ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.24074/tjrms.2025-109845

Comparison of Oral Contraceptives and Levonorgestrel Intrauterine Device Therapy in Isthmocele-Induced Intermenstrual Bleeding

İstmosel Kaynaklı İntermenstrüel Kanamada Oral Kontraseptifler ve Levonorgestrel Rahim İçi Araç Tedavisinin Karşılaştırılması

Ufuk ATLIHAN[a], Ferruh ACET[b], Onur YAVUZ[c], Burak ERSAK[d], Ali Cenk ÖZAY[e], Can ATA[f], Tevfik Berk BİLDACI[g], Hüseyin Aytuğ AVŞAR[h], Mehmet Emre PEKER[i], Selçuk ERKILINÇ[g]

[a]Private Karataş Hospital, Gynecology and Obstetrics Clinic, İzmir, Türkiye
[b]Ege University Faculty of Medicine, Health Application and Research Center, Department of Obstetrics and Gynecology, İzmir, Türkiye
[c]Dokuz Eylul University Faculty of Medicine, Department of Obstetrics and Gynecology, İzmir, Türkiye
[d]Ankara Bilkent City Hospital, Clinic of Gynecology and Obstetrics, Ankara, Türkiye
[e]Private Physician, TRCN
[f]Buca Seyfi Demirsoy Training and Research Hospital, Clinic of Gynecology and Obstetrics, İzmir, Türkiye
[g]İzmir Democracy University Faculty of Medicine, Buca Seyfi Demirsoy Training and Research Hospital, Department of Obstetrics and Gynecology, İzmir, Türkiye
[h]İzmir Tinaztepe University Private Galen Hospital Department of Obstetrics and Gynecology, İzmir, Türkiye
[i]Merkezefendi State Hospital, Clinic of Gynecology and Obstetrics, Manisa, Türkiye

ABSTRACT

Objective: To compare the effectiveness of combinedxcontraceptives (COC) and a levonorgestrell-releasiing-intrauteriine-device (LNG-IUD) in the treatment of intermenstrualx bleeding in patients with isthmocele diagnoses. **Material and Methods:** 104 patients who were diagnosed with isthmocele in our hospital between 2018-2024 and received COC or LNG-IUD treatment due to intermenstrual bleeding were compared retrospectively. All patients were investigated for histories of symptoms of dysmenorrhea, intermenstrual bleeding, dyspareunia, and persistent pelvic pain from patient files. **Results:** The mean age was significantllyxhiigher in the LNG-IUD group in comparison with the COCxgroup (p=0.042). The BMI value was significantly higher in the LNG-IUD group compared wiith the COC-group (p=0.044). The rate of smoking was significantllyxhiigher in the LNG-IUD group than in the COC-group (p<0.001). The rate of intermenstrual bleeding in the 12th-month follow-up was significantly higher in the LNG-IUD group in comparison with the COC group (p<0.001). The menstrual length in the 12th-month follow-up was significantly lower in the LNG-IiUD group compared with the COC group (p=0.048). The pelvic pain score in the 12th-month follow-up was significantlyxlower in the LNG-IiUD group than in the COCxgroup (p=0.042). **Conclusion:** This study provides important data comparing the efficacy of LNG-IUD and COC therapy in the treatment of intermenstrual bleeding. Although LNG-IUD appears to be more effective in reducing pelvic pain and menstrual duration, its effects on intermenstrual bleeding are more limited than COC therapy. Randomized controlled trials should be focused on investigating the mechanisms of different responses to treatment.

Keywords: Intermenstrual bleeding; isthmocele; levonorgestrel intrauterine device; oral contraceptives

ÖZET

Amaç: İstmosel tanısı almış hastalarda intermenstrüel kanamanın tedavisinde kombine oral kontraseptifler (KOK) ile levonorgestrel salgılayan rahim içi aracın (LNG-RİA) etkinliğini karşılaştırmaktır. **Gereç ve Yöntemler:** Çalışmamızda, 2018-2024 yılları arasında hastanemizde istmosel tanısı konulan ve intermenstrüel kanama nedeniyle KOK veya LNG-RİA tedavisi gören 104 hasta retrospektif olarak karşılaştırıldı. Tüm hastalar hasta dosyalarından dismenore, intermenstrüel kanama, dispareuni ve persistan pelvik ağrı semptomları öyküsü açısından araştırıldı. **Bulgular:** Ortalama yaş LNG-RİA grubunda KOK grubuna göre anlamlı yüksekxsaptandı (p=0.042). Vücut kitle indeksi değeri LNG-RİA grubunda KOK grubuna göre anlamlı yüksekxsaptandı (p=0.044). Sigara içme oranı LNG-RİA grubunda KOK grubuna göre anlamlı yüksekxsaptandı (p<0.001). 12. ay takipte intermenstrüel kanama oranı LNG-RİA grubunda KOK grubuna göre anlamlı yüksek saptandı (p<0.001). 12. ay takipte adet uzunluğu LNG-RİA grubunda KOK grubuna göre anlamlı kısa saptandı (p=0.048). 12. ay takipte pelvik ağrı skoru LNG-RİA grubunda KOK grubuna göre anlamlı düşük saptandı (p=0.042). **Sonuç:** Bu çalışma, LNG-RİA ve KOK tedavisinin intermenstrüel kanama tedavisindeki etkinliğini karşılaştıran önemli veriler sunmaktadır. LNG-RİA, pelvik ağrıyı ve adet süresini azaltmada daha etkili görünse de, intermenstrüel kanama üzerindeki etkileri KOK tedavisinden daha sınırlıdır. Randomize kontrollü çalışmalar, tedaviye verilen farklı yanıtların mekanizmalarını araştırmaya odaklanmalıdır.

Anahtar Kelimeler: İntermenstrual kanama; istmosel; levonorgestrelli rahim içi araç; oral kontraseptifler

Correspondence: Ufuk ATLIHAN
Private Karataş Hospital, Gynecology and Obstetrics Clinic, İzmir, Türkiye
E-mail: cfl.ufuk@gmail.com

Peer review under responsibility of Turkish Journal of Reproductive Medicine and Surgery.

Received: 04 Mar 2025 ***Accepted:*** 03 Apr 2025 ***Available online:*** 28 Apr 2025

The Cesarieanxsection (C/S) is one of the most frequentlly performed surgicall procedures worldwide, accounting for approximately one-third of all births.[1] Although it has revolutionized obstetric care and significantly reduced maternal and neonatal mortality rates, increasing C/S rates have drawn attention to long-term complications. Among these complications, uterine scar defects, called "niches" or "isthmoceles," have significant impacts on women's reproductive health and quality of life.[2] Isthmocele is a myometrial defect that occurs in the area of a previous cesarean scar and has been associated with various clinical symptoms such as abnormal uteriine bleeding, pelvic pain, infertiility, and cesarean scar pregnancies. Studies show that the incidence of isthmocele after cesarean varies between 43.4% and 75% depending on the diagnostic method used.[3-5]

Postmenstrual spotting and intermenstrual bleeding are the most common symptoms that affect the daily life and psychology of patients.[3-5] Despite advances in diagnostic methods such as transvaginal ultrasonography and saline infusion sonography, the underlying mechanisms of isthmocele-associated symptoms, especially abnormal uterine bleeding, are not fully understood.[6,7] Proposed theories include anatomic defects that cause menstrual blood to accumulate in the scar area and decreased contractile function and altered vascularization in the scar area.[8] There are a variety of options for treating symptoms associated with isthmoceles, ranging from hormonal therapies to hysteroscopic or laparoscopic surgical repair. Levonorgestrel-releasing intrauterine devices (LNG-IUD) have been shown to be effective in reducing intermenstrual bleeding, although conflicting results warrant further investigation.[9,10] Similarly, combined oral contraceptives (COC) are widely used to relieve bleeding symptoms, but their effectiveness compared with the LNG-IUD is not known.[11] Our study aimed to compare the effectiveness of COC and LNG-IUD in the treatment of intermenstrual bleeding in patients with isthmocele diagnoses.

MATERIAL AND METHODS

This study was desiigned as a retrospectiive observatiional study. The study was initiated after receiving ethics committee approval (Date: 26/02/25, Number: 2025/412) from the hospital ethics commiittee. The study was designed accordiing to the Helsinki Declaration and iinformed consent was obtained from all patiients. In our study, 1328 patients who presented to our hospital with intermenstrual bleeding symptoms between January 2018 and 2024 were evaluated retrospectively. The data of 426 patients who presented with the current symptoms and were diagnosed as having isthmocele were examined.

One hundred four patients who had intermenstrual bleeding symptoms due to isthmocele and were treated with COC or LNG-IUD were compared retrospectively. Sonographic evaluation of the cesarean scarxdefect was performed using a Voluson 730 Expert ultrasound device with a 7-9 MHz transvaginal probe. A cesarean scarxdefect was defined as the development of a hypoechoic area (filling defect) in the myometriium of the lower uteriinexsegment at the site of a previous cesarean iincision. After the definition of the cesarean scar defect, the myometrial defect was measured. In the evaluation of the myometrial defect, scar depth (vertical diistance between the base and the peak of the defect), scar width (length of the largest opening in the cervico-isthmic canal) and the thickness of the remaining myometrium were measured.[12]

In contrast to uterine retroflexion, i.e. posterior deviation of the axis, uterine anteflexion is defined as anterior deviation of the long axiis of the uterine endometriial cavity towards the cervical axis. The position of the uterus in all patients was additionally evaluated. Uterine retroflexion was defined as posterior deviation of the axis, and uterine anteflexion was defined as anterior deviation of the long axiis of the uterine endometrial cavity towards the cervical axis. If the patient had several ultrasound data during the study period, only the dimensions of the largest measurement were recorded. Body mass index (BMI), number of pregnancies, parity, number of cesarean deliveries, uterine position, cyclexllength, and menstrual duration were recorded for alll patients.

All patients were examined for symptoms of dysmenorrhea, intermenstrual bleeding, dyspareunia, and persistent pelvic pain from patient files. Exclusion criteria included endometrial pathology of atyp-

ical endometrial hyperplasia or malignancy, endometriosis, adenomyosis, contraindication to hormonal therapy, and intermenstrual bleeding from other causes. Patients in the COC group were administered a daily dose of 3 mg drospirenone + 0.02 mg ethinylestradiol starting from the third day of menstruation. Patients in the LNG-IUD group (20 ug/day) were administered and followed on the thirdxday of menstruation.

The examination records of all patients from 3, 6, and 12 months after treatment were reviewed. The presence of post-treatment breakthrough bleeding was based on verbal reports from patients. Reduction of menstrual bleeding was defined as a decrease in menstrual period by more than 3 days.[13] Visual analog scale (VAS) values of all patients who were diagnosed as having dyspareunia and dysmenorrhea were retrospectively examined from patient files.[14] On the VAS scale, 0 represents the lack of symptoms and 10 represents the worst conceivable symptoms. Dyspareunia, dysmenorrhea, and pelvic pain were scored by participants on axrange of 0 to 10.

STATISTICAL ANALYSIS

The SPSS version 26.0 software (IBM Inc., Chiicago, IL, USA) was used for statisticall analysis. The normallity of the distriibution was evaluated using the Kollmogorov Smiirnov and Shapiiro-Wilk tests based on whether the data demonstrated normal distribution. Fisher'sxexact and Chi-square tests were employed in categorical data analysis. Standard deviation (SD) was used for evaluating normally distributed data. Number (n) and percentage (%) were used for evaluating categorical data. The results were evaluated at 95% confiidence intervals (CI). P-values of <0.05 were regarded as statistiically significant.

RESULTS

The mean age was significantlly hiigher in the LNG-IUD group in comparison with the COC group (p=0.042). The BMI value was significantly higher in the LNG-IUD group compaired with the COC group (p=0.044). The rate of smoking was significantlly hiigher in the LNG-IUD group than in the COC group (p<0.001) (Table 1).

No signiificant diifference was found between the groups in terms of gynecologic data between groups before treatment (Table 2).

The rate of intermenstrual bleeding in the 12th-month follow-up was significantly higher in the LNG-IUD group in comparison with the COC group (p<0.001). The menstrual duration in the 12th month follow-up was significantly lower in the LNG-IiUD group compared with the COC group (p=0.048). The pelvic pain score in the 12th month follow-up was significantly lower in the iLNG-IUD group than in the COC group (p=0.042). No signifiicant diifference was found between the groups in terms of cycle length, and dysmenorrhea and dyspareunia scores between groups in the 12th month follow-up (Table 3).

DISCUSSION

Although there are many studies on isthmocele in the literature, few have compared the effectiveness of

TABLE 1: Comparison of demographic and ultrasonographic data between groups

	COC n=59	LNG-IUD n=45	
	X̄±SD		p value
Age (years)	30.38±2.68	31.94±2.78	0.042
BMI (kg/m^2)	23.12±2.88	23.86±2.92	0.044
Gravidity	2.92±1.24	3.12±1.36	0.630
Parity	1.74±0.72	1.82±0.68	0.580
Smoking, n (%)	17 (28.8%)	21 (46.6%)	<0.001
C/S number	1.62±0.68	1.72±0.64	0.490
Defect width (mm)	7.28±1.36	7.34±1.34	0.690
Defect depth (mm)	7.02±0.64	6.98±0.68	0.760
Residual myometrial thickness (mm)	4.46±0.52	4.40±0.56	0.780

BMI: Body mass index, C/S: Cesarean section

TABLE 2: Comparison of gynecologic data between groups before treatment

	COC n=59	LNG-IUD n=45	
	X̄±SD		p value
Cycle length (days)	29.5±2.26	30.2±2.38	0.380
Menstrual length (days)	10.12±2.18	10.28±2.22	0.660
Dysmenorrhea (VAS)	6.12±1.12	6.16±1.14	0.720
Dyspareunia (VAS)	5.34±0.86	5.38±0.92	0.770
Pelvic pain (VAS)	5.12±0.96	5.16±0.92	0.670

VAS: Visual analog scale

TABLE 3: Compariison of gynecologic data between groups at 12 months after treatment

	COC n=59	LNG-IUD n=45	
	X̄±SD		p value
Intermenstrual bleeding, n (%)	14 (23.7%)	19 (42.2%)	<0.001
Cycle length (days)	29.2±2.06	29.6±2.18	0.410
Menstrual duration (days)	3.12±1.02	2.88±0.98	0.048
Dysmenorrhea (VAS)	4.22±0.94	4.24±0.92	0.880
Dyspareunia (VAS)	3.54±0.78	3.58±0.82	0.840
Pelvic pain (VAS)	3.22±0.68	2.98±0.84	0.042

VAS: Visual analog scale

LNG-IUD and COC in the treatment of symptoms, especially intermenstrual bleeding due to isthmocele. In our study, the mean age and BMIi values of the patients in the LNG-IUD group were signiificantly higher than those in the COC group. The smoking rate in the LNG-IUD group was signiificantly hiigher than those in the COC group. After 12 months of treatment, the intermenstrual bleeding rate of patients in the LNG-IiUD group was signifiicantly hiigher than that of the COC group. After 12 months of treatment, menstrual duration and pelvic pain scores were signifiicantly lower in the iLNG-IUD group compared with the COC group. Wang et al. found that, in patients diagnosed with isthmocele, the average defect width was significantly larger in patients with intermenstrual bleeding compared with patients without intermenstrual bleeding.[15] This may be because smaller cesarean scar defects are not sufficient to accumulate blood and do not show spotting symptoms, whereas larger cesarean scar defects are thought to cause more blood accumulation and intermenstrual bleeding.[7,16] In our study, no signifiicant diifference was found in terms of defect depth and width between patients in the LNG-IUD and COC groups. Therefore, it eliminates patient selection bias in evaluating the effectiveness of these treatment methods.

Although the exact pathophysiology of cigarette smoking is not yet fully understood, in the study by Rahman et al., it was found that smoking damaged the vascular endothelium, produced superoxide anions, decreased nitric oxide (NO) production and bioavailability, and increased endothelin production, leading to serious vascular events such as endothelial dysfunction, thrombosis, atherosclerosis, and infarction.[17] Cigarette smoking has been associated with vascular changes that may affect uterine bleeding patterns, and this could potentially complicate the results. In our study, the smokiing rate was found to be higher in the LNG-IiUD group than in the COC group. The intermenstrual bleeding rate was also higher in the LNG-IiUD group than in the COC group. However, the high rate of intermenstrual bleeding in the LNG-IUD group was not attributed to smoking. Instead, it was attributed to the preference of the patient group who smoked to use the LNG-IUD.

In thexstudy conducted by Robinson et al., it was observed that high BMI could significantly affect the effectiveness of hormonal contraceptives by altering the absorptiion, distriibution, metaboliism, and excretiion processes of these drugs.[18] Similarly, BMI is a known factor affecting the pharmacokinetics of hormonal treatments and this may partially explain the variability in response between groups. In our study, BMI was significantly hiigher in the LNG-IUDx-group than in the COC group. Although patients in both groups received standardized doses of treatment regardless of their BMI, the lower intermenstrual bleeding rate in the COC group may be related to the lower mean BMI.

In the study by Baldini et al., COCs were shown to provide endometrial stabilization and regulate the menstrual cycle by reducing abnormal uterine bleeding associated with isthmocele.[19] In the study conducted by Gurbuz et al., oral contraceptives were evaluated as a rational option for suppressing bleeding and relieving symptoms.[20] Thurmond et al. investigated the effectiveness of COCs in four patients with spotting diagnosed as isthmocele, reporting that spotting decreased in one patiient and was unchanged in the other three.[21] In the study by Tahara et al., it was observed that spotting decreased and stopped completely in patients after three cycles of treatment with oral contraceptives and that scar dehiscence smaller than 3 mm disappeared after treatment.[22] In our studiy, it was found that intermenstrual bleeding symptoms improved by 76.7% of patients using COCs. However, no difference was found in isthmocele dimensions after treatment.

LNG-IUDs are commonly used to treat heavy menstrual bleeding. LNG-IUDs may reduce menstrual flow by causing endometrial thinning and stromal atrophy.[23,24] Zhang et al. evaluated surgical and nonsurgical treatments for patients with isthmocele, considering laparoscopy, vaginal repair, hysteroscopy, oral contraceptives, and LNG-IUDs. All investigated methods except LNG-IUD were useful in shortening the menstrual period in symptomatic patients.[25] Therefore, it has been emphasized that COCs might be a valiid option for symptomatiic women whoi do not want to become pregnant and prefer conservative treatment.[26] The study by Huang et al. supported that LNG-IUD was as effective as resectoscopy in reducing intermenstrual bleeding days associated with isthmocele and could be safely applied to patients without recent fertility aspiration.

It has been stated that patients with increased local vascularization observed during hysteroscopy may benefit more from LNG-IUD interventions than resectoscopy.[27] He et al. found LNG-IUD to be morexeffective than hysteroscopic isthmocele resection in the treatment of intermenstrual bleeding caused by isthmocele, and the effectiveness rate of LNG-IUD increased over time within 1 year.[28] In our study, the rate of intermenstrualxbleeding was higher in the LNG-IiUDxgroup than in the COC group after 12 months of follow-up. This result raises questions about the local hormonal effects of LNG-IUDs in patients with isthmoceles.

Although LNG-IUDs are designed to reduce endometrial proliferation and bleeding, structural and vascular changes associated with isthmoceles may limit these benefits. However, it is impossible to distinguish whether the bleeding is of isthmocele origin or is caused by possible adverse effects of LNG-IUDs. However, in the case of irregular spotting and ongoing intermenstrual bleeding, which may arise from both possibilities, patients may think that the LNG-IUD does not resolve their core symptoms and is therefore ineffective. Accordingly, it may make it difficult to achieve patient compliance and observe the effects of long-term treatment.

The lower rate of intermenstrual bleeding observed in patients treated with COCs suggests that the systemic hormonal regulation provided by COCs may have a more uniform effect on the endometrium. This finding supports the idea that COCs are a viable option for bleeding control in patients with isthmocele. The presence of congested endometrial folds and small polyps in the scar recess due to the isthmocele are potential causes of menorrhagiia and abnormal uteriine bleeding; lymphocytic infiltration and distortion of the lower uterine segment may contribute to chronic pelvic pain and dyspareunia, and iatrogenic adenomyosis limited to the scar may be responsible for dysmenorrhea.[15] In the study conducted by Gencer et al., it was found that LNG-IUDs might be an effectiive treatment option in patients with pelvic pain due to isthmocele.[29] The reduction in pelvic pain improves the quality of life of patients, emphasizing the value of LNG-IUDs in managing these symptoms. However, the persistence of intermenstrual bleeding in some patients may offset these benefits and highliight the need for a personaliized approach to treatment.

COCs do not have as significant an effect on pelvic pain scores as LNG-IUDs, which may limit their use in patients with multiple symptoms. In our study, although decreases in dyspareunia and dysmenorrhea (VAS) scores were detected in both treatment methods, no significant difference was detected between the groups. Pelvic pain is a significant problem for patients with isthmocele, and our study showed that LNG-IUDs were more effective than COCs in reducing pelvic pain scores after 12 months of treatment. This fiinding suggests that the local hormonal effects of LNG-IUDs may reduce inflammation.

The retrospective design of our study inherently limits the ability to establish causal relationships. The reliance on medical records and patient-reported outcomes may introduce potential biases, including recall bias. In addition, the relatively smalll sample size may limit the generalizabiliity of the findings. The strengths of the study iinclude its focus on a well-defiined patient population and the availability of follow-up data that provides a comprehensive understanding of treatment outcomes. The use of objective measures, such as VAS scores and ultrasound assessments, adds rigour to the analysis. These findings contribute to the growing body of evidence regarding the management of isthmocele-

related symptoms and highlight the need for tailored treatment strategies.

CONCLUSION

This study provides important data comparing the efficacy of LNG-IUD and COCxtreatment of intermenstrual bleeding. Although LNG-IUD appears to be more effective in reducing pelvic pain and menstrual duration, the high rate of intermenstrual bleeding is something that should be carefully considered in treatment planning. COCs, on the other hand, are more successful in controlling intermenstrual bleeding, but provide limited improvement in terms of pelvic pain. Future research should focus on randomized controlled trials to confirm these findings and to investigate the mechanisms underlying the different responses to treatment. In addition, studies examining the combination of medical and surgical interventions may provide new information on how to optimize outcomes for patients with isthmocele.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ufuk Atlıhan;* ***Design:*** *Ferruh Acet;* ***Control/Supervision:*** *Onur Yavuz;* ***Data Collection and/or Processing:*** *Burak Ersak, Mehmet Emre Peker;* ***Analysis and/or Interpretation:*** *Ali Cenk Özay;* ***Literature Review:*** *Can Ata, Hüseyin Aytuğ Avşar;* ***Writing the Article:*** *Tevfik Berk Bildacı, Ufuk Atlıhan;* ***Critical Review:*** *Selçuk Erkılınç.*

REFERENCES

1. World Health Organization Human Reproduction Programme, 10 April 2015. WHO statement on caesarean section rates. Reprod Health Matters. 2015;23(45):149-50.
2. Atlıhan U, Derundere Ü. Isthmocele; An overlooked cause of abnormal uterine bleeding and other gynecological complications. Turkish Journal of Reproductive Medicine and Surgery. 2024;8(1):1-6.
3. Atlıhan U. Approach to Abnormal Uterine Bleeding. In book: Current Studies in Obstetrics and Gynaecology I. Publisher: Livre de Lyon. 2025 p. 69-87
4. Murji A, Sanders AP, Monteiro I, et al. Cesarean scar defects and abnormal uterine bleeding: a systematic review and meta-analysis. Fertil Steril 2022; 118:758-66.
5. Bij de Vaate AJM, Brölmann HAM, van der Voet LF, et al. Ultrasound evaluation of the Cesarean scar: relation between a niche and post-menstrual spotting. Ultrasound Obstet Gynecol. 2011;37(1):93-9
6. Osser OV, Jokubkiene L, Valentin L. High prevalence of defects in Cesarean section scars at transvaginal ultrasound examination. Ultrasound Obstet Gynecol. 2009;34(1):90-7.
7. Fabres C, Aviles G, De La Jara C, Escalona J, Muñoz JF, Mackenna A, et al. The cesarean delivery scar pouch: clinical implications and diagnostic correlation between transvaginal sonography and hysteroscopy. J Ultrasound Med. 2003;22(7):695-700; quiz 701-2.
8. Pomorski M, Fuchs T, Rosner-Tenerowicz A, Zimmer M. Morphology of the cesarean section scar in the non-pregnant uterus after one elective cesarean section. Ginekol Pol. 2017;88(4):174-9.
9. Ou YC, Chen YY, Lan KC, et al. Levonorgestrel intrauterine system for the treatment of intermenstrual spotting in patients with previous cesarean delivery scar defect. J Obstet Gynaecol Res. 2022;48(1):155-60.
10. Kriplani A, Awasthi D, Kulshrestha V, Agarwal N. Efficacy of the levonorgestrel-releasing intrauterine system in uterine leiomyoma. Int J Gynaecol Obstet. 2012;116(1):35-8.
11. Tahara M, Shimizu T, Shimoura H. Preliminary report of treatment with oral contraceptive pills for intermenstrual vaginal bleeding secondary to a cesarean section scar. Fertil Steril. 2006;86(2):477-9.
12. Stegwee SI, Jordans IPM, van der Voet LF, Bongers MY, de Groot CJM, Lambalk CB, et al. Single- versus double-layer closure of the caesarean (uterine) scar in the prevention of gynaecological symptoms in relation to niche development - the 2Close study: a multicentre randomised controlled trial. BMC Pregnancy Childbirth. 2019;19(1):85.
13. Deng K, Liu W, Chen Y, et al. Obstetric and gynecologic outcomes after the transvaginal repair of cesarean scar defect in a series of 183 Women. J Minim Invasive Gynecol. 2021;28(5):1051-9.
14. Inal FY, Gul K, Yilmaz Camgoz Y, Daskaya H, Kocoglu H. Validation of the Turkish version of the Pain Sensitivity Questionnaire in patients with chronic pain. J Int Med Res. 2021;49(12):3000605211060158.
15. Wang CB, Chiu WW, Lee CY, et al. Cesarean scar defect: correlation between Cesarean section number, defect size, clinical symptoms and uterine position. Ultrasound Obstet Gynecol. 2009;34(1):85-9.
16. Uppal T, Lanzarone V, Mongelli M. Sonographically detected caesarean section scar defects and menstrual irregularity. J Obstet Gynaecol. 2011;31(5): 413-6.

17. Rahman MM, Laher I. Structural and functional alteration of blood vessels caused by cigarette smoking: an overview of molecular mechanisms. Curr Vasc Pharmacol. 2007;5(4):276-92.

18. Robinson JA, Burke AE. Obesity and hormonal contraceptive efficacy. Womens Health (Lond). 2013;9(5):453-66.

19. Baldini GM, Lot D, Malvasi A, Di Nanni D, Laganà AS, Angelucci C, Tinelli A, Baldini D, Trojano G. Isthmocele and Infertility. J Clin Med. 2024;13(8):2192.

20. Gurbuz AS, Gode F, Ozcimen N. Non-Invasive Isthmocele Treatment: A New Therapeutic Option During Assisted Reproductive Technology Cycles? J Clin Med Res. 2020;12(5):307-14.

21. Thurmond AS, Harvey WJ, Smith SA. Cesarean section scar as a cause of abnormal vaginal bleeding: diagnosis by sonohysterography. J Ultrasound Med. 1999;18(1):13-6; quiz 17-8.

22. Tahara M, Shimizu T, Shimoura H. Preliminary report of treatment with oral contraceptive pills for intermenstrual vaginal bleeding secondary to a cesarean section scar. Fertil Steril. 2006;86(2):477-9.

23. Costanzi F, De Marco MP, Colombrino C, Ciancia M, Torcia F, Ruscito I, et al. The treatment with Levonorgestrel Releasing Intrauterine System (LNG-IUS) in patients affected by menometrorrhagia, dysmenorrhea and adenomimyois: clinical and ultrasonographic reports. Eur Rev Med Pharmacol Sci. 2021;25(9):3432-9.

24. Atlıhan U, Ertan B, Özgözen E, Güney M. Comparison of patients with adenomyosis detected in hysterectomy material and patients with other benign pathologies: Retrospective study. Turkish Journal of Reproductive Medicine and Surgery. 2024;8(2):54-62.

25. Zhang X, Yang M, Wang Q, Chen J, Ding J, Hua K. Prospective evaluation of five methods used to treat cesarean scar defects. Int J Gynaecol Obstet. 2016;134(03):336-9

26. Iannone P, Nencini G, Bonaccorsi G, Martinello R, Pontrelli G, Scioscia M, Nappi L, et al. Isthmocele: From Risk Factors to Management. Revista Brasileira de Ginecologia e Obstetrícia. 2019;41(1):44-52.

27. Huang SY, Chen YY, Tsai CC, Lin H, Ou YC. Evaluating resectoscopy and the levonorgestrel intrauterine system for intermenstrual bleeding associated with cesarean scar defects: A retrospective study of treatment outcomes. J Obstet Gynaecol Res. 2024;50(2):253-61.

28. He X, Yan L, He C, Zhu C, Mol BW, Zhang J, Huirne JAF. The effect of a hysteroscopic niche resection compared with Levonorgestrel-releasing intrauterine device on postmenstrual spotting in patients with a symptomatic niche in the uterine cesarean scar: A prospective cohort study. Eur J Obstet Gynecol Reprod Biol. 2021; 265:66-73.

29. Ketenci Gencer F, Dincgez B, Yuksel S. Levonorgestrel-Releasing Intrauterine Device Use Can Be a Treatment Option in Symptomatic Patients with Isthmocele. Reprod Sci. 2022;29(10):2977-82.