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ORIGINAL ARTICLE

Severity of pain and circadian changes in uterine artery blood flow in primary dysmenorrhea

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Abstract
Objective To investigate the severity of pain and circadian changes in uterine artery blood flow in primary dysmenorrhea cases.
Materials and methods The study included 27 cases diagnosed as primary dysmenorrhea and 25 individuals who had no dysmenorrhea complaint. Bilateral uterine artery systole/diastole rates (S/D), pulsatility indices (PI) and resistance indices (RI) of all cases were measured using transvaginal colour Doppler at 12.00–02.00 p.m. and 12.00–02.00 a.m. Severity of pain was evaluated in dysmenorrhea cases at the same hours using a verbal pain assessment scale.
Findings Doppler measurements of dysmenorrhea cases conducted at 12.00–02.00 p.m. showed right uterine artery S/D: 3.37 ± 0.26, RI: 0.73 ± 0.07, PI: 2.38 ± 0.34 and left uterine artery S/D: 3.33 ± 0.37, RI: 0.74 ± 0.14, PI: 2.41 ± 0.15, while measurements carried out at 12.00–02.00 a.m. showed right uterine artery S/D: 3.88 ± 0.12, RI: 0.87 ± 0.14, PI: 2.94 ± 0.21 and left uterine artery S/D: 3.90 ± 0.27, RI: 0.92 ± 0.12, PI: 2.93 ± 0.21. Comparisons revealed significantly higher Doppler indices at night ($P < 0.05$) than in the day in dysmenorrhea cases. There was not any significant circadian difference in individuals who did not have dysmenorrhea ($P > 0.05$). Pain score in the verbal pain assessment of dysmenorrhea cases was found 3.6 ± 1.4 in the day and 5.8 ± 1.7 at night. The difference was found significant ($P < 0.05$).
Conclusion Uterine artery blood flow is reduced at night in dysmenorrhea cases. In correlation with this, the cases feel more pain at night. Our results may be important on the planning of working hours and their quality of life.

Keywords Uterin artery · Circadian rhythm · Primary dysmenorrhea

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Introduction

Dysmenorrhea is defined as a cramp-like pain in the lower part of the abdomen at the beginning of menstruation that associated with ovulatory cycle. Menstruation pain that results from a pathology that can cause pain in the pelvic area is called secondary dysmenorrhea, whereas pain without any pelvic pathology is called primary dysmenorrhea [1].

Prostaglandin (PG) and vasopressin levels, myometrial contractility and changes of uterine blood flow have an important role in etiopathogenesis of dysmenorrhea. It has been found that PG and vasopressin levels are higher in dysmenorrhea than healthy women [2]. Likewise, it has been found women with dysmenorrhea had significantly higher uterine blood flow indices than healthy controls in luteal and follicular phase [3]. In healthy women, it is known that PG and vasopressin secretion, myometrial contractility and changes of uterine blood flow, which are held responsible for the etiopathogenesis of dysmenorrhea, undergo diurnal and/or circadian changes [4–6]. However, it is not known that women had dysmenorrhea, whether or not have circadian changes in these etiologic factors.

In the present study, it is investigated whether or not there is a circadian difference in uterine artery blood flow changes and pain severity in dysmenorrhea cases.

Materials and methods

The study was conducted after the approval of Local Ethics Committee, was obtained on women with similar sociodemographic characteristics and educational level, who presented at Firat University Medical School, Obstetrics and Gynecology polyclinic and diagnosed as primary dysmenorrhea (*n*: 27) and normal (*n*: 25). All the cases included were informed about the study and their written consents were taken.

The groups and inclusion criterions

Control and study groups were selected randomly from normal with pain free and primary dysmenorrhea women, respectively. It was used as personal declaration for identification of groups. Diagnosis criteria for primary dysmenorrhea [7] were identified as follows: (1) having normal pelvic examination and ultrasound, (2) periodical pain history that began within 2 or 3 years after menarche, just before or during menstruation and continued for the first 2–3 days of the menstruation, (3) presence of colic-type pain history. Presence of at least one of such symptoms as nausea, vomiting, diarrhea, depression, syncope, and headache was evaluated as severe dysmenorrhea. All of the women, whose control group were pain free and normal.

Exclusion criterions

Cases who had hypertension, cardiac or pulmonary diseases, endocrine and metabolic diseases like diabetes, who were extremely obese (BMI > 30 and over), who had menstrual irregularities, who used oral contraceptives, intrauterine device, non-steroid antiinflammatory drugs, smoking who received ovulation induction, who had acute and chronic pelvic abdominal inflammatory disease story, and those who had previous pelvic surgery were not included in the study.

Doppler evaluations and verbal pain assessment

Doppler systole/diastole rates (S/D), pulsatility indices (PI) and resistance indices (RI) values of all cases were established on the own first menstrual day at 12.00–02.00 p.m. and 12.00–02.00 a.m. for uterine artery blood flow changes, and verbal pain scores were determined for pain severity. Women were asked to indicate the level of pain they perceived on the verbal scale immediately before Doppler evaluations. Doppler examinations were made by HITACHI EUB 525 Doppler Ultrasound device using a 6.5 mHz transvaginal probe. The area at the lateral level of uterine artery's cervicocorporeal junction was used for this purpose. The measurements were carried out by the same person and the average of three consecutive measurements was calculated.

Severity of pain was determined using a verbal pain assessment scale. The verbal pain scale consisted of a numerical scale with 11 points, graded from 0 to 10. Score 0 defines no pain, whereas score 10 designates the severest pain felt by the patient [8].

Statistical analysis

In the statistical analysis, Wilcoxon Rank test was used for the dependent variables and Mann–Whitney *U* test was employed for the independent variables in the comparisons between night and day, Doppler indices and pain scores. $P < 0.05$ was considered significant.

Results

Sociodemographic data about women who were included in the study are presented in Table 1. All women in the study group were married, with 88% of women in dysmenorrhea group and 86% of normal women having at least one child. Of the women surveyed in the study, 25% indicated that they used analgesics in their previous cycles due to dysmenorrhea. The most common additional symptom of women with severe dysmenorrhea is nausea, and it was present in 46% of the cases. Eighty-one per cent of normal women and 77% of dysmenorrheal women were nurses, while the rest had other professions. The first Doppler evaluations of the cases were conducted during the day in 58% of dysmenorrhea cases and at night in the remaining 42%, whereas the first measurements were carried out during the day in 53% of normal cases and at night in the other 47%. Night and day uterine artery Doppler evaluations of the groups are presented in Table 2. Comparisons did not show a significant difference between right and left uterine artery S/D, RI and PI values of dysmenorrheal and normal women ($P > 0.05$). Doppler values obtained from measurements

Table 1 Sociodemographic data of dysmenorrhea and control groups

	Dysmenorrhea (*n*: 27)	Normal (*n*: 25)	*P* value
Age	22.7 ± 1.4	23.1 ± 1.8	>0.05
Gravida	1.16 ± 0.36	1.12 ± 0.68	>0.05
Parity	0.86 ± 0.62	0.74 ± 0.52	>0.05
BMI	23.6 ± 1.4	24.1 ± 1.3	>0.05

BMI body mass indices

Table 2 Night and day uterine artery Doppler evaluations of dysmenorrhea and control groups

		Dysmenorrhea (*n*: 27)			Normal (*n*: 25)		
		12:00–14:00 p.m.	00:00–02:00 a.m.	*P* value	12:00–14:00 p.m.	00:00–02:00 a.m.	*P* value
Right uterine artery	SD	3.37 ± 0.26	3.88 ± 0.12*	<0.05	3.13 ± 0.13	3.16 ± 0.19	>0.05
	RI	0.73 ± 0.07	0.87 ± 0.14*	<0.05	0.72 ± 0.12	0.73 ± 0.14	>0.05
	PI	2.38 ± 0.34	2.94 ± 0.21*	<0.05	2.34 ± 0.24	2.23 ± 0.17	>0.05
Left uterine artery	SD	3.33 ± 0.37	3.90 ± 0.27*	<0.05	3.34 ± 0.23	3.42 ± 0.17	>0.05
	RI	0.74 ± 0.14	0.92 ± 0.12*	<0.05	0.71 ± 0.17	0.72 ± 0.23	>0.05
	PI	2.41 ± 0.15	2.93 ± 0.21*	<0.05	2.23 ± 0.21	2.31 ± 0.14	>0.05

S/D systole/diastole rates, *PI* pulsatility indices, *RI* resistance indices

* <0.05 significant

conducted at 12.00–02.00 p.m. were higher in women with dysmenorrhea, but the difference was not significant ($P > 0.05$). There was not any significant difference between night and day uterine artery Doppler values of normal women ($P > 0.05$). Doppler evaluations in dysmenorrhea cases were found significantly higher at night, in comparison to those found in the day ($P < 0.05$).

Pain score of dysmenorrhea cases as established by verbal pain scale was 3.6 ± 1.4 in the day and 5.8 ± 1.7 at night. The difference was significant ($P < 0.05$).

Discussion

It was established in our study that uterine artery blood flow decreased and accordingly, pain perception scores of dysmenorrhea cases increased at night. The observation of circadian rhythm of pelvic pains in women with dysmenorrhea and supporting this differentiation using Doppler findings is the first report in literature.

Our findings can be explained by current literature information. As it is known, the mechanism responsible for pain in dysmenorrhea is contraction of the myometrium and a consequent decrease in blooding. Many factors, with increased PGF2alpha levels as the leading factor among them, have been held responsible for the pain mechanism in dysmenorrhea. PGF2alpha, a potent myometrial stimulant and vasoconstrictor, causes myometrial contractions, and plays a part in the formation of pain due to the resulting ischemia [9]. It was found in a study by Eden et al. [10] that endometrial PG levels correlated with pain severity. Another hormone that is considered responsible for dysmenorrhea etiopathogenesis is vasopressin. It was reported in previous studies that vasopressin exacerbated myometrial contractions and reduced uterine artery blood flow, whereby it could be held responsible for dysmenorrheal pain [11–13]. Both PG and vasopressin exhibit a diurnal rhythm [4, 14]. Likewise, Doppler studies examining uterine artery blood flow in dysmenorrhea cases showed increased uterine artery pulsatility indices, which was reported to result from the increase in myometrial contractility [15]. Melatonin is the other hormone known as day time and night time secretion differences and it is shown that melatonin hormone increases uterine contractility in previous studies.

The exacerbation of pain severity at night, identified in our study, can be attributed to the increase in such hormones as PG, vasopressin and melatonin, which are secreted with a circadian rhythm and intensify myometrial contractions at night.

The peak incidence of dysmenorrhea is during late adolescence and in 20s [15]. Although it has as high an incidence as 92% in adolescents, it can be seen in later ages too, as shown in our study. Late 20s is a period when women are most active in terms of professional and academic life. Primary dysmenorrhea is a common problem among young women. As it appears in the young age group, it coincides with school and work life. In an epidemiological study, Klein and Litt [16] reported that 14% of dysmenorrhea cases could not attend school due to severe pain. Hence, primary dysmenorrhea is an important problem of health in community. Another study carried out in the United States showed that 10% of women with dysmenorrhea had to discontinue work because of severe pain, and the annual economic loss incurred there upon was estimated at 600 million work hours and 2 billion US dollars [17].

The decrease in quality of life brought about by dysmenorrhea has a remarkable impact on professional productivity and academic performance. Twenty-five per cent of working women use analgesics during dysmenorrhea, but no study has been conducted about their performance in this period. It is not possible for us to comment on work performance, as the number of our cases is not sufficient for a survey. However, our findings may provide a basis for further and more comprehensive studies and a scientific perspective on the arrangement of working hours so as to increase the performance of women with dysmenorrhea.

Other than limited number of cases, the weakness of this study is not being performed excluding endometriosis in dysmenorrhea cases. This is because there are some endometriosis cases reported as primary dysmenorrhea [18]. However, results of our preliminary study is still the first and only study until the further studies are performed, which are including higher number of cases and excluding endometriosis.

Conflict of interest statement None.

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