Özgün Araştırma / Original Article

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology - Obstetrics and Neonatoloogy

Comparison of the clinical and laboratory outcomes in adolescent and adults with polycystic ovary syndrome

Polikistik over sendromunun adolesan ve erişkinlerde klinik ve laboratuar parametreler açısından karşılaştırılması

Hasan Onur Topçu[1], Seda Topçu[2], Aslı Oskovi[1], Ali İrfan Güzel[1], Yaprak Engin-Üstün[1], Nedim Çiçek[1], Nafiye Yılmaz[1]

[1] Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey

[2] Ankara Diskapi Children's Hospital, Department of Pediatric, Department of Pediatrics, Ankara, Turkey

ÖZET

Amaç: Polikistik over sendromu (PKOS) kadınlarda anovulasyon, hirşutism ve infertilitenin en önemli nedenidir. Perimenarş döneminde başlayan ovulatuar disfonksiyon, hiperandrojenizm, hiperinsülinemi ve insülin resistansıyla ilişkilidir. Reprodüktif çağdaki kadınlarda prevelansı %3-23 arasında değişmektedir. Adolesanlarda PKOS tanısı için tanımlanmış kriterler mevcut değildir. National Institutes of Health ve Rotterdam kriterleri pratikte halen kullanılmaktadır. Biz çalışmamızda; Rotterdam kriterlerini tanı için kullandık ve polikistik over sendromu tanısı almış adolesan ve reprodüktif çağdaki kadınları klinik ve laboratuar parametreler açısından karşılaştırdık.

Gereç ve Yöntemler : Çalışmamıza Rotterdam kriterlerine göre PKOS tanısı konulmuş 14-18 yaşları arasındaki adolesan kızlar ve 25-32 yaşları arasında reprodüktif çağdaki kadınlar dahil edildi. Vücut kitle endeksi (VKI), bel-kalça oranı ve serum FSH, LH, E2, PRL, TSH, total testosteron, serbest testosteron, insülin, HOMA-IR düzeyleri her iki grupta hesaplandı.

Bulgular: VKI, bel-kalça oranı, serum FSH, E2, PRL, TSH ve LH/FSH oranı her iki grupta benzer bulundu. Ancak serum LH, total testosteron, serbest testosteron, insülin, HOMA-IR değerleri gruplar arasında istatistiksel olarak farklı bulundu.

Sonuç: Çalışmamızda, hiperandrojenizm ve insülin değerleri adolesan PKOS'larda erişkin çağdaki PKOS'lu kadınlara göre daha yüksek bulundu. Bize göre, bu bulgular ile pubertede meydana gelen metabolik değişiklikler arasında ilişki olabilir.

Anahtar Kelimeler: Polikistik over sendromu, adolesan, hiperandrojenism

ABSTRACT

Aim: Polycystic Ovary Syndrome (PCOS) is the leading cause of anovulation, hirsutism and infertility in women of all ages. It is associated with ovulatory dysfunction beginning in the perimenarchal period, hyperandrogenism, hyperinsulinemia, and insulin resistance. For adult women the prevalence of PCOS ranges from 3% to 23%. There are no established diagnostic criteria for the diagnosis of PCOS in adolescents. Both the National Institutes of Health and the Rotterdam criteria are used in practice. We used Rotterdam criteria for the diagnosis. In current study, we compared the clinical and laboratory outcomes in adolescents and adults with PCOS.

Material and Methods: Females aged 14 to 18 years old for the adolescent group and aged 25 to 32 years old for the reproductive age group with a diagnosis of PCOS using the Rotterdam criteria were enrolled in the study. Risk factors were recorded; body mass index (BMI), Waist/hip, FSH, LH, E2, PRL, TSH, Total Testosterone, Free Testosterone, Insulin, HOMA IR.

Results: There was no statistical significance between the groups in terms of BMI, waist/hip ratio, FSH, E2, LH/FSH, PRL, TSH. However, LH, total testosterone, free testosterone, insulin, HOMA-IR values were statistically significantly different between the groups.

Conclusion: Our study showed that hyperandrogenism, and insulin values are seen higher in adolescent PCOS in adult PCOS. In our opinion, there may be a likely relationship between these findings and metabolic differences in puberty.

Key Words: Polycystic Ovary Syndrome, Adolescent, Hyperandrogenism

Yazışma Adresi / Correspondence Address:
Dr. Hasan Onur TOPÇU
Zekai Tahir Burak Women Health Education and Research Hospital, Ankara, Turkey.
Tel: +90 532 635 95 38 - **Fax:** +90 312 306 59 17
e-mail: dronurtopcu@gmail.com

Geliş tarihi / Received : 02.05.2014
Kabul tarihi / Accepted : 22.05.2014

Introduction

Polycystic ovary syndrome (PCOS), which was first described in 1935 by Stein and Leventhal is a common endocrine disorder, affecting 5%-10% of reproductive-age woman (1). It is described with a composition of clinical, biochemical and radiological findings, mainly characterized with oligo-anovulation, hyperandrogenism and polycystic ovaries (2). Typical presentation of PCOS includes obesity, irregular menses, acne and hirsutism; which adversley affects the quality of life and can be more bothersome especially in adolescent patients (1). Due to Rotterdam ESHRE-ASRM study group in 2003, presence of at least two of the following criteria: clinical or biochemical hyperandrogenism, oligo-anovulation, polycystic ovaries were defined as PCOS (2). However, the nature of the adolescence is also characterized with physiologic anovulation and irregular menses in the first two years of menarche and acne, so the normal findings of this group may overlap with PCOS symptoms, which makes the diagnosis more problematic; since there are no diagnostic criteria described specificly for adolescent population and the feasibility of existing PCOS criteria on adolescent patients are still unclear (3).

The etiology of PCOS is controversial. Hypotalamic - pituitary and ovarian dysfunction, adrenal hyperresponsiveness, insulin resistance and obesity both play a role in development of androgen excess and adverse metabolic squeale in PCOS (4, 5).

PCOS is seen both in normal weight and obese woman and the severity of the clinical symptoms and metabolic sequele increases with the excessive body weight (6). Insulin resistance, hyperinsulinemia and hyperandrogenism may be a key mechanism underlying in this continuous sequence of hormonal and metabolic abnormalities in adolescents (7, 8).

During puberty, insulin sensitivity decreases (9, 10) while insulin requirements increase (11). Basal insulin levels are higher in the end of puberty than during prepuberty or adulthood. This suggests a role for hyperinsulinaemia in the development of PCOS, which occurs during the puberty stage of life. The nature of the puberty may cause different clinical and laboratory findings in adolescents with PCOS than adults with PCOS, therefore in this current study, we aimed to compare the clinical and laboratory findings between adolescents and adults with PCOS.

Material and Methods

This study was conducted at Zekai Tahir Burak Women's Health Care Education and Research Hospital, in Ankara, Turkey and was carried on participants who admitted to the adolescence and infertility department between June 2013 and September 2013. The study was approved by Institutional Review Board of Zekai Tahir Burak Women's Health Care Education and Research Hospital, and written informed consent was obtained from each participant.

The women with PCOS were divided into two groups: the adolescent age group and reproductive age group. Twenty-five adolescent girls aged 14 to 18 years old for the adolescent group with PCOS and twenty-five reproductive age women aged 25 to 32 years old with PCOS were enrolled into the study. Diagnosis of PCOS was based on the revised Rotterdam 2003 consensus on diagnosis criteria.

Body mass index (BMI), waist/hip ratio, FSH, LH, E2, LH/FSH, Prolactin, TSH, total testosterone, free testosterone, insulin and HOMA-IR (fasting plasma insulin X fasting plasma glucose)/22.5 were the risk factors recorded (12).

Numerical variables were evaluated for normality of data distribution by using the Kolmogorov-Smirnov test. Descriptive statistics were expressed as mean ± standard deviation (SD) according to the assumption of normal distribution. In case of normal distribution of data, independent samples t-test was performed to compare the means of the two groups. A $p<0.05$ was accepted as statistically significant. Data analysis was performed using the SPSS 15.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) software package.

Results

There were no statistically significant differences between two groups in terms of BMI, waist/hip ratio, LH/FSH ratio and serum FSH, E2, Prolactin, TSH levels. Serum LH, total testosterone, free testosterone, insulin values and HOMA-IR ratio were significantly higher in adolescent girls with PCOS than in reproductive age group with PCOS (Table 1).

Table 1. The clinical parameters of the groups

	Adolescent age group (n=25)	Reproductive age group (n=25)	P value
Age	16.24±2.5	27.8±4.3	**<0.001**
BMI (kg/m^2)	23.7±3.8	21.9±4.3	0.129
Waist/hip	0.7±0.05	0.7±0.04	0.061
FSH (mIU/ml)	6.0±1.3	6.3±1.4	0.489
LH (mIU/ml)	7.5±4.6	5.0±1.5	**0.013**
E_2 (pg/ml)	34.3±15.3	40.5±11.77	0.114
LH/FSH	1.1±0.9	0.8±0.2	0.088
PRL (ng/ml)	15.4±7.3	13.1±5.8	0.219
TSH (mIU/ml)	2.3±1.0	1.8±1.0	0.165
TT (ng/dL)	51.8±21.8	35.5±15.6	**0.004**
FT (ng/dL)	2.7±0.9	1.7±0.4	**<0.001**
Insulin (uIU/mL)	17.2±10.4	10.7±4.3	**0.006**
HOMA IR	3.9±2.6	2.4±1.0	**0.009**

Discussion

Sultan and Paris (13) proposed a definition of PCOS for adolescents with criteria; clinical hyperandrogenaemia (acne and hirsutism), biochemical hyperandrogenaemia (level of serum testosterone> 50ng/dl, LH/FSH ratio>2), insulin resistance and hyperinsulinaemia (impaired glucose tolerance, visceral adiposity, acanthosis nigricans), oligomenorrhoea persisting 2 years post menarche, polycystic ovaries on ultrasound. However, puberty has similar signs and symptoms with PCOS. In

particular; the physiologic and clinical changes in adolescents mimic the abnormal laboratory and clinical findings in PCOS.

The menstrual irregularities; such as oligomenorrhoea are a normal variant in the teen years because of the anovulatory cycles. In a study, it was showed that almost 50% of the girls between 15 and 18 years-old had oligomenorrhoea (14). Pelvic ultrasound is used in virgin adolescent population which is less sensitive for visualizing ovarian cysts than transvaginal ultrasound approach; amongst the adolescents with PCOS who underwent pelvic ultrasound, only 15% of the patients were reported to have ovarian cysts in one study (1). Also, multifollicular ovaries can be a normal finding in adolescents (4). These two situations can cause both over-diagnose and under-diagnose in adolescence. Moreover, androgen excess syptoms like acne and hirsutismus may be confused with normal pubertal signs and there is not enough normative data of biochemical values of androgen levels for adolescent population (4, 15). Those menstrual irregularities, physiological and clinical changes in puberty make it more difficult to distinguish the diagnosis of PCOS than physiological changes of puberty.

There is no consensus on appropriate laboratory tests for the assesment of PCOS (4). In a study, even the investigation of the adolescent girls with PCOS differed between pediatric endocrinology and gynecology clinics (1). In laboratory testing, the aim should be excluding other endocrinopathies such as late-onset congenital adrenal hyperplasia, hyperprolactinaemia, hypothyroidism, and Cushing's syndrome, androgen-secreting tumoursin differential diagnosis of hyperandrogenism and diagnosing dysglycemia and other metabolic abnormalities which accompany PCOS (16, 17). Obesity is strongly related to PCOS as 40-60% of woman with PCOS are obese (15). Even lean patients with PCOS had higher amount of body fat than lean controls and android pattern of body fat distribution while lean controls had gynoid pattern (18). Insulin resistance is blamed for playing a key mechanism under this metabolic syndrome as insulin resistance was present inapproximately 80% of women with PCOS in one study (19). Hyperinsulinism produces an androgenic state by increasing ovarian steroidogenesis and androgen and reducing production of sex hormon binding globulin (17, 20). In this study, we found that hyperandrogenism and hyperinsulinaemia are more common in adolescent girls with PCOS than in reproductive age group with PCOS.

Conclusion

Starting from adolescence, early diagnosis and intervention is essential in controling and preventing the long term metabolic sequels of PCOS. Therefore, discriminative criteria are needed for adolescent patients.

References

1. Orsino A, Van Eyk N, Hamilton J. Clinical features, investigations and management of adolescents with polycystic ovary syndrome. Paediatr Child Health. 2005;10:602-8.
2. Rotterdam ESHRE/ASRM - Sporsored PCOS consensus workshop groups. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19:41-7.
3. Cırık DA, Dilbaz B. What do we know about metabolic syndrome in adolescents with PCOS? J Turk Ger Gynecol Assoc. 2014;15:49-55.
4. Khan U. Polycystic ovary syndrome in adolescents. J Pediatr Adolesc Gynecol. 2007;20:101-4.
5. Lewy VD, Danadian K, Witchel SF, Arslanian S. Early metabolic abnormalities in adolescent girls with polycystic ovarian syndrome. J Pediatr. 2001;138:38-44.
6. Christensen SB, Black MH, Smith N, Martinez MM, Jacobsen SJ, Porter AH, et al. Prevalence of polycystic ovary syndrome in adolescents. Fertil Steril. 2013;100:470-7.
7. Eagleson CA, Gingrich MB, Pastor CL, Arora TK, Burt CM, Evans WS, et al. Polycystic ovarian syndrome: evidence that flutamide restores sensitivity of the gonadotropin-releasing hormone pulse generator to inhibition by estradiol and progesterone. J C Endocrinol Metabol 2000;85:4047-52.
8. Arslanian SA, Lewy VD, Danadian K. Glucose intolerance in obese adolescents with polycystic ovary syndrome: roles of insulin resistance and beta-cell dysfunction and risk of cardiovascular disease. J Clin Endocrinol Metab. 2001;86:66-71.
9. Bloch CA, Clemons P, Sperling MA. Puberty decreases insulin sensitivity. J Pediatr. 1987;110:481-7.
10. Amiel SA, Caprio S, Sherwin RS, Plewe G, Haymond MW, Tamborlane WV. Insulin resistance of puberty: a defect restricted to peripheral glucose metabolism. J Clin Endocrinol Metabol 1991;72:277-82.
11. Smith CP, Archibald HR, Thomas JM, Tarn AC, Williams AJ, Gale EA, et al. Basal and stimulated insulin levels rise with advancing puberty. Clin Endocrinol 1988;28:7-14.
12. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27:1487-95.
13. Sultan C, Paris F. Clinical expression of polycystic ovary syndrome in adolescent girls. Fertil Steril. 2006;86 Suppl 1:S6.
14. van Hooff MH, Voorhorst FJ, Kaptein MB, Hirasing RA, Koppenaal C, Schoemaker J. Endocrine features of polycystic ovary syndrome in a random population sample of 14-16 year old adolescents. Human Reprod 1999;14:2223-9.
15. Diamanti-Kandarakis E. PCOS in adolescents. Best Pract Res Clin Obstet Gynaecol. 2010;24:173-83.
16. Gooding HC, Milliren C, St Paul M, Mansfield MJ, Divasta A. Diagnosing Dysglycemia in Adolescents With Polycystic Ovary Syndrome. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2014.
17. Pasquali R, Gambineri A. Therapy in endocrine disease: treatment of hirsutism in the polycystic ovary syndrome. Eur J Endocrinol. 2014;170:R75-90.
18. Kirchengast S, Peterson B, Hauser G, Knogler W. Body composition characteristics are associated with the bone density of the proximal femur end in middle- and old-aged women and men. Maturitas. 2001;39:133-45.
19. Carmina E, Lobo RA. Use of fasting blood to assess the prevalence of insulin resistance in women with polycystic ovary syndrome. Fertil Steril. 2004;82:661-5.
20. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clin Epidemiol. 2013;6:1-13.