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ORIGINAL ARTICLE

Effects of epidural steroid injections on menstrual cycle in women: An observational study

Epidural steroid enjeksiyonlarının kadınlarda adet döngüsü üzerine etkileri: Gözlemsel bir çalışma

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Summary

Objectives: The aim of this study was to investigate the effect of epidural steroid injections on the menstrual cycle of women and to identify risk factors in those with changes.

Methods: A total of 78 women who had epidural steroid injections between the ages of 18 and 55 years were retrospectively analyzed. The patients were called by phone and asked whether there was any change in their menstrual cycles after the epidural injections. Data including demographic and clinical characteristics, body height and weight, education status, alcohol and smoking habits, comorbidities, number of children, birth control method, history of cesarean section, miscarriage, and abortion were recorded.

Results: Changes in the menstrual cycle were seen in five of 12 patients who underwent cervical interlaminar epidural steroid injection, in 27 of 56 patients who underwent lumbar transforaminal epidural steroid injection, in one of two patients who underwent lumbar interlaminar epidural steroid injection, and in three of eight patients who underwent caudal epidural steroid injection. The number of patients with obesity was higher in the patients with changes than those without, indicating a statistically significant difference (41.7% vs. 14.3%, respectively; p=0.007).

Conclusion: Our study suggests that epidural steroid injections are associated with changes in the menstrual cycle. Obesity is a risk factor for menstrual cycle changes after epidural steroid injections.

Keywords: Epidural injections; hypothalamo pituitary adrenal axis; menstrual disturbance; spinal injections; steroid.

Özet

Amaç: Bu çalışmanın amacı, epidural steroid enjeksiyonunun kadınlardaki menstrüel siklus üzerine etkisini araştırmak ve menstrüel değişiklikler yaşayanlarda risk faktörlerini belirlemektir.

Gereç ve Yöntem: Epidural steroid enjeksiyonu yapılan 18–55 yaş arası toplam 78 kadın retrospektif olarak incelendi. Hastalar telefonla aranarak epidural enjeksiyon sonrası adet döngülerinde bir değişiklik olup olmadığı soruldu. Demografik ve klinik özellikler, boy ve kilo, eğitim durumu, alkol ve sigara kullanımı, ek hastalıklar, çocuk sayısı, doğum kontrol yöntemi, sezaryen/doğum, düşük ve kürtaj öyküsü gibi veriler kaydedildi.

Bulgular: Servikal interlaminar epidural steroid enjeksiyonu yapılan 12 hastanın beşinde, lomber transforaminal epidural steroid enjeksiyonu yapılan 56 hastanın 27'sinde, lomber interlaminar epidural steroid enjeksiyonu yapılan iki hastanın birinde ve kaudal epidural steroid enjeksiyonu yapılan sekiz hastanın üçünde adet döngüsünde değişiklik görüldü. Obezite olan hasta sayısı, değişiklik gösteren hastalarda, olmayanlara göre daha fazlaydı ve bu istatistiksel olarak anlamlı bir farktı (sırasıyla %41,7 ve %14,3; p=0,007).

Sonuç: Çalışmamız, epidural steroid enjeksiyonlarının adet döngüsündeki değişikliklerle ilişkili olduğunu düşündürmektedir. Obezite, epidural steroid enjeksiyonlarından sonra adet döngüsü değişiklikleri için bir risk faktörüdür.

Anahtar sözcükler: Epidural enjeksiyonlar; hipotalamus hipofiz adrenal aks; menstrüel düzensizlikler; spinal enjeksiyonlar; steroid.

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Introduction

Epidural steroid injections (ESIs) have been widely used in pain practice for many years. The epidural space of the cervical, thoracic, and lumbar region is accessed with intermittent fluoroscopy images via the transforaminal, interlaminar, or caudal routes.[1] Particulate steroids such as methylprednisolone, triamcinolone, or betamethasone, or nonparticulate steroids such as dexamethasone, are used in these regions.[2] With anti-inflammatory effects, the steroid reduces inflammation and provides pain relief.[3]

It is well known that steroids given to the epidural area have systemic effects. Several studies have demonstrated that fasting blood glucose increases after ESI.[4–6] Therefore, caution is recommended in diabetic patients with insufficient blood glucose control.[7] The relationship between ESI and osteoporosis is still controversial. Nevertheless, it is recommended that postmenopausal women with a high bone fracture risk should be initiated with an anti-osteoporotic medication before the procedure.[8]

Previous studies have shown that ESI affects the hypothalamic-pituitary-adrenal axis by decreasing serum adrenocorticotropic hormone (ACTH) and free cortisone.[9,10] The development of Cushing syndrome was also reported in case reports after ESI.[11] The interaction of local steroid injections with the hypothalamic-pituitary-ovarian axis has also been demonstrated in many studies.[12,13] Saketos et al.[12] showed that glucocorticoids inhibited the hypothalamic-pituitary-ovarian axis, mainly affecting hypothalamic function. Mens et al.[13] reported that 39 (50.6%) of 77 premenopausal women had disturbances in menstrual cycles after triamcinolone injection into the joint or into soft tissues such as bursa, tendon, or tendon sheath.

However, the number of data in the literature is limited regarding the possible effects of ESI on the menstrual cycle and associated risk factors. In the present study, therefore, we aimed to investigate the effect of ESI on the menstrual cycle of women and to identify possible risk factors.

Material and Methods

This retrospective, observational study was conducted at the interventional pain clinic of the Department of Physical Medicine and Rehabilitation of a tertiary care center between January 2019 and March 2020. Women between the ages of 18 and 55 years who underwent ESI for various indications were screened from the hospital database. Patients who underwent any procedures in addition to ESI, such as facet intra-articular injections, were excluded. All screened patients were called by phone. During the phone call, patients who were in the postmenopausal period, had an irregular menstrual cycle or a regular menstrual cycle with medication, pregnancy, received any steroid injections after epidural administration, and those who did not give consent for participation were excluded. Finally, a total of 78 women who had ESI were included in the study. The study flow chart is shown in Figure 1. Verbal consent was obtained from each patient during the telephone interview to use the data obtained in the study. The study protocol was approved by the institutional Ethics Committee (09.2020.811). The study was conducted in accordance with the principles of the Declaration of Helsinki.

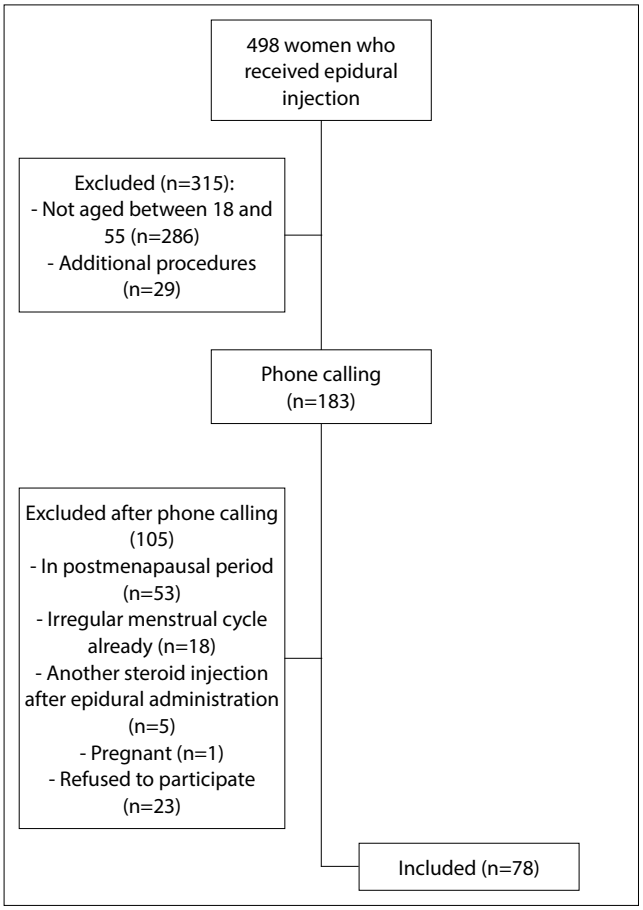

Figure 1. Flowchart.

The patients were called by phone and asked whether there was any change in their menstrual cycles after the epidural injection. Data including demo-

Table 1. Baseline demographic and clinical characteristics of patients

Age, years (±SD)	40.1 (± 6.7)
BMI, kg/m^2 (IQR)	26.5 (22.7-30.8)
Education status, n (%)	
Litarate	2 (2.6%)
Primary school	26 (33.3%)
Middle school	6 (7.7%)
High school	18 (23.1%)
University	26 (33.3%)
Smoking habit, n (%)	27 (34.6%)
Alcohol habit, n (%)	3 (3.8%)
Comorbidity, n (%)	29 (37.2%)

Data are given in mean±SD, median (IQR) or number and percentage, unless otherwise stated. SD: Standard deviation; IQR: Interquartile range; n: Number; BMI: Body mass index.

graphic and clinical characteristics, body height and weight, education status, alcohol and smoking habits, comorbidities, medications, number of children, history of cesarean section, miscarriage or abortion, and birth control method were recorded. If a change in the menstrual cycle was described, treatments applied were questioned. The diagnosis and route of the administration of ESI were obtained from our registry system. If more than one injection was administered, only changes in the menstrual cycle after the last injection were questioned.

40 mg of triamcinolone, 0.5 ml of physiological saline, and 0.5 ml (0.5%) of bupivacaine for lumbar transforaminal epidural injections; 40 mg of triamcinolone, 1 ml of physiological saline, and 1 ml (0.5%) of bupivacaine for lumbar interlaminar epidural injections; 40 mg of triamcinolone, 5 ml of physiological saline, and 2 ml (0.5%) of bupivacaine for caudal epidural injections; 40 mg of triamcinolone and 2 ml of physiological saline for cervical interlaminar epidural injections were used in each patient participating. After the epidural injection, no acute major complications were reported.

Statistical Analyses

Statistical analysis was performed using the SPSS for Windows version 24.0 software (IBM Corp., Armonk, NY, USA). Continuous data were presented as mean±standard deviation (SD) or median (interquartile range [IQR]), while categorical variables were presented as number and frequency. The normality test was carried out using the Shapiro-Wilk test. The Student t-test or Mann–Whitney U test was performed for the comparison of quantitative variables. Comparison of qualitative variables was performed using the Pearson chi-square or Fisher exact tests according to fulfillment of assumption requirements. A p value of <0.05 was considered statistically significant.

Results

A total of 78 women were included in the study. Baseline demographic and clinical characteristics of the patients are summarized in Table 1.

Indications for ESI were cervical disc herniation (CDH) (15.4%), lumbar disc herniation (LDH) (62.8%), lumbar spinal stenosis (LSS) (6.4%), post-laminectomy syndrome (PLS) (10.3%), and coccygodynia (5.1%). Administrations of steroids into the epidural space were cervical interlaminar (CIL) (15.4%), lumbar transforaminal (LTF) (71.8%), lumbar interlaminar (LIL) (2.6%), and caudal (10.3%).

36 patients (46.2%) had a change in their menstrual cycle. The menstrual patterns are shown in Table 2.

Table 2. Menstrual patterns after epidural steroid injections

Variable	n	%
No change in menstrual cycle	42	53.8
Earlier than expected but same volume and duration	9	11.5
Later than expected but same volume and duration	2	2.6
Reduced blood volume and shorter duration but on expected time	5	6.4
Increased blood volume and longer duration but on expected time	1	1.3
Earlier than expected with reduced blood volume and shorter duration	3	3.8
Excessive bleeding irregularly and more frequently of menstrual cycles	16	20.5

Data are given in number and percentage, unless otherwise stated.

Table 3. The comparison of patients with and without changes in the menstrual cycle after epidural steroid injection

	Pts with changes (n=36)	Pts without change (n=42)	p
Age, years (±SD)	40 (±6.5)	39.9(±6.9)	0.86
BMI, kg/m² (IQR)	28.7 (22.6–32)	25.5 (22.7–28.8)	0.1
Obesity (BMI>30 kg/m²), n (%)	15 (41.7%)	6 (14.3%)	**0.007**
Education status, n (%)			
Literate	1 (2.8%)	1 (2.4%)	0.07
Primary school	17 (47.2%)	9 (21.4%)	
Middle school	1 (2.8%)	5 (11.9%)	
High school	9 (25%)	9 (21.4%)	
University	8 (22.2%)	18 (42.9%)	
Smoking habit, n (%)	13 (36.1%)	14 (33.3%)	0.79
Alcohol habit, n (%)	0	3 (7.1%)	0.1
Comorbidity, n (%)			
Thyroid dysfunction	6 (16.7%)	4 (9.5%)	0.9
Diabetes	2 (5.6%)	1 (2.4%)	
Hypertension	6 (16.7%)	4 (9.5%)	
Astma	4 (11.2%)	2 (4.8%)	
C/section, n (%)	9 (25%)	13 (31%)	0.56
Miscarriage /abortion, n (%)	13 (36.1%)	10 (23.8%)	0.23
Parity			
Nulliparity, n (%)	6 (16.7%)	8 (19%)	0.88
Primiparity, n (%)	5 (13.9%)	7 (16.7%)	
Multiparity, n (%)	25 (69.4%)	27 (64.3%)	
Birth control method, n (%)			
None	16 (44.4%)	23 (54.8%)	0.48
Condom	14 (38.9%)	10 (23.8%)	
Intra uterine device	3 (8.3%)	6 (14.3%)	
Tubal ligation	3 (8.3%)	3 (7.1%)	

Data are given in mean±SD, median (IQR) or number and percentage, unless otherwise stated. SD: Standard deviation; IQR: Interquartile range; n: Number; BMI: Body mass index.

Changes in the menstrual cycle were seen in five of 12 patients who underwent cervical interlaminar epidural steroid injection, in 27 of 56 patients who underwent lumbar transforaminal epidural steroid injection, in one of two patients who underwent lumbar interlaminar epidural steroid injection, and in three of eight patients who underwent caudal epidural steroid injection. The menstrual patterns are shown in Table 2. Only seven out of 36 patients visited the gynecology and obstetrics clinics, and their bleeding was controlled with medication. The time to return to normal cycle, regardless of whether with medication or not, was 1 month in three patients (8.3%), 1 to 3 months in 10 patients (27.8%), 3 to 6 months in seven patients (19.4%), and longer than six months in 16 patients (44.4%).

The comparison of patients with or without changes in the menstrual cycle after ESI is shown in Table 3. The number of patients with obesity was statistically significantly higher in patients with changes in the menstrual cycle than those without (41.7% vs. 14.3%, respectively; p=0.007).

The diagnosis and routes of the administration of ESI are summarized in Table 4.

Discussion

In the present study, we investigated the effect of epidural steroid injection (ESI) on the menstrual cycle of women and identified possible risk factors. According to the study results, 36 of 78 (46.2%) women

Table 4. The diagnosis and routes of the administration of ESI

	Pts with changes	Pts without changes	p
Diagnosis			0.94
CDH	5 (13.9%)	7 (16.7%)	
LDH	23 (63.9%)	26 (61.9%)	
LSS	3 (8.3%)	2 (4.8%)	
PLS	3 (8.3%)	5 (11.9%)	
Coccygodynia	2 (5.6%)	2 (4.8%)	
Epidural administration			0.93
CIL	5 (13.9%)	7 (16.7%)	
LTF	27 (75%)	29 (69%)	
LIL	1 (2.8%)	1 (2.4%)	
Caudal	3 (8.3%)	5 (11.9%)	

Data are given in number and percentage, unless otherwise stated. ESI: Epidural steroid injection; CDH: Cervical disc herniation; CIL: Cervical interlaminar; LDH: Lumbar disc herniation; LIL: Lumbar interlaminar; LSS: Lumbar spinal stenosis; LTF: Lumbar transforaminal; PLS: Postlaminectomy syndrome.

experienced changes in their menstrual cycle with different patterns. Only seven of the 36 women, whose menstrual cycles changed, applied to the gynecology and obstetrics clinics.

There are a limited number of studies investigating the effect of ESI on the menstrual cycle in the literature. In an observational cohort study, Suh-Burgmann et al.[14] examined abnormal vaginal bleeding after ESI. They included 8166 ESI procedures performed on 6926 non-hysterectomized women with a diagnosis of low back pain. Of these, 197 women (201 procedures) presented to the outpatient clinic with abnormal vaginal bleeding. The authors found that women were 2.8 times more likely to have abnormal vaginal bleeding when compared 60 days before and 60 days after the injection, based on patients presenting to a medical service provider. However, the authors might not have included all women whose menstrual cycles changed after injection. In this study, we included all women who met the inclusion criteria. Therefore, we found more women with abnormal bleeding after ESI.

Hirsch et al.[15] reported a case series of four women, two of whom were premenopausal. These two premenopausal patients received caudal ESI using triamcinolone 80 mg. After the procedure, abnormal and prolonged menstrual bleeding was reported. Both patients had a history of previous low back surgery, and one of them also had a diagnosis of migraine. In another case report, Gitkind et al.[16] used 2 ml of betamethasone sodium phosphate in a premenopausal woman with heavy menstrual bleeding after bilateral L4-L5 transforaminal ESI. The patient had coexisting hypertension. Additionally, Çok et al.[17] reported a case series of two premenopausal women. Caudal ESI was administered to one of them, and lumbar interlaminar ESI to the other, using methylprednisolone 80 mg. After a few days, they experienced abnormal vaginal bleeding. In these cases, after ESI, the patients had excessive menstrual bleeding which was a condition requiring medical treatment. Most women may underestimate the change after ESI. Therefore, in this study, we attempted to include all women experiencing any change in their menstrual cycle. Only seven of 78 (9%) women included in the study visited the gynecology and obstetrics clinics for medical treatment. However, 36 women (46.2%) described a change in their menstrual cycle after ESI.

In the current study, we also identified risk factors for changes in the menstrual cycle after ESI. Obesity was another significant risk factor for menstrual cycle changes after ESI (41.7% vs. 14.3%, respectively; p=0.007). Previous studies have shown a strong relationship between obesity and abnormal vaginal bleeding, and therefore weight loss is recommended as a conservative therapy.[18] It is thought that excessive adipose tissue may cause endometrial hyperplasia by producing prolonged and continuous estrogen.[19] This may predispose women to menstrual cycle alterations after ESI. However, further large-scale, well-designed studies are needed to better understand the effect of obesity on the menstrual cycle after epidural injections.

The clinical efficacy of long-acting particulate and short-acting non-particulate steroids used in ESI is still controversial. Some authors have suggested that particulate steroids can provide a longer duration of efficacy than non-particle steroids,[20] while others have shown similar efficacy.[21] However, it has been shown that there is more suppression of cortisol in insoluble steroids such as triamcinolone than in water-soluble forms such as dexamethasone after

ESI.[22] This may be attributed to the fact that the hypothalamic-pituitary-adrenal axis is suppressed for a longer period by insoluble steroids than by water-soluble steroids. In our study, particulate long-acting insoluble triamcinolone was used. Therefore, further studies examining the effects of different forms of steroids on menstrual bleeding are required.

Nonetheless, there are some limitations to this study. First, bupivacaine, a long-acting local anesthetic, was used in combination with steroids for lumbar and caudal injections. The relationship between irregular menstruation and bupivacaine was not considered. Studies involving ESI without local anesthetic may be required to fully demonstrate the effects of epidural steroid applications on menstrual bleeding. Second, the effects on menstrual bleeding after epidural injection were evaluated via telephone interviews. Patients may have remembered the effects of the injection incorrectly. Third, factors such as stress, excessive exercise, diet, or medications could be reasons for abnormal uterine bleeding; however, these factors were not evaluated in our study.

Although the findings should be interpreted with caution due to these limitations, this study has certain strengths. First, there are few cases in the literature, and this is the first study to examine the effects of epidural injections on menstrual bleeding and risk factors in patients with irregular bleeding. Second, previous findings in the literature on menstrual cycle alterations after ESI were related to lumbar region injections. In the present study, we also reported patients who experienced changes in the menstrual cycle after cervical epidural injection for the first time. Third, most women did not regard the change in menstrual bleeding after the injection as significant and thus did not visit gynecology outpatient clinics. Therefore, telephone interviews regarding the change in menstrual bleeding revealed the effects of ESI more accurately.

In conclusion, our study suggests that ESI is associated with changes in the menstrual cycle. Obesity and comorbidities are risk factors for menstrual cycle alterations after epidural steroid applications. Based on these findings, it should be kept in mind that irregular menstrual bleeding may occur after ESI, particularly in women with obesity or having comorbidities.

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Ethics Committee Approval: The Marmara University Clinical Research Ethics Committee granted approval for this study (date: 24.07.2020, number: 09.2020.811).

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