

Evaluating the Efficacy of Levonorgestrel Intrauterine System and Danazol for Relief of Postoperative Pain in Endometriosis

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ABSTRACT

Introduction: Endometriosis is an oestrogen-dependent disorder, manifests during reproductive years and is associated with pain and infertility. There is considerable debate about the effectiveness of various interventions for pain relief.

Aim: To evaluate the efficacy of Levonorgestrel Intrauterine System (LNG-IUS) and Danazol in postoperative pain relief for patients with endometriosis.

Materials and Methods: Hundred patients with diagnosis of endometriosis, who were treated laparoscopically, entered the study to receive either danazol (600 mg once daily) or LNG-IUS (inserted during immediate post operative period) postsurgery,

for pain relief. Patients were analysed for pain relief according to VAS score and recurrence of disease using ultrasonography at third and sixth months of follow up.

Results: There were 50% patients in stage IV of endometriosis. Majority of them presented with complaint of infertility (49%) and pelvic pain (43%). It was observed that LNG-IUS was significantly more effective in relieving pain compared to danazol (65.2% vs 38.0%, $p < 0.05$). Recurrence rate was significantly lower in LNG-IUS users compared to other group.

Conclusion: LNG-IUS was found to be more effective in relieving pain compared to danazol.

Keywords: Infertility, Pain relief, Pelvic pain

INTRODUCTION

Endometriosis is an oestrogen-dependent chronic disease that results in substantial morbidity like pelvic pain, infertility and multiple operations. Its prevalence is significantly high in reproductive age group [1]. Timely diagnosis and treatment is very important not only for disease-associated pain and infertility, but also for saving the women from future risk of cancer, as these patients are at higher risk of cancer and autoimmune disorders [2]. There is considerable debate over the effectiveness of various interventions for pain relief [3].

Medical interventions are effective but are not curative and more-over treatment is required for long term or until the woman desires pregnancy. Pain can also be treated by excising peritoneal implants, deep nodules and ovarian cysts or inducing lesion suppression by abolishing ovulation and menstruation through hormonal manipulation with progestins, oral contraceptives and gonadotropin-releasing hormone agonists [4]. Combined surgery and medical therapy represents the best treatment for endometriosis according to various studies [5].

This study was undertaken to evaluate the efficacy of LNG-IUS and danazol for pain relief in patients with different grades of endometriosis who had undergone conservative treatment laparoscopically. Recurrence rate was also studied and compared.

MATERIALS AND METHODS

It was a non-randomized prospective study conducted in the Department of Obstetrics and Gynaecology in tertiary care hospital, Punjab, India, from 2014-2015. Hundred women with endometriosis stage I-IV were enrolled for the study. The inclusion criteria were, women requiring pain relief postsurgery and did not want to conceive for six months or more after surgery.

A detailed history including symptoms like infertility, chronic pelvic

pain, dyspareunia were noted. A general physical and gynaecological examination was carried out before surgery. Patients were subjected to transvaginal sonography for size of endometriomas. All the patients were taken up for laparoscopic staging and cystectomy. After the surgery, patients were divided into two groups of 50 each. Group A was started on danazol 600 mg once daily. In Group B, LNG-IUS was inserted during immediate post operative period.

All patients were monitored with clinical and gynaecological examination. Relief of pain was assessed using a Visual Analogue Scale (VAS) on a scale of 1-10 after 3rd and 6th months of surgery. The adverse effects [6] of danazol and LNG-IUS were also noted. The number of patients willing to retain the device at the end of study was assessed as a response to treatment. Transvaginal sonography was done at the end of 3rd and 6th months of surgery to look for size of lesions more than 3 cm as possible evidence of recurrence. Four patients of Group A were non-compliant to treatment and four lost during follow up. Four patients of Group B had their LNG-IUS removed due to abnormal uterine bleeding.

Study protocol was approved by Ethical Committee of Institution. Informed and written consent was taken from all the patients.

STATISTICAL ANALYSIS

Mean and standard deviation were computed. The results were analysed using percentages and Chi-square test. The level of significance was taken as 0.05. The data were statistically analysed by using SPSS 20.0.

RESULTS

The mean age of patients at presentation was 30.26±2.5 and 30.14±2.36 years respectively in each group. [Table/Fig-1] shows number of patients in each stage of endometriosis. Fifty percent patients were in stage IV. There was almost equal distribution of patient's stage wise in both the groups. Eight and four patients from

group A and B respectively were lost during follow up [Table/Fig-1]. Most patients presented with complaint of infertility and pelvic pain (49% and 43% respectively). Only 8% patients presented with other complaints like dysmenorrhoea, deep dyspareunia, dyschezia and dysuria.

Pain was assessed using the VAS score on a scale of 0 to 10. Pain relief was significantly more with increase in period of treatment in both the groups. In Group A- 23.8% patients got pain relief after three months of treatment and this increased to 38.0% after six months. In Group B- 32.6% patients reported pain relief after three months and 65.2% after six months. It was observed that LNG-IUS was significantly ($p < 0.05$) more effective in relieving pain compared to danazol. It was further observed that more number of Stage IV patients showed pain relief compared to other stages in both the groups [Table/Fig-2].

The recurrence rate as measured on ultrasound after 3rd and 6th months of study is shown in [Table/Fig-3]. It can be seen that it is significantly lower in Group B compared to Group A.

The adverse effects observed with danazol were weight gain (20%) and acne (10%). Few patients (2-7%) complained bleeding and nausea as well. In LNG-IUS users, the only side effect noted was irregular uterine bleeding which decreased with time (65.2%, 50% and 43.47% patients after 1, 3 and 6 months of surgery respectively).

Sixty eight percent of patients were willing to retain LNG-IUS at the end of six months.

DISCUSSION

Endometriosis is a chronic gynaecological disorder of ectopic endometrium. Mean age at presentation in our patients was 30.2 ± 2.4 years. Similar age of presentations has been reported by other workers. Preciado Ruiz R et al., reported an incidence of 35% with an average age at presentation of 30 years [7]. In our study

Stage	Number of patients		Presenting complaint		
	Group A (n=50)	Group B (n=50)	Pelvic pain	Infertility	Others
I (n=12)	6	6	4	6	2
II (n=18)	9	9	6	10	2
III (n=20)	8	10	10	8	2
IV (n=50)	19	21	23	25	2
Total (n=100)	42*	46**	43	49	8

[Table/Fig-1]: Distribution of patients presenting with various symptoms in each stage.
*8 and **4 patients lost during follow up.

Stage	3 months		6 months	
	Group A	Group B	Group A	Group B
I	2 (33.3)	1 (16.6)	3 (50.0)*	3 (50.0)**
II	2 (22.2)	2 (22.2)	2 (22.2)	4 (44.4)**
III	2 (25.0)	3 (30.0)	3 (37.5)	5 (50.0)**
IV	4 (21.0)	9 (42.85)*	8 (42.1)*	18 (85.7)**
Total	10 (23.8)	15 (32.6)*	16 (38.09)*	30 (65.22)**

[Table/Fig-2]: Distribution of patients showing pain relief after 3 and 6 months of treatment.

Figures in parentheses indicate percentage
*Group A vs Group B $p < 0.05$
+ 3 months vs 6 months $p < 0.05$

Groups	3 months	6 months
Group A (n=42)	8 (19.0)	3 (7.1)*
Group B (n=46)	5 (10.9)*	1 (2.1)**

[Table/Fig-3]: Distribution of patients with recurrence of disease.

Figures in parentheses indicate percentage
*Group A vs Group B $p < 0.05$
+ 3 months vs 6 months $p < 0.05$

50% patients presented in stage IV directly because signs and symptoms of endometriosis are non-specific and the diagnosis becomes difficult. The gold standard of diagnosis remains to be laparoscopy [8].

In our study 43% of patients presented with the complaints of chronic pelvic pain. This symptom is characteristic of advanced stage endometriosis (stage III and IV). The severity of pain in endometriotic lesions is related to the recurrent, cyclic, micro bleeding in the implants [9]. This explains the chronic pelvic pain in severe lesions. Similar complains of pain and infertility in endometriosis patients have been reported by other studies as well [10].

The treatment options for endometriosis include- ovarian suppression therapy, surgical or a combination of both the strategies. Through surgery visible areas of endometriosis are removed and the anatomy is restored by division of adhesions. Medical therapy aims to inhibit the growth of endometrial implants by suppression of ovarian hormones [11]. Due to its high recurrence rate, both surgical and medical management is required. Significant pain relief was observed in patients using LNG IUS as compared to danazol users. The release of LNG appears to have a direct effect on endometrial deposits through peritoneal fluids possibly by a haematogenous spread. LNG decreases blood flow in uterine artery and spiral arterioles causing reduction in dysmenorrhoea and reduction of recurrence [12]. Danazol has been shown to be more effective in stage I or II [13]. It acts by producing high levels of androgen and low levels of oestrogen in the body. This hormonal environment stops menstruation and suppresses the growth of endometrial implants, causing them to degenerate. The effect of danazol was not significant in stage III and IV.

Recurrence of endometriosis after conservative surgery is not infrequent [14]. Recurrence of pain decreases with LNG-IUS for symptomatic endometriosis [11]. The use of LNG-IUS is an effective alternative for the medical treatment of women having recurrence of endometriosis and chronic pelvic pain [11]. In the present study recurrence rate was not appreciable with LNG-IUS but 19.0% and 7.1% recurrence was noted in danazol users at 3rd and 6th months [15]. Recurrence rate was significantly lower at 6th month compared to 3rd month in both the groups and further recurrence was significantly lower in Group B compared to Group A. These patients with recurrence of pain were managed effectively with NSAID.

Of the adverse effects, irregular bleeding was reported with LNG-IUS. This has been documented earlier as well. The common adverse effects with danazol were weight gain and acne. Few patients complained bleeding and nausea as well. Many of the side effects are due to its androgenic action [16].

In Group B majority (68%) of patients were willing to continue with LNG-IUS at the end of the study. Patient satisfaction itself shows the efficacy of the drug. This percentage was comparable to the study by Lockhat FB et al. [17].

LIMITATION

It was a small study with limited participants. Larger trials are required to comment on the effectiveness of LNG-IUS and danazol for the relief of postoperative pain in endometriosis.

CONCLUSION

Postoperative pain in endometriosis is very distressing. Various methods to decrease the postoperative pain in endometriosis include danazol and LNG-IUS. LNG-IUS is found to be an effective method in our study. Larger studies are required to conclude the same.

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