Taiwanese Journal of Obstetrics & Gynecology 53 (2014) 178–182

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Clinical and biochemical characteristics of women with menstrual disturbance

Szu-Yu Shen [a,e], Shih-Yi Huang [b,e], Ching-Hung Hsieh [c], Ming-I Hsu [a,*], Chih-Yu Cheng [d], Chun-Sen Hsu [a]

[a] Department of Obstetrics and Gynecology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan
[b] School of Nutrition and Health Sciences, College of Public Health and Nutrition, Taipei Medical University, Taipei, Taiwan
[c] Department of Obstetrics and Gynecology, Clinic of Fu Jen Catholic University, Taipei, Taiwan
[d] Institute for Labor Research, National Chengchi University, Taipei, Taiwan

ARTICLE INFO

Article history:
Accepted 26 July 2013

Keywords:
amenorrhea
hyperandrogenism
insulin resistance
metabolic syndrome
oligomenorrhea

ABSTRACT

Objective: Menstrual irregularity is one of the major complaints in women of reproductive age. The aim of this study was to evaluate the complications in women with different menstrual disturbances.
Materials and methods: This is a retrospective study. A total of 576 women were screened first, and 470 women were included later [257 women with oligo/amenorrhea (149 hyperandrogenic and 108 non-hyperandrogenic women) and 213 normocyclic controls]. Endocrine and metabolic parameters and insulin resistance were compared among different menstrual patterns.
Results: The average duration of menstrual cycle length was positively correlated with age, levels of androgens and prolactin, lipid profiles, and the parameters of insulin resistance. Hyperandrogenic women with amenorrhea had higher levels of androgens and more lipid profiles disorders than hyperandrogenic women with oligomenorrhea. However, nonhyperandrogenic women with amenorrhea had a degree of insulin resistance and metabolic disturbance similar to that of nonhyperandrogenic women with oligomenorrhea. Interestingly, for women with normal prolactin levels, serum prolactin levels were significantly lower in amenorrhea than oligomenorrhea in both hyperandrogenic and nonhyperandrogenic groups.
Conclusion: The degree of menstrual disturbances does not correlate with the severity of insulin resistance and metabolic disturbances in women without excess levels of androgen. For women with normal prolactin levels, amenorrheic patients had significantly lower serum prolactin levels than oligomenorrheic patients.

Introduction

Hyperandrogenism and chronic anovulation are the major components associated with polycystic ovary syndrome (PCOS). The morbidity of PCOS is associated with insulin resistance, type 2 diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, and low-grade chronic inflammation [1]. A recently reviewed study found that not all women with PCOS should be considered as being similar in terms of cardiovascular risk profiles [2]. Irregular menstrual cycles are associated with insulin resistance [3] and increased risk of cardiovascular disease [4]. Ovulatory dysfunction is associated with a wide range of menstrual disturbances, including irregular cycles and clinical amenorrhea. Menstrual disorders are easy-to-use parameters in the clinical setting. Amenorrhea and oligomenorrhea represent different types of menstrual disturbances. However, the correlation between menstrual interval and biochemical parameters remains unclear in women with chronic anovulation. The association between the severity of menstrual disorders and endocrine and metabolic parameters is controversial [3–7]. We conducted this retrospective study to examine the relationship between menstrual disorders and the metabolic syndrome (MBS).

* Corresponding author. Center of Reproductive Medicine, Wan Fang Hospital, Taipei Medical University, Number 111, Section 3, Xinglong Road, Taipei 11696, Taiwan.
E-mail address: hsumingi@yahoo.com.tw (M.-I. Hsu).
[e] S.-Y.S. and S.-Y.H. contributed equally to this work.

http://dx.doi.org/10.1016/j.tjog.2014.04.009

Methods

We retrospectively reviewed the medical records of female patients who visited the Reproductive Endocrinology Clinic at the Wan Fang Medical Center at Taipei Medical University from January 1, 2009 to November 31, 2011. The chief complaints of these patients were menstrual disturbance, dysmenorrhea, infertility, and acne/hirsutism. The following patients were excluded: (1) women who had been diagnosed with congenital adrenal hyperplasia, androgen-secreting tumor, Cushing's syndrome, disorders of the uterus (e.g., myoma, adenomyosis, Asherman's syndrome, Müllerian agenesis), and chromosomal anomalies (e.g., Turner syndrome); (2) women who had had menarche less than 3 years before evaluation or who were older than 46 years; (3) women with inadequate clinical/biochemical records; and (4) women who received hormones or drugs for major medical diseases. A total of 576 women were initially screened.

Modified Ferriman–Gallwey (mF–G) scores were recorded by one investigator. Hirsutism was defined as an mF–G score $\geq$ 6. Biochemical hyperandrogenemia was defined as total serum testosterone $\geq$ 2.78 mmol/L. Hyperandrogenism was defined as hirsutism and/or biochemical hyperandrogenemia.

Amenorrhea was defined as no menstrual bleeding over a period of at least 3 months and oligomenorrhea was defined as fewer than nine cycles per year [8]. Normocyclic controls were defined as having regular menstrual intervals of 24–34 days. To simplify the experimental groups, 106 women were further excluded due to primary amenorrhea ($N = 9$), premature ovarian failure ($N = 10$), hyperprolactinemia (serum prolactin $>$ 26.4 μg/L or 1.15 nmol/L; $N = 59$), and irregular cycles without oligomenorrhea/amenorrhea ($N = 28$). Finally, the 470 women were classified into three subgroups, namely, normocyclic ($N = 213$) and oligomenorrhea/amenorrhea ($N = 257$; 147 women had oligomenorrhea and 110 women had amenorrhea). To further evaluate the clinical and biochemical characteristics of women with amenorrhea and oligomenorrhea, the 257 women were classified as hyperandrogenic ($N = 149$, oligomenorrhea = 83, amenorrhea = 66) and non-hyperandrogenic ($N = 108$, oligomenorrhea = 64, amenorrhea = 44).

PCOS was diagnosed according to the 1990 National Institutes of Health diagnostic criteria, which required both oligomenorrhea or amenorrhea and hyperandrogenism for a diagnosis of PCOS. Of the 470 cases, 149 women with PCOS and 321 women without PCOS were considered separately.

The number of menstrual cycles during the previous year was recorded. Menstrual cycle length was defined as the average duration/year. Body mass index was defined as body weight in kilograms divided by body height in meters squared (kg/m^2).

Medical histories included detailed menstrual and medical/surgical records as well as anthropometric measurements. The dates and assays for blood sampling have been previously described [9]. The timing of blood sampling was either in the early follicular phase (Days 1–5 for normocyclic women) or more than 35 days after the previous menstrual bleeding (for oligo/amenorrheic women). The following components were evaluated: (1) total testosterone, androstenedione, dehydroepiandrosterone sulfate, 17-α-hydroxyprogesterone, and free androgen index (FAI); FAI = T (nmol/l) × 100/sex hormone-binding globulin (SHBG) (nmol); (2) fasting insulin, fasting glucose, 2-hour oral glucose tolerance test glucose level, and the homeostasis model assessment of insulin resistance index (HOMA-IR); HOMA-IR = [fasting insulin (μU/mL) × fasting glucose (mg/dL)]/405; (3) serum thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin; (4) total cholesterol, triglycerides (TGs), high-density lipoprotein (HDL), and low-density lipoprotein (LDL); and (5) SHBG and anti-Müllerian hormone (AMH).

The MBS (2005 National Cholesterol Education Program-Adult Treatment Panel III) was defined as the presence of at least three of the following criteria: abdominal obesity (waist circumference $>$ 80 cm), serum TG $\geq$ 1.7 mmol/L, serum HDL $<$ 1.3 mmol/L, blood pressure $\geq$ 130/$\geq$ 85 mmHg, and fasting plasma glucose $\geq$ 5.6 mmol/L.

Statistical analysis

Statistical analysis was performed using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA). We evaluated the correlation between menstrual cycle length and PCOS-related parameters with Pearson's correlation coefficients using the two-tailed method. Data are presented as the mean ± standard deviation. We used the Chi-square and Fisher's exact tests to compare categorical variables and analysis of variance to compare continuous variables (Tables 1 and 2). Differences between the groups were considered significant when $p < 0.05$.

Results

The average duration of menstrual cycle length was positively correlated with the following parameters: age ($r = -0.133$, $p = 0.004$), AMH ($r = 0.199$, $p < 0.001$), SHBG ($r = -0.174$, $p < 0.001$), ferritin ($r = 0.319$, $p < 0.001$), LH ($r = 0.123$, $p = 0.008$), prolactin ($r = -0.217$, $p < 0.001$), HOMA-IR ($r = 0.234$, $p < 0.001$), fasting insulin ($r = 0.220$, $p < 0.001$), total cholesterol ($r = 0.207$, $p < 0.001$), LDL ($r = 0.200$, $p < 0.001$), total testosterone ($r = 0.169$, $p < 0.001$), androstenedione ($r = 0.169$, $p < 0.001$), and FAI ($r = 0.165$, $p < 0.001$).

Table 1 shows the clinical and biochemical characteristics of 470 patients. The normocyclic group (A) had 213 cases and the oligo/amenorrhea group (B) had 257 cases. Compared with the controls, the women with oligo/amenorrhea had a higher prevalence of hyperandrogenism and MBS. Women with oligo/amenorrhea suffered from higher disturbances in the parameters of insulin resistance and lipid profiles than women with normal menstrual cycle.

Table 2 shows biochemical and clinical characteristics of normocyclic controls and oligo/amenorrhea in women without PCOS. The LH/FSH ratio was significantly higher in women with oligomenorrhea/amenorrhea than in women with normal cycle (Table 2); however, the LH/FSH ratio was not significantly different between women with oligomenorrhea and women with amenorrhea (Table 2). Androgens levels (total testosterone, androstenedione, and FAI), lipid profiles, and insulin resistance were similar between oligomenorrheic and amenorrheic women without PCOS (Table 2).

Table 3 shows the comparison of biochemical characteristics of PCOS women with oligomenorrhea or amenorrhea. For PCOS, amenorrheic women had significantly higher androgens, lower SHBG levels, and more lipid profile disturbances than oligomenorrheic women. In both the PCOS and non-PCOS groups, the insulin resistance and risk of MBS were not significantly different between the oligomenorrheic and amenorrheic subgroups (Tables 2 and 3). Interestingly, serum prolactin levels were significantly higher in oligomenorrheic compared with amenorrheic women for both PCOS and non-PCOS.

Discussion

Ovulatory dysfunction, defined as oligomenorrhea and amenorrhea, is a common complaint in women of reproductive age. The long-term complications of ovulatory dysfunction have not been well studied. Hyperandrogenemia is thought to increase cardiovascular and metabolic risks in women with PCOS [2,5]. Our results showed that serum androgens were correlated with the severity of menstrual disturbances. Therefore, we compared the clinical and biochemical