

A COMBINATION APPROACH TO THE TREATMENT OF SEVERE ENDOMETRIOSIS : OPERATIVE LAPAROSCOPY AND DANAZOL

M.L.GOENKA

SUMMARY

Fiftysix patients with severe endometriosis (stage III and stage IV) were treated with pelviscopic surgery and high dose danazol (600 to 800 mg). Pelviscopic surgery was done in two to three sittings at 3 months interval. Danazol was given concomitantly for 6-9 months. 39 patients conceived with a pregnancy rate of 69.6%. There were no surgical complications. None of the patients had any serious side effect due to high dose of danazol.

INTRODUCTION

Endometriosis is the commonest cause of infertility in female over the age of 25 years, since endometriosis is seen in 15 to 40% of all infertile women. Earlier it was thought to be a disease of white women but since the introduction of diagnostic laparoscopy, it is found that the disease is equally prevalent in Asia and Africa. From April 1983 to September '90 we have preformed 1150 diagnostic laparoscopies for infertility patients and endometriosis was found in 264 cases with an incidence of about 23%.

The exact cause of infertility in patients with endometriosis is unknown. It is difficult to say whether endometriosis causes infertility or long periods of infertility lead to endometriosis. The

mechanical factor definitely plays a role in severe endometriosis. The tubes are usually patent, but peritubal & periovarian adhesions are frequently found with an adherent and retroverted uterus. This results in inadequate tubo-ovarian motility and imperfect ovum acceptance by fimbriae. Extensive destruction of ovarian tissue or replacement by endometrial cysts obviously can interfere with ovulation, while extensive periovarian adhesions can prevent the normal egress of the ovum.

There is no consensus as to the optimal form of treatment for endometriosis. Laparoscopic cauterisation of endometriosis for fertility with electrocautery and more recently, laser, has been advocated by several authors (with pregnancy reported to occur in 50% to 75% patients.) We have combined laparoscopic cauterisation with medical therapy (DANAZOL).

Dept. of Obst. & Gyn. Relief Nursing Home & Maternity Clinic, Guwahati.

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MATERIAL AND METHODS

Over a period of three years from July 1987 to September '90 fifty six patients having severe (stage III and stage IV endometriosis according to revised classification of AFS) endometriosis were treated with laparoscopic cauterisation and danazol. Thirty one (55.4%) patients were having stage III and twenty five (44.6%) were having stage IV endometriosis.

RESULTS

All couples underwent a complete infertility evaluation that included assessment of ovulatory status, semen analysis, post coital testing, hysterosalpingography, hysteroscopy and diagnostic laparoscopy with chromotubation to assess the tubal status. Patients who had an ovulatory factor contributing to infertility were included in the analysis. Patients with male factor infertility (less than 20 million sperm per ML, less than 50% motility, or less than 60% normal morphology) were not included. Patients with Azoospermia were included.

The mean age of the patients was 30.5 years with a range of 22 to 39 years. Fifty four patients were of primary infertility and two were having secondary infertility. The mean duration of infertility was $4.2 \pm$ years. In 48 patients endometriosis was the only cause for infertility and 6 patients had associated anovulation. 2 patients of stage III endometriosis had azoospermia.

During the first diagnostic laparoscopy Table I, once the diagnosis of endometriosis was

made, peritoneal endometriotic implants were coagulated with bi-polar cautery. Lysis of adhesions was performed, using electrocautery or blunt techniques. The cautery was applied until the lesion and surrounding tissue blanched. The adhesions were first co-agulated and then incised with scissors. Chocolate cysts were initially aspirated of their contents. Their wall co-agulated by electrocautery and incised with scissors. They were irrigated with heparinised lactated Ringer's solution (5,000 U heparin in 1 L). The diluted ovarian contents were then suctioned from the pelvis with a 5 mm suction irrigation probe. Whenever possible, the capsule was stripped away from the ovarian stroma using blunt dissection. If the capsule could not be teased free, the internal cyst lining was then cauterised with electrocautery and left open. At the end of each procedure, after confirming adequate hemostasis, 200 to 300 cc of fresh heparinised Ringer's solution was left intraperitoneally.

We preferred bipolar electrocautery because unipolar cautery have 1) Unpredictable route of the electrical current and its potential thermal damage and necrosis to vital structures (e.g. bowel) and 2) the relatively large area of thermal damage and necrosis that is not visible at the time of surgery.

All procedures were done under general endotracheal anesthesia. A standard three-or four-puncture technique was used. No stitches were given to abdominal wounds. All the patients were discharged on second post-operative day. Patients were made ambulatory after 6-8 hours of

Table - I

Period of study	Stage of disease	Number of patients
July 1987 to September 1990	Stage III	31 (55.4%)
	Stage IV	25 (44.6%)

operation. Atmospheric air was used for pneumoperitoneum. There was no intra-operative and post-operative complication in any of the cases. Most patients had vomiting on first day and shoulder pain for 3-4 days.

The danazol was started in a dose of 600 mg daily. Most of the patients had break-through bleeding in first month but later on complete suppression of menstruation was possible in 54 patients. 2 patients of stage IV endometriosis had intermittent break-through bleedings where dose of danazol was increased to 800 mg daily. In case of stage IV endometriosis having dense adhesions with involvement of intestines and complete obliteration of POD, danazol was started in a dose of 800 mg daily. As the half life of danazol is only six hours, it was given in equally 3 or 4 divided doses.

Second pelviscopic surgery was done after 3 months treatment of danazol. During second pelviscopic surgery most adhesions between ovaries, tubes, broad ligaments and uterus could be separated even by blunt dissection with probe and atraumatic holding forceps. These separated area were cauterised to stop bleeding and to prevent adhesion formation.

Complete adhesiolysis was possible after second pelviscopic surgery in 28 patients of stage III and 10 cases of stage IV endometriosis. In these cases danazol was further continued for 3 months in same dose of 600-800 mg daily.

In remaining patients danazol was continued in same dose and third pelviscopic surgery was

performed after 3 months of second. Complete adhesiolysis and fulguration of all endometriotic implants was possible in remaining three patients of stage III and thirteen patients of stage IV endometriosis. Two remaining patients, where adhesiolysis was no possible even at third pelviscopic surgery, had almost frozen pelvis. Small intestines, pelvic colon, uterus, ovaries were so firmly adherent to each other that even laparotomy did not help much in removing these dense adhesions. In all these 18 patients danazol was continued for another 3 months (total 9 months), in the same dose of 600-800 mg daily.

All patients above the age of 35 and patients having ovulatory dysfunction were followed by ovulation stimulation and intra-uterine insemination. AID was done in two patients having azoospermia.

Danazol was increased to 800 mg/day (200 mg QID) if there was no improvement at second pelviscopic surgery and three months of treatment with 600 mg of danazol.

The pregnancy rate (PR) for the patients is shown in table III. PR ranged from 71% in stage III to 68% in stage IV disease with an overall PR of 69.64% of the 39 pregnancies two resulted in spontaneous abortion. Both patients conceived again and had term deliveries. There was no case of ectopic pregnancy. Two pregnancies resulted in patients who had laparotomy for excision of endometriosis 2 years before operative laparoscopy.

There was no significant difference between

Table - II

Correlation between No. of Pelviscopies and Achievement of Complete Adhesiolysis

Pelviscopy	No. of patients (Stage - III)	No. of patients (Stage - IV)	Total
Second	28	10	38 (64.28%)
Third	03	13	16 (28.57%)

Table - III

Incidence of Post - Treatment Pregnancies

Stage of disease	No. of patients treated	No. of patients conceived	PR in %	Over - all PR %
Stage III	31	22	71%	69.6%
Stage IV	25	17	68%	

patients with anovulation (after ovulation induction) and those who ovulated normally regardless of the stage of disease. AID was done in the two patients with azoospermia and both conceived within six months.

The mean length of follow-up was 7.9 months for all patients. A mean time interval from stoppage of danazol to conception was 5.9 months with a range of 1 to 25 months. Of the total number of patients who conceived, 70% did so within 6 months and 90% within 1 year.

DISCUSSION

In severe endometriosis there are too much of dense fibrous adhesions which are mostly difficult to deal with in one sitting. Concomitant use of high dose (600 to 800 mg) danazol will soften the adhesions. Most endometriotic implants will shrink and the pelvis becomes less congested. During second pelviscopic surgery adhesions

can be removed with much ease and there is little oozing from the raw surfaces. It has been seen that in 95% cases there was no readhesion. The reason being early ambulation, less tissue handling, no exposure to atmosphere, no infection.

Even after complete adhesiolysis danazol was continued in same doses (600 to 800 mg) for three months more to treat nonpigmented subtle endometriotic lesions, microscopic foci, lesions in difficult areas like in the course of ureter, major vessels and bowels. This will also help in proper healing of raw areas after adhesiolysis.

In conclusion, there is presently much interest in advanced operative laparoscopy both for endometriosis and other pelvic pathology. Our encouraging results in this series without complication confirm that severe endometriosis can be successfully treated with pelviscopic surgery and danazol.