeks	3rd Instil.	Occlusion after 6 to 8 months
1. M.V.	31	5 3 2	HO	R+	Yes	R- H4	-	-
2. N.O.	31	3 3 0	HO	H4	-	-	-	H4
3. C.B.	30	3 3 0	HO	R+	Yes	R- H2	-	H3
4. F.B.	35	3 3 0	HO	R- H4	+	-	-	H4
5. M.C.	30	2 2 0	HO	R- H2	-	-	-	H4
6. L.P.	30	3 3 0	HO	R+	Yes	R- H4	-	H4
7. J.P.D.	34	4 4 0	R+	R- H4	-	-	-	-
8. Y.P.	15	220	R+	R-	I-I	-	I-I	-
9. R.R.	37	3 3 0	R+	R- H2	-	-	-	-
10. P.B.	34	2 2 0	Rt	Rt	Yes	R+	Yes	H4
11. C.A.	36	2 2 0	R+	Rt	Yes	R+ HO	Yes	R+
12. C.B.	30	2 2 0	Rt	R- H2	-	-	-	H3
13. L.R.	36	4 4 0	Rt	R+	Yes	R- H3	-	-
14. L.P.	36	4 4 0	Rt	Rt	Yes	-	R- H2	-
15. M.S.	33	2 2 0	Rt	R- H4	-	-	-	H4
16. C.G.	39	1 1 0	R+	R- H2	-	-	-	-
17. J.G.	38	3 3 0	R+	R+	Yes	R- H2	-	-
18. J.B.	35	3 3 0	HO	R+	Yes	R- H3	-	-
19. V.B.	34	3 3 0	R+	R+	Yes	R- H4	-	-
20. G.M.	30	3 3 0	R+	R+	Yes	R+ HO	-	-
21. Y.L.	32	3 3 0	R+	R+	Yes	R- H4	-	-
22. J.Be	36	5 4 1	R+	R- H2	-	-	-	H2
23. P.A.	41	3 3 0	R+	R+	Yes	R+ HO	-	-
24. H.B.	42	3 3 0	R+	HO	-	-	-	-
25. C.N.	35	3 2 1	R+	R- H3	-	-	-	H2
26. L.G.	33	2 2 0	R+	R- H4	-	-	-	-
27. O.P.	30	2 2 0	R+	R+	Yes	R+	Yes	H4
28. L.L.	33	3 3 0	R+	R+	Yes	R+ HO	-	-
29. L.T.	34	2 2 0	R+	R+	Yes	H2	-	-
30. N.H.	33	1 1 0	R+	R+	Yes	H4	-	-

+ = RUBIN TEST POSITIVE (+)
 - = RUBIN TEST OR NEGATIVE (-)
 H = HYSTEROSALPINGOGRAPHY
 GRADE 0, 1: Patency of both tubes
 GRADE 2, 3, 4: occlusion

occurred after the first instillation; 22 out of 29 possible cases were successful after one or two instillations and 25 out of 26 possible occlusions were produced on patients who received up to 3 instillations.

Among the 25 patients with occlusion, 10 were taking contraceptive medication before, during and after the procedure and 15 were not protected against pregnancy by any means. For the 5 patients without occlusion, the respective frequencies were 2 and 3. Apart from the first patient who experienced vaginal reaction during the instillation, 4 patients had side effects. They were characterized by abdominal pain of variable intensity and moderate abdominal distension. These symptoms lasted from 1 to 5 days and disappeared without any sequelae and necessitated only mild analgesics. One of the patients with side effects was very nervous and had to be hospitalized. Mild chemical inflammation on the peritoneum was diagnosed because of her mild fever, abdominal tenderness and slight distension. This happened on her second instillation; no pain was reported on the first. All laboratory and radiological examinations (flat plate i.v. pyelography, barium meal and barium enema) failed to show any pathology. She was treated with bed rest and mild analgesics. Discharged from the hospital three days later, she has been well ever since. Control hysterosalpingography after 6 weeks showed total bilateral tubal occlusion.

DISCUSSION

The study shows that we obtained an 83.3% occlusion rate, about the same as Zipper's. With only one instillation, the percentage is 43.3%; it rises to 76.6% with two instillations. Depending on the response of the three patients still waiting for their third instillation, the overall percentage may even be higher than 83.3%. So far, hysterosalpingography in 11 patients after 6 to 8 months shows a definite tubal occlusion.

In the six patients from whom the first instillation was done under fluoroscopic control, it was obvious that the quinine solution entered the two Fallopian tubes: the contrast medium was cleared progressively as the syringe piston was pushed. Although the entering of the solution in both tubes is necessary, it alone is not sufficient for achieving complete occlusion; more than one instillation were needed in 3 of these first patients.

The contrast medium was completely cleared from the tubes before the end of the instillation; thus the quinacrine solution must have overflowed into the abdominal cavity in all 6 patients under fluoroscopy. Three of these patients had significant abdominal pain when the instillation was done immediately after salpingography. Since only one other patient manifested this symptom (under different treatment conditions), it is possible that the contrast medium was involved in the production of pain. Hence only one case of pain was clearly associated with quinacrine alone. Including all possible cases with atropine in the procedure, the incidence of side effects was 14% (4/29), with 95% confidence limits of 4 and 31%.

Occasional spasms of the tubes could be observed under fluoroscopy; they corresponded to augmented resistance against the pushing thumb of the gynaecologist. Atropine may have helped to overcome these spasms without difficulty.

The influence of contraceptive medication, postulated by Davidson and Wilkins (2), was not confirmed in this study. The success rate of patients receiving such a medication does not seem significantly different from the rate of those not receiving it.

The procedure is simple and does not seem to cause serious side effects. Since inflammation was always found after a single instillation (2), one should not wait for a decrease of the tubal reaction; a higher percentage of occlusion might be obtained if three instillations were to be performed at weekly intervals. This procedure would certainly deserve to be tried on patients when surgery under general anesthesia is ruled out for medical or technical reasons.

REFERENCES

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