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Are there any association between polycistic ovary syndrome and congenital abnormalities of Müllerian ducts

Da li postoji udruženost sindroma policističnih ovarijuma i urođenih anomalija Milerovih kanala

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Abstract

Background/Aim. There are many specificities of merital infertility and sometimes surprising connections between some thinks with no connections at first sight. Examinations of these patients imply diagnostic actions such as the blood basal hormone sample, doing hysterosalpingography, ultrahysterosonography, ultrasound examinations, and sometimes laparoscopy and hysteroscopy if there are necessary. The aim of the study was to determine the characteristics of the connection between policystic ovary (PCO) syndrome (Sy) and congenital Müllerian ducts abnormalities. **Methods.** This study included 356 patients treated in the period from January 1, to December 31, 2009, in the Department of Infertility of the Clinic for Obstetrics and Gynecology in Niš, Serbia. Exclusion criteria were no myoma, ovary cysts, tubal and male factors of infertility. **Results.** A total of 180 patients were divided into 3 groups: the group I with PCO sy, the group II with uterine congenital malformation and the group III with a combination of these disorders. The middle age of patients was 29.6 ± 4.8, body mass index (BMI) was 26.1 ± 4,8 kg/m² the middle thicknes of endometrium was 5.2 + 2.7 mm, and there were no significant differences between the examined groups. There were no significant among in a number of miscarriages in the examined groups. We found that PCO Sy and congenital abnormalities of Müllerian ducts were conjoint in 30% of examined patients. **Conclusion.** Conjoined PCO Sy and congenital abnormalities of Müllerian ducts do not result in a higher number of misscarriages than only either PCO Sy or abnormalities of Müllerian ducts. It is important to check BMI, basal level of follicle stimulating hormone and number of antral follicles because the induction protocol and concentracion of inductors depends on these characteristics, thus, the succsessful cycles and pregnancy.

Key words:
polycystic ovary syndrome; uterus; congenital abnormalities; comorbidity; risk assessment.

Apstrakt

Uvod/Cilj. Postoje mnoge specifičnosti u ispitivanju bračnog steriliteta koje ponekad mogu da nas iznenade svojom pojavom, povezanošću ili mogućom zajedničkom genskom ekspresijom. Tako, moguća je i povezanost sindroma policističnih ovarijuma (PCOS) i kongenitalnih malformacija Milerovih kanala. Cilj rada bio je da se utvrde karakteristike povezanosti PCOS i kongenitalnih malformacija Milerovih kanala. **Metode.** Studijom je bilo obuhvaćeno 356 infertilnih žena lečenih u periodu od 1. januara 2008. do 31. decembra 2009. u Ginekološko-akušerskoj klinici u Nišu. Pacijentkinje sa miomima, cistama jajnika, tubarnim sterilitetom, kao i infertilni muškarci nisu uključeni u studiju. **Rezultati.** Ukupno 180 pacijentkinja bilo je podeljeno u tri grupe: grupa sa kongenitalnim malformacijama Milerovog kanala, grupa sa PCOS i grupa sa udružene obe pojave. Prosečna starost pacijentkinja iznosila je 29,6 ± 3,7 g, srednja vrednost indeksa telesne mase (BMI) 26,1 ± 4,8 kg/m2, a srednja vrednost debljine endometrijuma 5,2 ± 2,7 mm. Nije utvrđena statistički značajna razlika među grupama za navedene parametre izuzev za BMI. Nije bilo značajne razlike u broju pobačaja među ispitivanim grupama. Kombinacija PCOS i kongenitalnih malformacija Milerovih kanala utvrđena je kod 30% ispitivanih pacijentkinja. **Zaključak.** Udruženost ispitivanih pojava nema uticaja na povećanje incidencije spontanih pobačaja, ali treba obratiti pažnju na prateće faktore kao što je BMI, bazalni uzorak folikulostimulirajućeg hormona i broj antralnih folikula jer oni, takođe, govore o kvalitetu jajnih ćelija koje sazrevaju.

Ključne reči:
jajnik, policistični, sindrom; materica; anomalije; komorbititet; rizik, procena.

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Introduction

In everyday work sometimes some specific and uncommon thinks at first sight can be found. Examinations such as blood basal hormone samples, hysterosalpingography, ultrahysterosonography, ultrasound examinations and sometimes laparoscopy and hysteroscopy are perfomed sometimes. But there are some investigations with the aim to find the connections between polycystic ovary syndrome (PCO sy) [1] and congenital abnormalities of Müllerian ducts [2] as well as different genes expressions. In that case there is no difference between mild or other forms of congenital Müllerian abnormalities. Genes which are maybe involved are WNT genes probably WNT 4. WNT4 gene has influence on growth factor for development of kidney, adrenal glands, mammary glands, pituitary glands and female reproductive tracts. With late development of that gene locus, masculasations happens in female fetus as well as stronger steroidogenesis [3]. WNT5, WNT7, HOXA 10 and HOXA 11 genes locus have a very important part in regulation uterus stroma as well as production estrogens and progesterons. WNT and HOXA genes are both important in developing anteroposterior axis of reproductive tract. It means that in special conditions their expression influences the different development of Müllerian ducts and ovaries.

The aim of the study was to determine if the connections between PCO sy and congenital Müllerian ducts abnormalities exist.

Methods

This study included 356 patients treated in the period from January 1, 2008 to December 31, 2009, in the Department of Infertility in Clinic for Obstetrics and Gynecology in Niš. All the patients with myoma, ovary cists, tubular and male factors of infertility were excluded. A total of 180 patient left, so they were divided into 3 groups: the group I with PCO sy, the group II with uterine congenital malformations and the group III with a combination of these disorders.

The patients were examined using the protocols: basal blood hormone sample, hysterosalpingography or ultrahisterosonography. If the diagnosis of PCO sy was made oral insulin glucose test with the level of insulin, ultrasound examination, and endoscopic procedures, if necessary, were also performed.

Also, we investigated variables like body mass index (BMI), age, as well as the number of miscarriages.

All the results were statistically analyzed and shown as mean values standard deviation. The difference was statistically significant when $p < 0.05$.

Results and discussion

The percentage of association between PCO sy and Müllerian duct congenital abnormalities was about 30 but as we cannot find the similar datas in the literature, it is hard to compare. The clinical and epidemiological features of the group of patients with PCO sy and the group with the combination of PCO sy and congenital Millerian abnormalities are shown in Table 1. There is no significant difference between the examined groups in any variables except BMI (Table 2). Also, there were no significant differences in a number of misscarrigies among the groups (Table 3). If we compare congenital Müllerian abnormalities in our study (Table 4) and the literature data the percentage of them is similar, except uterus bicornis and arcuatus which differs a little; there were more bicornis than other abnormalities. Usually, the biggest prevalence had uterus arcuatus (Table 5). It could be the result of

Table 1

Clinical and epidemiological characteristics of the patients

Characteristics	PCO sy and congenital Müllerian abnormalities	PCO sy	Total
Patients (n)	60	60	120
Age (years) x ± SD	29.7 ± 3.5	30.1 ± 3.6	29.6 ± 3.7
BMI (kg/m^2), x ± SD	25 ± 0.46	27.1 ± 4.5	26.1 ± 4.6
Duration of infertility (years), x ± SD	3.4 ± 2.4	3.6 ± 2.3	3.5 ± 2.4
Endomerial thickness 2–4 days (mm), x ± SD	4.8 ± 2.2	5.8 ± 3.2	5.2 ± 2.7
FSH 2–4.days (miV/mL), x ± SD	6.1 ± 2.0	5.9 ± 1.9	5.2 ± 2.7
The antral follicle count (n), x ± SD	18.3 ± 14.2	21.5 ± 16.2	20.2 ± 15.7

PCO sy – policystic ovary syndrome; BMI – body mass index; FSH – follicle stimulating hormone.

Table 2

Body mass index (BMI) in the studied groups of patients

Groups of patients	BMI (kg/m^2)		
	< 20	20–29	> 20
PCO Sy, n	6*	49	5
Mixed, n	0	55	5

PCO sy – policystic ovary syndrome; Mixed – PCO sy and congenital Müllerian abnormalities; *PCO sy *vs* mixed $p < 0.05$ (statistically significant).

Table 3

The number of miscarriages in the studied groups of patients

Groups of patients	Miscarriages		
	One	Two	≥ Three
Mixed, n (%)	3 (5)	2 (3.3)	2 (3.3)
PCO Sy, n (%)	6 (10)	1 (1.7)	0 (0)

PCO sy – policystic ovary syndrome; Mixed – Müllerian ducts abnormalities conjoined with policystic ovary syndrome.

Table 4

Congenital anomalies of Müllerian ducts in the different groups

Group of patient	Anomalies					
	Arcuatus	Bicornis	Unicornus	Duplex	Subseptus	Septus
Mixed, n (%)	24 (40)	20 (30.3)	2 (3.3)	2 (3.3)	10 (16.5)	2 (3.3)
Müllerian ducts abnormalities, n (%)	24(40)	24 (40)	4 (6.6)	4 (6.6)	4 (6.6)	4 (6.6)

Mixed – Müllerian ducts abnormalities conjoined with policystic ovary syndrome.

Table 5

The number of miscarriages depending on the type of anomaly

Anomalies	Miscarriages (n)	
	Mixed group	Müllerian abnormalities group
Arcuatus	2	2
Bicornus	2	1
Unicornus	0	0
Duplex	0	2
Subseptus	1	1
Septus	0	1

Mixed – Müllerian ducts abnormalities conjoined with policystic ovary syndrome.

different diagnosis procedures such as hysterosalpingography, hysteroscopy, ultrasound, and it is also possible that the investigator can have his/her personal opinion.

There are no significance differences between miscarriages in the group with PCO sy and the group PCOsy and Müllerian congenital abnormalities, so it means that perinatal outcome is not worse if we have there two problems conjoined. It means that if we make good diagnostic procedures we can treat PCO sy as well as congenital Müllerian abnormalities and have good results. Literature data have reported successful results between 10% and 65%, our were about 11%.

Some studies prove a significant difference between those with uterine malformations and those with normal uterus in the abortion rate, and preterm deliveries. It is expected, but we did not have a group with the normal uterus because it was not the aim of our study. The patients with didelphys and unicornuate uterus have similar effect on reproduction, because we can considered that didelphys is symmetrical duplication of unicornuate uterus. Patients with bicornuate uterus also have a poor pregnancy outcome, so patients with partial bicornis have a better pregnancy outcome than patients with a complete one. Even if there are no differences between the number of miscarriages, the highest number is in the group with PCO sy with one miscarriage, two had only one, and more than two none. It means that patients after one miscarriage go to concluding and other diagnostic procedures (ultrasound or hysteroscopy) as well as resection of septum, metroplasty or medicaments for PCO sy.

It seems that the patients with uterine malformations have high abortion and delivery rates as well as low delivery rates from their first pregnancy to the every next pregnancy.

It is very interesting, if there are any differences between BMI in different groups, what are the values of basal blood hormone samples, and the measurements of endometrium on the day 4 following ultrasound. Our results demonstrated that the middle age of patients was 29.6 ± 3.7, BMI 26.1 ± 4.8 kg/m^2 and the middle thicknes of endometrium 5.2 ± 2.7 mm with no significant differences among the groups.

The number of miscarriages was equal in the groups and similar to the literature data (from 10% to 60%), and if similar multicentric investigatations are performed, we can have good results, for instance higher number of ovulations can improve perinatal outcome. It means that the improved quality of ovarian cells will result in good ovulation and pregnancy [4]. Some studies have examined the pregnancy outcome in patients with untreated uterine malfomations and their pregnancy rate is exactly the same in their first and later pregnancies as the abortion, and the preterm delivery rates [5–7].

It has been very imoprant to identify all endocrinological, clinical and ultrasound disorders which can influnce ovulations.

We do not speak about the level of basal follicle stimulating hormone (FSH), which is also very important for the protocol of induction of ovulations, as well as the types of drugs and their effects.

BMI, and age are also important. Women with higher BMI could have more antral follicles, but lower intermediate and higher, as we can see in many multicentric studies. It should be kept in mind and, if necessery, to use different protocol of ovulation.

Conclusion

Conjoined PCO sy and congenital abnormalities of Müllerian ducts do not result in the higher number of miscarriages. It is important to check BMI, basal level of FSH and number of antral follicles because the induction protocol and concentration of inductors depend on these characteristics, and consequently the successesful cycles and pregnancy.

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