GENERAL GYNECOLOGY

Prevalence of hyperprolactinemia in adolescents and young women with menstruation-related problems

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OBJECTIVE: The aim of this study was to evaluate the prevalence of hyperprolactinemia in adolescents and young women with menstrual problems.

STUDY DESIGN: This study included 1704 young women with menstruation-related problems. The patients were classified into group I (age, 11-20 years) or group II (age, 21-30 years); the prevalence of hyperprolactinemia was analyzed according to age and categories of menstruation-related problems.

RESULTS: For primary amenorrhea and oligomenorrhea, the prevalence of hyperprolactinemia was low in both groups. However, hyperprolactinemia was a relatively common cause of secondary amenorrhea (5.5% for group I and 13.8% for group II, respectively); it was more frequent in group II ($P = .001$); the prevalence of prolactinoma was also higher in group II ($P = .015$). For abnormal uterine bleeding, hyperprolactinemia was more common in group II (2.6% for group I and 9.4% for group II; $P < .001$), but causes were similar.

CONCLUSION: Hyperprolactinemia is not rare in young women with menstruation-related problems; its prevalence varies according to age and manifestations.

Key words: adolescent, hyperprolactinemia, menstruation-related problem, young women

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Menstrual disturbances such as primary or secondary amenorrhea, oligomenorrhea, and other patterns of abnormal uterine bleeding (AUB) are common problems among female adolescents.[1] During the first years after menarche, anovulatory cycles are common,[2] and the immaturity of the hypothalamic-pituitary-gonadal axis may be the major cause for irregular menstruation. Although the frequency of ovulatory cycles rises thereafter and in many cases menstruation-related problems can be resolved with time, evaluations for other etiologic factors should be performed.

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Among them, hyperprolactinemia, which is one of the most common endocrine disorders of the hypothalamic-pituitary axis in young women, is associated with ovulatory dysfunction that results in menstrual irregularities. Aside from high prolactin levels during pregnancy and lactation, prolactinoma is the most frequent cause of persistent hyperprolactinemia.[3,4] Additionally, there are a number of causes that alter the neuroendocrine control of prolactin secretion, such as stress and exercise and certain medications.[5]

Hyperprolactinemia can occur at any age, and the prevalence varies from 0.4% in the normal adult population to as high as 9-17% in women with menstrual problems such as amenorrhea or polycystic ovarian syndrome.[6,7] Although a recent study reported that the highest incidence rate of dopamine agonist–treated hyperprolactinemia was found in women 25-34 years old,[8] there has been little information about hyperprolactinemia in young women including adolescents, especially in relation to menstrual problems such as amenorrhea, oligomenorrhea, or AUB. Therefore, this study was conducted to investigate the prevalence of hyperprolactinemia in young women with menstrual problems according to age and manifestations.

Materials and Methods

This study included 1704 women with menstruation-related problems who visited the Young Lady Clinic at Samsung Medical Center from February 1995 to December 2010. The patients were classified into 2 groups according to age: group I (age, 11-20 years old; n = 1002) and group II (age, 21-30 years old; n = 702). This study was approved by the institutional review board of Samsung Medical Center.

A detailed history was taken, and a complete physical examination and laboratory tests were performed. Patients were asked about their growth and development, menstruation, medications, and any medical problems. Physical examinations included height, weight, and secondary sexual characteristics, and the presence of clinical hyperandrogenism signs was determined. Hormone studies included gonadotropins (luteinizing hormone, follicle-stimulating hormone [FSH]), sex hormones (estradiol, progesterone, free testosterone), prolactin, thyroid-stimulating hormone, and beta–human chorionic gonadotropin. Luteinizing hormone and FSH were measured with an immunoradiometric assay kit (DIAsource ImmunoAssays, Nivelles, Belgium). Interassay variations for luteiniz-

TABLE 1
Menstruation-related problems according to age group

Symptom	Group I, n (%)[a]	Group II, n (%)[b]
Amenorrhea	484 (48.3)	339 (48.3)
Primary	192 (19.2)	50 (7.1)
Secondary	292 (29.1)	289 (41.2)
Abnormal uterine bleeding	420 (41.9)	233 (33.2)
Oligomenorrhea	98 (9.8)	130 (18.5)

[a] n = 1002 patients 11-20 years old; [b] n = 702 patients 21-30 years old.

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ing hormone and FSH were 8.0% and 4.4%, respectively; intraassay variations were 3.9% and 2.0%, respectively. Prolactin was measured with an immunoradiometric assay kit (Siemens Healthcare Diagnostics, Marburg, Germany), and inter- and intraassay variations were 2.4 and 1.9%, respectively. If indicated, imaging studies such as gynecologic ultrasonography, brain or pelvic magnetic resonance imaging, and hematologic studies, which included a complete blood cell count and coagulation test, were performed to identify potential organic causes. Prolactinoma was diagnosed with magnetic resonance imaging with gadolinium enhancement and classified into microadenoma (<10 mm) or macroadenoma (≥10 mm) according to the size.

Menstruation-related problems were categorized as amenorrhea (primary/secondary), oligomenorrhea, or AUB. *Primary amenorrhea* was defined as an absence of menstruation by 14 years of age without secondary sexual characteristics or no menarche by 16 years of age with secondary sexual characteristics. *Secondary amenorrhea* was defined as the cessation of menstruation for >3 cycles or >6 months once they had begun. *Oligomenorrhea* was defined as infrequent menstruation that occurred at intervals of >35 days in adults and >45 days in adolescents. *AUB* was defined as any type of bleeding that was irregular in amount, duration, or frequency. In addition, *hyperprolactinemia* was defined as the presence of abnormally high levels of prolactin in the blood (>20 ng/mL); polycystic ovary syndrome (PCOS) was diagnosed according to the Rotterdam consensus.[9]

Statistical analyses were performed with PASW Statistics software (version 17; SPSS Inc, Chicago, IL). Data are presented as a number (percent) or mean ± SD. Variables on a nominal scale were analyzed with the use of Fisher's exact or χ^2 test as indicated. Probability values of $< .05$ were considered statistically significant.

TABLE 2
Etiologic classification of patients with primary amenorrhea

Classification	Group I, n (%)[a]	Group II, n (%)[a]
Hypergonadotropic hypogonadism		
Chromosomally incompetent	42 (21.9)	5 (10.0)
Chromosomally competent	19 (9.9)	3 (6.0)
Hypogonadotropic hypogonadism		
Nonspecific	41 (21.3)	13 (26.0)
Constitutional delay	36 (18.7)	0
Acquired		
Congenital adrenal hyperplasia	0	2 (4.0)
Cushing's syndrome	1 (0.5)	0
Hyperprolactinemia	1 (0.5)	0
Hypothyroidism	2 (1.0)	0
Craniopharyngioma	1 (0.5)	0
Eugonadism		
Anatomic		
Müllerian anomaly	35 (18.2)	25 (50.0)
Vaginal agenesis	4 (2.0)	0
Imperforated hymen	2 (1.0)	0
Cervical agenesis	1 (1.0)	0
Intersex disorder: androgen insensitivity	7 (3.5)	2 (4.0)

[a] n = 192 patients 11-20 years old; [b] n = 50 patients 21-30 years old.

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RESULTS

Table 1 presents the distribution of clinical manifestations in the 2 groups. Among the 1704 young women with menstrual disturbances, amenorrhea was the most frequent occurrence (48.3% for both groups), followed by AUB (41.9% for group I and 33.2% for group II). In patients with amenorrhea, the proportion of primary amenorrhea was significantly higher in group I (39.7%) than in group II (14.7%). The frequency of AUB was significantly higher in group I than in group II, and oligomenorrhea was more common in group II than in group I ($P < .001$ for all comparisons).

Tables 2 and 3 list the etiologic classifications of patients with amenorrhea. Among the 1704 women, hyperprolactinemia was the cause of menstrual problems in 110 women (25 for group I and 85 for group II). The mean of prolactin levels in patients who had elevated prolactin was 69.6 ng/mL (range, 27.7–163.0 ng/mL) in group I and 235.4 ng/mL (range, 26.6–2691.0 ng/mL) in