
Patient satisfaction and Quality of life after dienogest treatment versus surgical excision of ovarian endometrioma

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Abstract

Background: Endometriosis is a chronic condition affecting females in the reproductive period. Variable medical treatment options have been provided with comparable results to surgery.

Objective: Comparing dienogest treatment and surgical excision of endometrioma regarding patients' satisfaction and Quality of life.

Study design: This randomized clinical trial was conducted at a tertiary hospital from Nov 1, 2020, to Jul 31, 2022. We recruited patients according to specific inclusion and exclusion criteria. The study population was randomly allocated into two groups; group one received Dienogest, and group two had laparoscopic cystectomy. Group one patients received medical treatment with Dienogest (2mg/day) starting on the first day of the first menstrual cycle for three months. After three months, patients were subjected to clinical evaluation, including cyst diameter, recurrence after surgical excision, evaluation of patient satisfaction using the endometriosis treatment satisfaction questionnaire (ETSQ), and Quality of life using the SF-36 questionnaire.

Results: The recurrence rate after excision was 12/60 (20%). There was a significant difference in patient satisfaction after medical treatment rather than surgical excision. This was noted in each item of the satisfaction questionnaire and the total score (p-value <0.05). There was a significant improvement in all aspects of the Quality of life with dienogest therapy rather than surgical treatment (p-value <0.05).

Conclusion: Dienogest greatly improved patients' Quality of life and satisfaction rather than surgical intervention.

Keywords: Endometrioma; Dienogest; Surgical excision; Satisfaction; Quality of life.

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Introduction

Endometriosis is a benign chronic condition affecting females with variable presentations such as infertility and chronic pelvic pain (1). When it affects the ovary, an endometrioma develops that requires surgical intervention (2). Laparoscopic excision of endometrioma is the mainstay treatment; however, concerns regarding decreased ovarian reserve due to accidental removal of healthy ovarian tissue or impaired vascularity due to electrocoagulation are paramount (3). Also, recurrence after surgery represents a significant challenge (4). Non-surgical options have proved effective in the management of endometriosis (3). These include non-steroidal anti-inflammatory drugs, combined hormonal contraception, gonadotropin-releasing hormone agonists, and progestogens. They were effective in reducing pain and endometrioma size (5). Dienogest is a synthetic progestogen with moderate anti-gonadotropic properties and no androgenic activity (6, 7). It also has anti-inflammatory and anti-proliferative activities (8). Studies have focused on the effectiveness of dienogest in reducing pain compared to other medical options (9, 10). A study reported a 20-37% dissatisfaction rate after norethisterone acetate treatment (11). Few studies reported patient satisfaction after dienogest therapy compared to surgical intervention (12, 13). This study evaluated patient satisfaction after dienogest versus surgical excision of endometrioma.

Methods

This randomized clinical trial was conducted at the obstetrics and gynecology department at Suez Canal university hospital from Nov

1, 2020, to Jul 31, 2022, after approval of the research ethics committee. We recruited patients according to specific inclusion and exclusion criteria. Inclusion criteria: a) unilateral endometrioma, b) size of 2-8 cm, c) age 18-45 years, d) regular cycles, and e) no previous ovarian operations in the last three months. Exclusion criteria: a) suspected or confirmed malignancy, b) women within two years of menarche, and c) women on progesterone or combined hormonal contraception.

After a detailed explanation of the study procedure, informed consent was obtained from all eligible patients accepting participation in the study. The study population was randomly allocated into two groups using the random generation of numbers through computer software in a 1:1 manner. Group one received Dienogest, and group two had laparoscopic cystectomy. Randomization was done after evaluating the participants for eligibility. The allocation sequence was concealed from the researcher, enrolling and assessing participants using opaque sealed envelopes. Patients and researchers were aware of group allocation, but outcome assessors and data analysts were kept blinded.

Eligible patients were subjected to the following:

1. Complete personal and medical history.
2. Complete physical examination and local examination to evaluate pelvic pain.
3. Ultrasound examination, either transabdominal for virgins or transvaginal for sexually active women, to diagnose ovarian endometrioma. This was done after demonstrating a unilocular cystic lesion with a ground glass echogenicity of the fluid and a regular thick wall (14).
4. Group one patients received medical treatment with Dienogest (Visanne VR, Bayer AG, Soficopharm) (2mg/day) starting on the first day of the first

- menstrual cycle for three months.
5. Group two patients had laparoscopic ovarian cystectomy.
 6. After three months, patients were subjected to clinical evaluation, including cyst diameter, recurrence after surgical excision, and evaluation of patient satisfaction using the endometriosis treatment satisfaction questionnaire (ETSQ). The questionnaire included six questions that evaluated patient satisfaction after surgical excision of the endometrioma regarding endometriosis-related pain before or during periods, during or after sexual activity, endometriosis-related pain, any bleeding or spotting, tolerability, and overall satisfaction. Each question has seven scales to answer, ranging from extremely satisfied to extremely dissatisfied, with scores of 6 to 0. A higher score indicates a more remarkable improvement (15).
 7. Quality of life was evaluated using the SF-36 questionnaire. It included 36 questions addressing the following eight scales: physical function, role limitation due to physical health, body pain, general health, vitality, social functioning, role limitation due to emotional problems, and emotional well-being. Each item was scored, and the average was obtained according to the instructions of the RAND corporation website. A higher score represented better Quality of life (16, 17).

This study represents the secondary outcome measure of a clinical trial that evaluated both groups' ovarian reserve before and after the intervention.

Sample size: - The sample size was calculated using the following formula (18):

$$n = 2 \left[\frac{(Z_{\alpha/2} + Z_{\beta}) * \sigma}{\mu_1 - \mu_2} \right]^2$$

n = Sample size in each group.

$Z_{\alpha/2} = 1.96$ (The critical Value corresponds to a 95% confidence level).

$Z_{\beta} = 0.84$ (The critical value corresponding to 80% power of the study).

μ_1 = Percentage of change of AMH in the Dienogest group (10.1±3.1) (19)

μ_2 = Percentage of change of AMH in laparoscopic cystectomy group (11±6) (20)

σ = estimate of pooled standard deviation [=2.5].

Dropout = 12% [Sampling error].

According to the previous equation, the sample size was 120 patients, with 60 patients in each group.

Ethical approval: this study was conducted after approval of the Scientific Research Ethics Committee on 27/7/2020 with a reference number of 4255#.

Statistical analysis

Data were statistically described as mean and standard deviation, frequencies (number of cases), and percentages when appropriate. P values of less than 0.05 were considered statistically significant. All statistical calculations were done using the computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA), release 23 for Microsoft Windows. The Chi-square test was used for categorical variables and the (t) test for continuous variables with normally distributed data. Non-normally distributed data were tested using Fisher's exact for categorical variables and Mann-Whitney U tests for continuous variables.

Results

One hundred twenty-five women were eligible for the study, three declined to participate, and one refused medical treatment. Another one was lost for follow-up, leaving 120

women divided into two groups for the final analysis (**Figure 1**).

There was no difference in the primary demographic data of the studied population, as demonstrated in **table 1**.

The recurrence rate after excision was 12/60 (20%). There was a significant difference in the endometrioma size with dienogest therapy from 5.42 ± 1.47 cm to 1.99 ± 0.54 cm (p-value <0.001).

There was a significant difference in patient satisfaction after medical treatment rather than surgical excision. This was noted in each item of the satisfaction questionnaire as well as the total score (p-value <0.05) (**Table 2**). This was evidenced in each group before and after the intervention, also.

There was a significant improvement in all aspects of the Quality of life with dienogest therapy rather than surgical treatment (p-value <0.05) (**Table 3**). Both interventions resulted in a significant improvement in the patient's Quality of life.

Discussion

The recurrence rate was 20% in the surgical excision group. A high recurrence rate was reported previously, ranging from 29-56% after two years and 43% after five years (21). A low recurrence rate of 6.4% was also documented (22). The current study provided no medical treatment after surgery, while the follow-up period was only three months. Recurrent endometriosis was rendered to the effects of immune cells and extracellular matrix metalloproteinase leading to the proliferation and survival of endometriotic cells (23). The variability in recurrence rates was rendered to the different factors attributing to its recurrence as the definition of recurrence, whether depended on subjective pain sensation or imaging diagnosis, the type of endometriosis, disease severity, method of excision, surgical skills, and time to recurrence reported (4). When

accounting for symptoms, higher recurrence rates are reported, with a poor correlation between pain and actual recurrence (24)—the current study evaluated recurrence using ultrasound after three months of excision.

There was a significant improvement in the satisfaction scores between both groups. Dienogest provided a better satisfaction score than surgical excision. Surgical excision was associated with improved patient satisfaction as 43.8%- 45.2% were very satisfied at 3-12 months after ablative surgery for endometriosis and endometrioma (25). In a study comparing dienogest and norethisterone acetate, dienogest was associated with better satisfaction (50% and 26%, respectively). The overall satisfaction was insignificant between both groups, despite better tolerability of dienogest (26). A study evaluating patients' satisfaction after surgical treatment and progestin (norethisterone acetate) therapy reported that 43% of patients were satisfied after surgical treatment versus 59% after progestin therapy. This showed varied rates as time elapsed from 3- 12 months after intervention (13). Higher satisfaction rates were reported by Cho et al. (75.5%) (27). Tolerability is an essential factor in determining patients' satisfaction. It represents the ability to tolerate the medication's side effects, making it suitable for long-term treatment (28). Of note, no patient discontinued dienogest therapy in the current study. Satisfaction with the treatment option was rendered to improve dysmenorrhea, dyspareunia, and overall pelvic pain. Greater satisfaction after medical treatment was explained by its long-lasting effect, while surgery was associated with recurrences that resulted in pain occurring six months after the operation (13).

The Quality of life was improved significantly after both interventions. When the groups were compared, a significant improvement was in favor of dienogest therapy. An earlier study reported a significant improvement in the Quality of life after dienogest therapy with remarkable improvement in the

dysmenorrhea score (26). Another reported improved endometriosis health profile after undergoing dienogest therapy for six months (12). This was rendered to the fact that dienogest is effective in pain control with few side effects increasing its tolerability (29). The current study recruited women who had endometrioma excision only without any additional procedures. Dienogest has potential benefits, such as being progesterone receptor selective with anti-inflammatory properties that decrease cytokine production by the endometriotic implants (30). In addition, it affects pain modulation and transmission, even in the absence of significant changes in endometriotic spots (12), explaining the significant difference between the study groups.

Strength and limitations: Few studies evaluated patient satisfaction after dienogest therapy compared to surgical excision of endometrioma. The evaluation was limited to 3 months only. Patient satisfaction was represented as the mean score; the percentage of satisfied and dissatisfied patients was not presented. There was no evaluation of the stage of endometriosis for the recruited patients. The evaluation was based on validated scales; however, the SF-36 questionnaire failed to assess dyspareunia.

Conclusion

Dienogest therapy is an excellent alternative to surgical intervention for women with declining endometriosis surgery with long-lasting effects and few tolerable side effects. This significantly impacted the patient's Quality of life and satisfaction after dienogest therapy than after surgical intervention.

Conflict of interest: None

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Tables:

Table 1: Basic demographic data of the studied population

Group		Medication (60)	Operation (60)	p-value
Age (years) (Mean ± SD)		32.77 ± 8.09	30.33 ± 7.95	0.099 ^a
Occupation N (%)	Not working	37 (61.67%)	29 (48.33%)	0.142 ^b
	Working	23 (38.33%)	31 (51.67%)	
Residence N (%)	Urban	30 (50%)	28 (46.67%)	0.715 ^b
	Rural	30 (50%)	32 (53.33%)	
Marital status N (%)	Virgin	27 (45%)	30 (50%)	0.583 ^b
	Married/Divorced/Widowed	33 (55%)	30 (50%)	
Parity (Mean ± SD)		1.09 ± 0.68	1.27 ± 0.69	0.297 ^c

^a Independent samples t-test, ^b Chi-squared test, ^c Mann-Whitney U test

Table 2: Patient satisfaction after both modalities of treatment

Group	Medication	Surgery	P value
Endometriosis-related pain before or during periods	4.38 ± 1.06	3.43 ± 1.13	<0.001^a
Endometriosis-related pain during or after sexual activity	4.58 ± 1.05	3.43 ± 1.2	<0.001^a
Endometriosis related pain	4.68 ± 1.19	3.68 ± 1.14	<0.001^a
Any bleeding or spotting	4.5 ± 1.14	3.8 ± 1.2	<0.001^a
Tolerability	4.22 ± 1.11	3.33 ± 1.05	<0.001^a
Overall satisfaction	4.5 ± 1.11	3.53 ± 1.19	<0.001^a
ETSQ total score	26.87 ± 2.55	21.22 ± 2.93	<0.001^b

^a Independent sample t-test, ^b Mann- Whitney U test.

Table 3: Comparison of the Quality of life between both groups

Group	Medication	Operation	p-value
Variable	Mean ± SD	Mean ± SD	
Physical functioning	68.58 ± 12.2	62.97 ± 7.73	0.003^a
Role limitations due to physical health	70.28 ± 12.07	61.22 ± 7.9	<0.001^b
Role limitations due to emotional problems	69.42 ± 12.03	63.13 ± 6.72	0.001^a
Energy/Fatigue	69.22 ± 10.75	63.17 ± 7.88	0.001^a
Emotional well-being	71.47 ± 12.25	63.5 ± 7.13	<0.001^a
Social functioning	69.83 ± 11.37	63.02 ± 7.48	<0.001^a
Pain	69.87 ± 12.25	63.78 ± 8.04	0.002^a
General Health	69.22 ± 11.72	62.92 ± 7.96	0.002^b
Total SF-36	69.74 ± 4.42	62.96 ± 2.67	<0.001^a

^a Independent sample t-test, ^b Mann- Whitney U test.

Figure legend:
Figure 1: Patients' flow chart
Enrollment

