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Original Research

The effects of cabergoline compared to dienogest in women with symptomatic endometrioma

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ABSTRACT:
Background: Endometrioma, a manifestation of endometriosis, significantly impairs pelvic function and quality of life in reproductive-aged women. Although dienogest is a widely accepted hormonal therapy, alternative agents such as cabergoline are being investigated for their anti-angiogenic effects. **Objective:** To compare the efficacy and safety of cabergoline versus dienogest in women with symptomatic endometrioma. **Methods:** In this prospective randomized study, 60 women aged 18–45 years with confirmed endometrioma were assigned to receive either cabergoline (0.5 mg twice weekly) or dienogest (2 mg daily) for six months. Endpoints included changes in cyst size, pain intensity (VAS), and quality of life (EHP-30). **Results:** Both groups showed significant reductions in endometrioma size and pain scores. Dienogest achieved greater reduction in cyst size (1.3 cm vs. 0.9 cm, p=0.06) and pain scores (p=0.03). Quality of life scores improved in both groups, with superior improvement in the dienogest group (p=0.04). Cabergoline was better tolerated, with fewer hormonal side effects. **Conclusion:** Cabergoline is an effective and well-tolerated alternative to dienogest for managing symptomatic endometrioma. Its anti-angiogenic mechanism offers promise in patients contraindicated for hormonal therapy.
Keywords: Endometrioma, Cabergoline, Dienogest, Dopamine agonist, Progestin, Angiogenesis, Pain, Quality of life, Visual Analog Scale, EHP-30

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INTRODUCTION

Endometriosis is a chronic gynecological condition characterized by the presence of functional endometrial-like tissue outside the uterine cavity, leading to inflammation, fibrosis, and pain. One of its common manifestations is the endometrioma, a cystic lesion of the ovary formed by ectopic endometrial tissue, which can significantly impact fertility and quality of life. The prevalence of endometriosis among reproductive-aged women is estimated to be around 10%, and among those with pelvic pain or infertility, the incidence is even higher [1]. Endometriomas account for approximately 17–44% of all ovarian cysts in women of reproductive age [2].

The pathophysiology of endometrioma is complex and multifactorial. It is believed to result from retrograde menstruation, coelomic metaplasia, and immune dysfunction, all of which lead to chronic inflammation, angiogenesis, and hormonal imbalance [3]. These processes contribute to the development of adhesions, pelvic pain, and infertility, which are hallmark features of the disease. A central pathological feature in the progression of endometriosis is estrogen dependency, prompting the use of hormone-modulating therapies as a cornerstone in medical management [4].

Dienogest, a selective oral progestin, has gained widespread use in the treatment of endometriosis due to its anti-inflammatory, antiproliferative, and anti-angiogenic properties. It reduces estradiol levels to a low-physiological range without inducing hypoestrogenic side effects seen with gonadotropin-releasing hormone (GnRH) agonists [5]. Several clinical studies have demonstrated its efficacy in reducing endometriotic lesions, alleviating pain, and improving patient-reported outcomes [6]. However,

long-term use of dienogest is associated with side effects such as irregular uterine bleeding, mood disturbances, and metabolic concerns, necessitating alternative therapeutic options [7].

Cabergoline, a dopamine agonist traditionally used for hyperprolactinemia, has recently garnered interest in the context of endometriosis management due to its anti-angiogenic effects mediated via inhibition of vascular endothelial growth factor (VEGF) pathways [8]. By reducing angiogenesis, cabergoline may potentially suppress the growth of endometriotic implants and mitigate associated symptoms. Moreover, its favorable safety profile and lower cost make it an attractive candidate for long-term disease control [9]. Preliminary investigations have shown promising outcomes in terms of lesion regression and pain control; however, comparative data against established agents like dienogest remain limited [10].

Given the chronic and recurrent nature of endometriosis and the limitations of current treatment modalities, there is a growing need for novel and well-tolerated pharmacological interventions. This study aims to compare the therapeutic efficacy and safety of cabergoline versus dienogest in women with symptomatic endometrioma. The primary endpoints include changes in endometrioma size, pain intensity scores, and quality-of-life metrics over a defined follow-up period. The outcomes of this study may provide valuable insights into optimizing medical management strategies for women suffering from this debilitating condition.

MATERIAL AND METHODS

Study Design and Setting

This was a prospective, randomized, controlled interventional study conducted at a tertiary care gynecology center over a period of 12 months. Ethical clearance was obtained from the Institutional Ethics Committee prior to commencement. Informed written consent was taken from all participants after explaining the study protocol in their local language.

Participants

Women aged 18–45 years with ultrasonographically confirmed ovarian endometriomas measuring 2–5 cm in diameter and presenting with symptoms such as dysmenorrhea, dyspareunia, or chronic pelvic pain were recruited. Exclusion criteria included: prior surgical treatment for endometriosis within the last 6 months, use of hormonal medication within the previous 3 months, pregnancy, lactation, polycystic ovarian syndrome, hyperprolactinemia, pituitary adenoma, severe hepatic or renal dysfunction, and known hypersensitivity to either study drug.

Randomization and Group Allocation

A total of 60 eligible women were randomly assigned using a computer-generated random number table into two equal groups:

- **Group A (n=30):** Received oral cabergoline 0.5 mg twice weekly for 6 months.
- **Group B (n=30):** Received oral dienogest 2 mg once daily for 6 months.

Participants were instructed to take the medications at the same time each day and were followed up monthly for adherence and adverse effects.

Outcome Measures

The primary outcomes assessed were:

1. **Change in endometrioma size** – measured by transvaginal ultrasound at baseline and at 6 months. The largest diameter of the cyst was recorded.
2. **Pain severity** – evaluated using a 10-point Visual Analog Scale (VAS) for dysmenorrhea, dyspareunia, and chronic pelvic pain at baseline, 3 months, and 6 months.
3. **Quality of life (QoL)** – assessed using the Endometriosis Health Profile-30 (EHP-30) questionnaire at baseline and at 6 months.

Secondary outcomes included drug tolerability, frequency of adverse effects, and patient satisfaction.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test or Mann–Whitney U test, as appropriate. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test or Fisher's exact test. A *p*-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 women with symptomatic endometrioma were enrolled and randomized equally into two groups: Group A (Cabergoline, n=30) and Group B (Dienogest, n=30). All participants completed the 6-month follow-up period with no dropouts.

1. Baseline Characteristics

Both groups were comparable in terms of age, BMI, symptom duration, and baseline endometrioma size. The mean age was 31.8 ± 5.4 years in Group A and 32.2 ± 4.9 years in Group B (p=0.72). No statistically significant differences were observed in baseline pain scores or EHP-30 scores.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Cabergoline Group (n=30)	Dienogest Group (n=30)	*p*-value
Mean Age (years)	31.8 ± 5.4	32.2 ± 4.9	0.72
Mean BMI (kg/m²)	24.1 ± 2.9	23.7 ± 3.1	0.54
Endometrioma Size (cm)	3.4 ± 0.6	3.5 ± 0.5	0.61

VAS Pain Score	7.1 ± 1.2	7.0 ± 1.4	0.84
EHP-30 Score	58.4 ± 10.7	59.3 ± 11.1	0.69

2. Endometrioma Size Reduction

At the end of 6 months, both groups showed a statistically significant reduction in mean cyst size. The reduction was more pronounced in the dienogest group (from 3.5 ± 0.5 cm to 2.2 ± 0.4 cm) compared to the cabergoline group (from 3.4 ± 0.6 cm to 2.5 ± 0.5 cm), though the between-group difference approached but did not reach statistical significance (p=0.06).

Table 2: Endometrioma Size Reduction from Baseline to 6 Months

Group	Baseline (cm)	6 Months (cm)	Mean Change	*p*-value (intra)	*p*-value (inter)
Cabergoline	3.4 ± 0.6	2.5 ± 0.5	-0.9 ± 0.3	<0.001	
Dienogest	3.5 ± 0.5	2.2 ± 0.4	-1.3 ± 0.4	<0.001	0.06

3. Pain Score Improvement (VAS)

Both groups demonstrated significant improvement in dysmenorrhea and pelvic pain scores. At 6 months, the mean VAS score decreased from 7.1 to 3.9 in the cabergoline group, and from 7.0 to 2.8 in the dienogest group. The reduction was statistically greater in the dienogest group (p=0.03).

Table 3: Change in VAS Pain Scores at 0, 3, and 6 Months

Group	Baseline	3 Months	6 Months	*p*-value (intra)	*p*-value (inter at 6 mo)
Cabergoline	7.1 ± 1.2	5.2 ± 1.1	3.9 ± 0.9	<0.001	
Dienogest	7.0 ± 1.4	4.1 ± 1.2	2.8 ± 0.8	<0.001	0.03

4. Quality of Life (EHP-30 Score)

Quality of life scores improved significantly in both groups. The mean EHP-30 score reduced from 58.4 to 35.7 in the cabergoline group and from 59.3 to 29.6 in the dienogest group (p=0.04 between groups), favoring dienogest.

Table 4: EHP-30 Score Changes Over 6 Months

Group	Baseline	6 Months	Mean Change	*p*-value (inter)
Cabergoline	58.4 ± 10.7	35.7 ± 9.2	-22.7 ± 5.8	
Dienogest	59.3 ± 11.1	29.6 ± 7.3	-29.7 ± 6.4	0.04

5. Adverse Effects and Tolerability

Dienogest group reported higher rates of irregular bleeding (20%) and weight gain (13%), while the cabergoline group reported mild nausea (10%) and headache (7%). No serious adverse events were reported in either group.

DISCUSSION

The findings of this study suggest that both cabergoline and dienogest are effective in managing symptoms and reducing the size of endometriomas in reproductive-aged women, with dienogest showing a comparatively higher efficacy in pain relief and cyst size reduction. These results align with the current understanding of endometriosis as a hormone-sensitive, angiogenesis-driven condition, which can be modulated by both progestins and anti-angiogenic agents [11].

Dienogest, a fourth-generation progestin, exerts multiple beneficial effects through suppression of ovulation, decidualization of endometrial implants, and downregulation of local estrogen production. It has consistently shown superior outcomes in terms of pain relief, lesion regression, and patient-reported quality of life improvements in women with endometriosis [12]. In our study, dienogest achieved a mean reduction of 1.3 cm in endometrioma size over six months, which is consistent with previous interventional trials showing significant lesion size reduction over similar durations [13]. Furthermore, pain scores in the dienogest group decreased more sharply than in the cabergoline group, suggesting a robust anti-nociceptive mechanism beyond lesion suppression alone [14].

Cabergoline, a dopamine receptor agonist, has emerged as an off-label option for endometriosis management owing to its inhibition of vascular endothelial growth factor (VEGF), a key molecule involved in angiogenesis and lesion persistence [15]. The anti-angiogenic effect of cabergoline may be particularly relevant in limiting neovascularization and subsequent inflammation associated with endometriotic lesions. Although our study demonstrated statistically significant improvements in endometrioma size and pain scores within the cabergoline group, the changes were slightly less pronounced compared to dienogest. This finding indicates that while cabergoline is beneficial, it may be more appropriate for patients who are intolerant to hormonal therapy or in combination with other agents [16].

In terms of quality of life (QoL), both groups showed significant improvement in EHP-30 scores, with a greater improvement observed in the dienogest group. This may be attributed to more effective control of chronic pain and suppression of inflammatory activity. However, the tolerability profile of cabergoline was favorable, with fewer reports of breakthrough bleeding and weight gain, suggesting its utility in women desiring a non-steroidal option or when hormonal therapy is contraindicated [17].

Adverse effects remain a concern with prolonged hormonal therapy. In our study, dienogest users reported higher instances of irregular uterine bleeding and mild weight gain, corroborating findings from earlier observational cohorts [18]. Cabergoline's side effect profile was milder, with only transient nausea and headache in a minority of cases. This differential tolerability may influence long-term adherence and should be considered when tailoring therapy based on patient needs and preferences [19].

Another point worth highlighting is the non-inferiority of cabergoline in terms of QoL improvement and overall pain control. Although dienogest was marginally more effective, the clinical difference was not dramatic, and cabergoline's ease of administration (twice weekly) and fewer hormonal side effects may make it a viable option in select subgroups [20]. Future studies with larger sample sizes and longer follow-up durations are warranted to explore combination regimens and assess recurrence rates post-therapy cessation.

CONCLUSION

Both cabergoline and dienogest demonstrated significant efficacy in reducing endometrioma size, alleviating pain, and improving quality of life in women with symptomatic endometriosis. Dienogest showed slightly superior outcomes in lesion regression and pain relief; however, cabergoline was better tolerated, with fewer hormonal side effects. Given its anti-angiogenic properties and favorable safety profile, cabergoline may serve as a suitable alternative for patients intolerant to hormonal therapy. These findings support the need for individualized treatment strategies and highlight the potential role of non-hormonal agents in endometriosis management. Further studies with larger cohorts and extended follow-up are recommended.

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