# Goserline Versus Danazol in the Treatment of Endometriosis

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**Objective:** The objective of this study was to achieve symptoms relief of endometriosis with a drug having better efficacy and least side effects. **Study Design:** Experimental. **Place & Duration of Study:** Lady Willingdon Hospital, Lahore from March, 2003 to Feb. 2005. **Subjects & Methods:** The trial was conducted on two groups; one group (n = 20) received goserline and other group (n=20) received danazol for 6 months. Patients were followed for relief of symptoms including dysmenorrhoea, dyspareunia, lower abdominal pain and menstrual irregularity and appearance of side effects. **Results:** The results depicted that in Danazol group 50% pain relief was found in 5 patients (25%) while in goserline group in 4 patients (20%). 75% pain relief was seen in 7 patients (35%) in danazol group and 8 patients (40%) in goserline group. 100% of improvement in pain found in equal number of patient that is 8(40%) in both groups. Both drugs were effective in pain relief (P >0.05), Goserline had less side effects as compared to Danazol (P<0.05). **Conclusion:** Goserline and Danazol are equally effective in symptomatic relief of endometriosis while side effects favoured use of GnRH agonist.
**Key words:** Danazol, Goserline, Endometriosis.

Endometriosis is often a perplexing medical condition for both the physician and the patient. The symptom can be severe enough in many patients to interfere significantly with normal life and justify treatment[1]. The dependence of endometriotic tissue for its continued growth on ovarian steroid hormones, particularly estrogen has resulted in medical treatment aimed at inducing ovarian suppression[2]. The development of treatment strategies according to the need of patient is highly desirable.

The pharmacological therapies currently include combined oral contraceptives, danazol, GnRH analogue, progestin. Although, these agents show efficacy in relieving pain, all differ in their side effects making it difficult to achieve balance between efficacy and safety[3].

Danazol which is an isoxazole derivative of 17 α ethinyl testosterone with androgenic and anabolic properties has been first choice by many gynaecologist because of its proven efficacy, however, not well tolerated by patients.

Continued exposure of the pituitary gonadotropes to agonistic analogues of gonadotrophin releasing hormones (GnRH-a) result in down regulation with resultant reduction in circulating serum gonadotrophin levels and inhibition of ovarian steroidogenesis.

These effects thus offered alternative medical therapy for endometriosis which is most popular preparation at present time. The objective of this study was to achieve symptoms relief of endometriosis with a drug with better efficacy and least side effects.

**Patients and Methods:** This was experimental study carried out on 40 patients in Lady Willingdon Hospital Unit-III from March. 2003 to Feb. 2005. Convenience sampling method was used.

**Inclusion Criteria**: All patients where the diagnosis of endometriosis was made at Laparoscopy or Laparotomy, included in the study.

**Exclusion Criteria:** Patients with poor compliance or who required radical surgery as primary treatment because of advanced disease and patients with recurrent disease.

**Methodology:** Patients fulfilling the inclusion criteria selected. Evaluation of patient was done by detailed history, examination and investigations. Diagnosis of endometriosis was made at Laparoscopy or Laparotomy. Patients were randomized into two group to receive either goserline (n=20) 3.6mg S/C monthly or danazol capsule (n=20) 200mg three and four times a day. No hormonal agents were allowed during 8 weeks before starting therapy and barrier contraception advised. Treatment started between one to seven days of menstrual cycle. Patients were followed for 6 months for dysmenorrhoea dyspareunia, Lower abdominal pain and menstrual irregularity and adverse effects (headache, depression, weight gain, hirsutism, acne, oily skin/hair, voice changes, increased appetite, reduced breast size and libido, psychological upset, vaginal bleeding, hot flushes and atrophic vaginitis. Data was analysed on SPSS and tests of significance applied.

**Results:**

In Danazol group patients (n=20) received Danazol and in Goserline group (n=20) received goserline accetate. The age of patients ranged from 18-40yr mean ± SD(28.4 ± 6.15). Endometriosis was most common in age group of 28-37 years. There were 14(35%) parous and 26(65%) nulliparous patients. Presented with different symptoms including Lower abdominal pain in 36 patients (90%), dysmenorrhoea in 34(85%), Dyspareunia and infertility in 28(70%) and menstrual irregularly in 8 patients (20%). (Table 1)

Among the patients having Lower abdominal pain, 9(25%) had mild pain, 16(44%) had moderate and 11(31%)had severe pain.

Table I.Frequency of symptoms of Endometriosis

| Symptoms | Number | Percentage |
|---|---|---|
| Lower abdominal pain | 36 | 90 |
| Dysmenorrhoea | 34 | 85 |
| Dyspareunia | 28 | 70 |
| Infertility | 28 | 70 |
| Menstrual irregularity | 8 | 20 |

*(P >0.05) NS*

Table II shows that in Danazol group 50% pain relief was found in 5(25%) patients while in goserline group 4 (20%) patients. 75% pain relief was seen in 7 patients (35%), in Danazol group and 8 patients (40%) in goserline group. 100% of improvement in pain found in equal number of patients 8(40%) in both groups. The statistical analysis of results showed, that both drugs were effective in pain relief (P>0.05).

Table II: Comparison of pain relief by Danazol Vs Goserline in patient of Endometriosis

| Pain relief | Danazol Group n=20 | | Goserline Group n=20 | |
|---|---|---|---|---|
| 50% | 5 | 25% | 4 | 20% |
| 75% | 7 | 35% | 8 | 40% |
| 100% | 8 | 40% | 8 | 40% |

*(P > 0.05) N.S*

Although menstrual irregularity was least likely symptoms, (Table II). Statistically, there was no significant difference in correcting menstrual irregularity in both drugs (P>0.05) (Table III).

Table III: Correction of menstrual irregularity by Danazol Vs Goserline in patients of Endometriosis

| Correction of menstrual irregularity | Danazol Group (n=3) | | Goserline Group (n=5) | |
|---|---|---|---|---|
| 25% | 1 | 33.3% | | |
| 50% | 1 | 33.3% | 3 | 60% |
| 75% | - | | 1 | 20% |
| 100% | 1 | 33.3% | 1 | 20% |

*(P>0.05)*

The adverse effects reported in study are summarized in Table IV.

Androgenic side effects were more common in patients receiving danazol including weight gain, hirsutism, acne, oilyskin/hair, increased appetite, and reduced breast size (P <0.05) where as estrogen deficiency symptoms were more common in patients treated with goserline including hot flushes, psychological upset and atrophic vaginitis.

Table IV: Side effects of two drugs

| Side effects | Danazol Group n=20 | | Goserline Group n=20 | | P.Value |
|---|---|---|---|---|---|
| Headache | 17 | 86% | 13 | 65% | P>0.05 |
| Wt gain | 16 | 80% | 2 | 10% | P<0.05 |
| Hirsutism | 16 | 80% | - | - | P<0.05 |
| Reduced breast size | 14 | 70% | 5 | 25% | P<0.05 |
| Hot flushes | 7 | 35% | 19 | 95% | P<0.05 |
| Increased appetite | 13 | 65% | - | - | P<0.05 |
| Depression | 13 | 65% | 12 | 60% | P>0.05 |
| Acne | 14 | 60% | - | - | P<0.05 |
| Oily Skin/hair | 8 | 40% | - | - | P<0.05 |
| Reduced Libido | 6 | 30% | 7 | 35% | P>0.05 |
| Psychological upset | 2 | 10% | 8 | 40% | P<0.05 |
| Irregular bleeding | 2 | 10% | 4 | 20% | P>0.05 |
| Voice changes | 1 | 5% | - | - | P>0.05 |
| Atrophic Vaginitis | - | | 6 | 30% | P>0.05 |

**Discussion:**

Endometriosis is a common condition in the reproductive years with a peak incidence between 30-45 years of age, although it is increasingly being diagnosed in much younger women as the threshold for investigations for gynaecological symptoms utilizing diagnostic Laparoscopy has altered[4,5]. In this study endometriosis was more common in the age group of 28-37 years. The frequency of symptoms of endometriosis were lower abdominal pain (90%), dysmenorrhoae (85%), dyspareunia and infertility (70%), incontrast, Shaw described the likely frequency of symptoms of endometriosis as dysmenorrhoea (60-80%), lower abdominal pain (30-50%), dyspareunia (25-40%)[4]. Vassiliades addressed that endometriosis is tightly linked to infertility[6]. The patient were divided into two group, one received danazol and other group received GnRH a for at least 6 months.

Danazol which is isoxazole derivative of 17 α ethinyl testosterone causes suppression of hypothalamic pituitary axis with interference in pulsatile gonadotrophin secretions and inhibition of the mid cycle gonadotrophin surge but no change in basal gonadotrophin level. There is direct inhibition of ovarian steroidogenesis and competitive blockage of androgen, estrogen and progesterone receptor in the endometrium. An increase in free testosterone occurs because of reduction in sex hormone binding globulin which is responsible for androgenic side effects[4]. On the other hand, the GnRH analogues induce pituitary gonadotrophin desensitization via down regulation of GnRH receptors and an eventual state of hypogonadotrophic hypogonadism.

This study revealed nearly equal symptomatic relief in both drug groups. Barbiere and Evan described that Danazol's efficacy in treating mild to moderate endometriosis is equivalent to that of a variety of GnRH

agonist. More than 80% of patients experienced pain relief in two months of treatment[7,8]. Two randomized trial by Lemay, Malta & Shaw addressed that symptomatic improvement was seen in 72-90% of patient[9,10,2].

Similarly, Rock & Truglia concluded in their studies that goserline is as well tolerated and as effective as danazol in the treatment of endometriosis[11]. Comparable results were produced in a double blind randomized clinical trial done by Wheeler & Knittle in 1993[12].

There was marked difference of side effect in both drugs, there were significantly more androgenic side effects including weight gain, hirsutism, acne, oily skin/hair, increased appetite, reduced breast size in danazol group ($P<0.05$) Table IV. Barbiere et al reported that 85% of patients had androgenic side effects[7,13].

In contrast, the Goserline group showed hypoestrogenic side effects including hot flushes, atrophic vaginitis (Table IV).

Matta and Shaw proved that both symptomatic relief and resolution of endometrial deposit, there was no significant differene in comparative trial between GnRHa and danazol. However, the patients acceptability and the profile of side effects may be slightly in favour of GnRH analogues[10,14].

**Conclusion:**

Goserline and Danazol are equally effective in symptomatic relief of endometriosis while side effects pattern favoured use of GnRH agonists.

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