Evaluation of utero-ovarian hemodynamics in relation to fertility and stage of endometriosis

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Summary

Objective: The aim of this study was to compare hemodynamic changes in the uterine and ovarian arteries between infertile women with moderate and/or severe endometriosis and healthy women. In this prospective study, 99 women in their generative age were subjected to color Doppler ultrasonography to measure hemodynamic parameters from July 2010 to January 2011. The examination was performed during the proliferative or ovulatory phase of the natural menstrual cycle in a random sample of 54 women treated for endometriosis-induced infertility and 45 healthy women were included in control examination procedure. Irrespective of considered stage, endometriosis was most often found in the ovaries, in the sacro-uterine ligaments, peritoneum, and rectovaginally. Resistance to blood flow expressed as the resistance index (RI) in the measured arteries, was significantly higher in severe endometriosis compared to moderate form. Average values of pulsation index (PI) and RI are significantly higher, in both endometriosis stages, compared to measured values in healthy women.

Key words: Uterine and ovarian blood flow; Endometriosis; Infertility.

Introduction

Endometriosis refers to whenever a functioning endometrium is found outside the uterine cavity. Consequences are numerous and the most serious is infertility that occurs in 20-50% of women [1, 2].

While medication proved to be an adequate therapy for mild stage endometriosis, laparoscopic treatment is often the only solution for moderate and severe stages.

A prerequisite for the fertility capacity of female genital tract includes, among others, optimum utero-ovarian and endometrial blood flow. These parameters have been separately studied from a number of perspectives, particularly in in vitro fertilization (IVF) programs, as important predictors of the implantation success [3-5].

Endometriosis is most often accompanied by essentially altered hemodynamics of the uterus and ovaries. This is a consequence of the endometrial hot-beds that often and deeply infiltrate the uterine tissue, oviducts, as well as other, surrounding structures. Therefore the stage of the disease, as well as the site of endometriosis hot-bed are essential in the assessment of utero-ovarian hemodynamics and, consequently, of the fertility capacity. The aim of this study was to determine whether and to what extent utero-ovarian blood flow differs between a group of women with moderate and/or severe endometriosis versus a group of healthy women.

Materials and Methods

During the period from July 2010 to January 2011, color Doppler ultrasonography findings of 54 infertile women finally diagnosed with endometriosis in moderate (35 cases) or severe form (19 cases), and for 45 women without endometriosis (without any infertility-inducing disease).

Patients were subjected to conventional transvaginal and color Doppler examination using 5 MHz transvaginal transducer.

The examination was performed during the proliferative or ovulatory phase of the menstrual cycle (11th to 14th day), with patients in the same position, at approximately the same time of the day, whereby conditions were created to ensure objectivity and comparability of the findings.

Color Doppler mode was used for blood flow imaging. After obtaining continuous image of the flow waveform flow imagery, the average of three to five cardiac cycles was determined for the electronic calculation of PI and RI values from the Doppler spectrum, using the following relationships:

RI = peak systolic frequency – end-diastolic frequency / peak systolic frequency

PI = peak systolic frequency – end-diastolic frequency / mean systolic frequency

Statistical analysis was performed using the SPSS software package, version 13.0. Statistical significance between the examined groups was assessed using Fisher's exact test, Chi – square test, Student's test, Mann – Whitney U test. Results were considered significant when the and p value was less than 0.05.

Results

Regarding most of the demographic features, there were no substantial differences between the test and control group. Only the average age of patients with severe-stage endometriosis was significantly higher (34.4 ± 4.28 years), compared to both: the control group (30.8 ± 4.28 years) and the group of patients with moderate-stage endometriosis. (31.2 ± 5.92 years, p = 0.047). Duration of infertility was significantly longer (7.11 ± 2.98 years versus 5.4 ± 2.90 years), and the mean parity was significantly lower in the group of patients with severe endometriosis (1.05 ± 0.23 versus 1.34 ± 0.48).

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Dismenorea, dispareunia, and annovulation were present in a significantly large number of cases (about 70% - 95% cases) both in moderate and severe endometriosis. Somewhat greater probability of all stated symptoms in severe endometriosis was not statistically significant, on the accepted level of reliability. The exception is pelvic pain which appeared significantly more often in Stage IV endometriosis. Irrespective of considered stage, endometriosis was most often found in the ovaries, sacro-uterine ligaments, peritoneum, and rectovaginally. Regarding severe endometriosis, it is significantly more often found in the ovaries and rectovaginally, compared to moderate endometriosis (Table 1).

Blood PI in both uterine and ovarian arteries, did not differ significantly in relation to the endometriosis stage. However, the average RI in these arteries was of significantly higher value in the severe forms of endometriosis. Comparison of either studied stages of endometriosis with the control group shows that both hemodynamic values were significantly higher at the level of the uterus and ovaries (Table 2).

Table 1. — *Clinical parameters in the test groups with moderate and severe endometriosis*

Endometriosis	Moderate (n = 35)	Severe (n = 19)	*p*
Symptoms			
Pelvic pain	26 (74.3%)	18 (94.7%)	**0.030***
Dismenorea	28 (80.0%)	18 (94.7%)	0.071
Dispareunia	28 (80.0%)	16 (84.2%)	0.352
Annovulation	24 (68.6%)	16 (84.2%)	0.106
Localization			
Peritoneum	20 (57.1%)	10 (52.6%)	0.375
Sacro-uterine ligament	17 (40.6%)	12 (63.2%)	0.056
Rectovaginally	10 (28.6%)	10 (52.6%)	**0.041***
Bowels	13 (37.1%)	4 (21.1%)	0.634
Ovary	26 (74.3%)	18 (94.7%)	**0.033***
Oviduct	5 (14.3%)	5 (26.3%)	0.139
Other	5 (14.3%)	6 (31.6%)	0.066

Data are represented as the median value ± standard deviation or the number of cases (%).
* significant $p < 0.05$.

Table 2. — *Comparison of hemodynamic parameters between the test groups with moderate/severe endometriosis and the control group*.

	Moderate endometriosis[1] (n = 35)	Severe endometriosis[2] (n = 19)	Control group[3] (n = 45)	p^{12}	p^{13}	p^{23}
Uterus						
PI	2.74 (2.31 - 3.80)	2.80 (2.26 - 3.58)	2.60 (1.56 - 2.97)	0.814	**< 0.001***	**0.001***
RI	0.83 (0.76 - 0.92)	0.89 (0.83 - 0.92)	0.65 (0.57 - 0.73)	**0.016***	**< 0.001***	**< 0.001***
Ovary						
PI	0.94 (0.80 - 1.09)	0.94 (0.80 - 1.26)	0.77 (0.46 - 0.96)	0.079	**< 0.001***	**< 0.001***
RI	0.85 (0.78 - 0.97)	0.88 (0.81 - 0.97)	0.60 (0.30 - 0.81)	**0.011***	**< 0.001***	**< 0.001***

PI: pulsatility index; RI: resistance index; Median (range); * significant $p < 0.05$.

Discussion

Pain and infertility are the primary manifestations of the presence of endometriosis, and the dominant one in cases classified as Stage III and IV of this disease [6-8]. Negative effects of the presence of endometriosis are manifested through the anamnestic indicators, particularly in case of severe endometriosis. Patients with this stage of the disease are on the average older, with longer duration of infertility and with lower parity. Based on these results, a conclusion appears obvious regarding the importance of timely application of an adequate treatment for the mild and moderate stage of endometriosis.

The results of this study indicate that particular attention should be paid to the symptoms according to the individual stages of endometriosis. It appears that the symptoms do not differ significantly in studied stages, except for the presence of pain that is much more often a symptom in severe endometriosis. Considering more common locations on the oviducts, rectovaginally, and on sacro-uterine ligament, as well as the deep infiltration of the lesions in case of severe endometriosis, the larger number of cases with the pain is quite logical. Earlier studies have confirmed that the localization of endometrial deep-infiltrated lesions, as a specific entity, is similar and that they are mostly responsible for the presence of pain [6, 8, 9-11].

The association between endometriosis and infertility is related to the fact that endometriosis may induce inflammation of the pelvis minor organs and the peritoneum. In advanced stage of endometriosis, female reproductive function is hindered on all levels.

Disturbed anatomic relations inside the pelvis minor are determined by the presence of adhesive fibrous formations, and jeopardized fertility capacity is further compromised with increased level of inflammation mediators. Consequences of such anatomic-functional mismatches are inadequate hemodynamic parameters, as indicated by altered blood flow to the ovaries and uterus.

Hemodynamics of the mentioned arteries is also altered due to previously established, most often localizations of the endometrial lesions in the immediate vicinity.

In the control group of healthy women, the average values of blood perfusion parameters in the uterine and ovarian arteries correspond to those which, according to the available studies, ensure favorable conditions for conception [3, 4, 12, 13]. In case of moderate and severe endometriosis, the average PI and RI, both at the level of uterus and ovary, have significantly higher values, whereby the possibilities of conception and implantation are considerably reduced.

Comparison of hemodynamic parameters between the group with moderate and severe stage of endometriosis, showed that only the resistance to blood flow in uterine and ovarian arteries is considerably higher (worse) in severe endometriosis, at both examined levels. PI values are in both cases similar to the groups with endometriosis. Thereby RI stands out as the parameter of greater sensitivity in the prediction of worsened hemodynamics determined by the progressed stage of endometriosis.

Conclusion

The hemodynamic parameters of uterine and ovarian arteries are considerably different in women with moderate and severe stage of endometriosis compared to

healthy women. Resistance to blood flow in uterine and ovarian arteries and in their branches shows greater sensitivity as the indicator of higher stage, progressed endometriosis, compared to the PI value.

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