

Original Article

LONG TERM OUTCOME OF PATIENTS WITH ENDOMETRIOSIS ON MEDICAL TREATMENT

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Objective: To evaluate long term outcome of patients with endometriosis on medical treatment (OCP's, progestin, clomiphene citrate according to need of patients), in terms of symptomatic relief, successful conception, recurrence & treatment failure.

Material & Methods: This quasi experimental study was conducted in Shalamar Hospital Lahore. All patients who had confirmed diagnosis of endometriosis by laparoscopy or by laparotomy were included in the study after informed consent. Type of medical management was decided according to the need of the patients. The patients who did not want to conceive were given medical treatment in the form of combined oral contraceptive pills or progesterone. Patients who wanted to conceive, were given clomiphene citrate. Patients were followed up for 1 to 9 years. Study outcome was expressed in terms of symptomatic relief, pregnancy, recurrence and treatment failure. Data was analyzed using SPSS version 16.

Results: Initially, there were 94 patients who had confirmed endometriosis and were included in the study. Out of these, 18 patients lost follow up, and were excluded from study. The mean age of these patients was 25 ± 4.73 years and 50 percent presented with pelvic pain and 36% with infertility. They were followed for 1-9 years. The mean duration of follow up was 4.37 ± 2.29 years. 61.8% cases became symptom free, 15.8% conceived successfully, whereas 9.2% had persistence of pain. 11.8% had recurrence rate over 12-14 months after discontinuation of medical treatment.

Conclusion: Long term follow up of patients with endometriosis showed that medical treatment of endometriosis with COCPs, progestogens, and clomiphene citrate has promising results with less than 20% cases requiring other modes of treatment.

Keywords: Long term follow up, Endometriosis, COCPs, Progestogens, Clomiphene citrate.

Introduction

Endometriosis is a common, benign, chronic gynaecological disorder in which endometrium like tissue is present outside the uterus^{1,2} which results in substantial morbidity, including pelvic pain, progressive dysmenorrhea, infertility and repeat surgeries.^{2,3} A definite diagnosis of endometriosis is rarely possible in general practice. There is no diagnostic test for diagnosis of endometriosis and no diagnostic strategy is supported by evidence of effectiveness, so laparoscopy is the gold standard for diagnosis of endometriosis.^{4,5} The primary goal of medical treatment is to halt growth and activity of these ectopic lesions which help to resolve symptoms, encourage fertility, eliminate endometrium like lesions and restore anatomy of pelvis.² The various therapies available, include combined oral contraceptive pills (COCPs), progestogens, danazol, gonadotrophin releasing hormone analogue, (GnRH-analogue) gestrinone. All are equally effective, and have shown similar efficacy.⁶ Combined oral contraceptive pills and progestogens are drugs of

choice because of safety profile, tolerability and cost.⁷ Gonadotrophin releasing hormone analogues are very expensive whereas danazole is associated with androgenic side effects.⁸ Clomiphene citrate has its own role in patients who desire fertility.⁹ As endometriosis is present throughout reproductive life, if not monitored and treated properly recurrence rate is high. This study was designed to see response of simple, easily available cheap medication (OCP's, progestins, clomiphene citrate according to need of patients) and then followed and monitored to study its long term outcome in terms of symptomatic relief, conception rate, recurrence and treatment failure.

Material & Methods

This quasi experimental study was done in Department of Obstetrics and Gynecology Shalamar Hospital Lahore from January 2001 to 31st December 2009. All of patients, who underwent either laparoscopy or laparotomy and had a confirmed diagnosis of endometriosis on

direct visualization of chocolate coloured/ powdered burn lesions, were included in the study. Patients in whom endometriosis was not confirmed by direct visualization using laparoscopy or laparotomy were excluded from the study. Patients who had other associated problem besides endometriosis e.g fibroid were also excluded from the study.

All patients who fulfilled the inclusion criteria were recruited after informed consent. Type of medical management was decided according to the need of the patients. The patients who did not want to conceive were given medical treatment in the form of combined oral contraceptive pills, progesterones; patients who wanted to conceive were given clomiphene citrate. These patients were followed up

for 1 to 9 years to study outcome in terms of symptomatic relief, pregnancy, recurrence and treatment failure. Data was analyzed using SPSS version 16.

Results

Initially, 94 patients with confirmed endometriosis were included in the study. Out of these, 18 patients lost follow up and were excluded. The mean age of these patients was 25 ± 4.73 years. 50 percent presented with pelvic pain and 36% with infertility. They were followed for 1-9 years & mean duration of follow up was 4.37 ± 2.29 years. **Table 1** shows percentage of patients with symptomatic improvement, pregnancy, recurrence, persistent pain and

Table-1: Outcome of patients with endometriosis after medical treatment.

Variables	Response Seen		No Response seen	
	No.	Percentage	No.	Percentage
Symptomatic relief	47	61.8	29	38.2
Successful conception	12	15.8	64	84.2
Recurrence	09	11.8	67	88.2
Persistent Pain	07	9.2	69	90.8
Miscellaneous	07	9.2	69	90.8

Discussion

Endometriosis is a chronic, progressive inflammatory disease characterized by endometrial lesions, cyst, or adhesions in pelvic cavity causing chronic pelvic pain and infertility in women of reproductive age.^{10,11} In our study the mean age of patients was $25 + 4.73$ years. In one study conducted at Karachi only 7% of patients with endometriosis were between 20-30 years.¹² 50% patients had complaint of chronic pelvic pain and 36% presented with infertility. A study done at Islamabad showed that frequency of endometriosis in infertile women was 24%.¹³

Although various drug options are available for endometriosis other than COCPs and progestogens like danazol, GnRH-analogue, gestrinone etc, the rationale for use of COCPs and progestogens in our study was that all therapies (medical) available for endometriosis are equally effective.⁶ Secondly COCPs and progesterones are drug of choice because of safety profile, tolerability, easy availability and low cost.^{7,14} Thirdly COCPs and progesterones reduce the nerve fiber density and nerve growth factor and nerve growth factor receptor p 75 expression in peritoneal endometriotic lesions, thus relieving pain related to endometriosis.¹⁵ Regarding GnRH analogue, they are very expensive and there is

little or no difference in the effectiveness of GnRH against and with other medical treatment for endometriosis.¹⁴ Androgenic effect of danazol limits its use.⁸ So in our study COCPs and oral progesterones were given to patients with proven endometriosis and were followed initially after one month, then three months, then six months and then on yearly basis. Unfortunately during follow up 18 patients were lost and they were excluded from the study. 62% of patient got symptomatic relief from pain, dysmenorrhea or dyspareunia with COCPs and progesterones.

Regarding the effectiveness of ovulation suppression endometriosis agents (COCPs, progestogens) in the treatment of endometriosis associated subfertility, there is no evidence of benefit in the use of ovulation suppression in women with endometriosis who wish to conceive.¹⁶ So we used clomiphene citrate for ovulation induction immediately after laparoscopic confirmation of endometriosis as was done by Parveen N et al.⁹ Out of 36% of the patients who had infertility and given clomiphene citrate, 16% conceived successfully. But we did not have follow up about pregnancy

outcome. (It was not the objective of our study). Endometriosis is one of most common gynaecological disease which persists throughout reproductive life; long term follow up is required to know about recurrence. Although surgical and endocrine therapies successfully suppress pelvic pain it often recurs after the completion of treatment.¹⁷ Recurrence rate was found to be 12% in our study over a mean follow up period of 4.5 ± 2.29 years. Guo SW reported recurrence rate of endometriosis as 21.5% at 2 years and 40-50% at 5 years.¹⁸ 9.2% of cases (4 patients) had persistent pain with use of COCPs and progestogens which we labeled as treatment failure; these patients required other drugs such as danazol or GnRH agonist or repeat surgery⁷ & 3 patients were advised for IVF treatment (In Vitro

Fertilization) as IVF is an effective treatment option for infertility in severe endometriosis.¹⁹

Conclusion

Long term follow up of patients with endometriosis showed that medical treatment of endometriosis with COCPs, progestogens and clomiphene citrate has promising results with less than 20% cases requiring other modes of treatment.

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