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SHORT REPORT

Menstrual cycle pattern during the first gynaecological years in girls with precocious puberty following gonadotropin-releasing hormone analogue treatment

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Our aim was to longitudinally investigate menarche timing and menstrual cycle (MC) pattern during the first five gynaecological years in 101 girls with idiopathic central precocious puberty (CPP) who had been treated with gonadotropin-releasing hormone agonists (GnRHa) for at least two years. Our girls received Decapeptyl Depot (60 μg/Kg) every 28 days from a chronological age (CA) of 7.8 years (range 3.3–8.9) and for 24–96 months (median 43) till the age of 11.3 years (range 9.6–13.8). All of them exhibited adequate compliance with the GnRHa regimen, as elsewhere reported [1].

Bone age (BA) was evaluated both at entry and at the end of GnRHa therapy and was, respectively, 10 and 13.6 years.

From therapy withdrawal onwards the girls were semestrally re-examined until menarche. Menarcheal age (MA) was assessed by a semistructured interview and calculated by decimal year according to birthday.

Mothers' MAs were confirmed by patients' mothers.

After menarche the patients were regularly re-evaluated at 1-year intervals for at least five years in order to get information about MC pattern. Menstruation frequency was determined from monthly diaries maintained by girls and their families.

Definitions of MC pattern [6] include: (a) secondary amenorrhea, the absence of menstruation for 180 days or more; (b) oligomenorrhea (OM), average length of MC between 42 and 180 days; (c) polymenorrhea (PM), average length of MC 21 days or less; and (d) regular or irregular MC (RMC or IMC), average length of MC between 22 and 41 days; either none or a single MC with a length of less than 22 or more than 41 days during the past year (RMC); two or more MC with a length of less than 22 or more than 41 days during the past year (IMC).

For statistical purposes, χ^2 linear trend analysis was performed to study the effect of gynaecological age (GA) on the prevalence of OM, PM, and both RMC and IMC. Correlation regression analysis was used to evaluate the influence of other factors on menarche timing.

Median MA was 12.6 years (range 10.6–15.2), i.e. significantly higher ($p<0.0005$) with respect to that of their

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Table 1 Distribution (%) of menstrual cycle (MC) patterns of our 101 patients by gynaecological age

	Gynaecological age (months)				
	1–12	13–24	25–36	37–48	49–60
Regular and irregular MC	49.5	65.3	85.2	92.1	96.0
Oligomenorrhea	46.5	33.7	14.8	7.9	4.0
Polymenorrhea	4.0	1.0	0	0	0
Secondary amenorrhea	0	0	0	0	0

mothers (11.6; range 8–14). MA in our patients was positively related to both CA (x=12.5, y=11.2, r 0.51, p<0.001) and BA at the end of treatment (x=12.5, y=12.8, r 0.32, p<0.01). Moreover, it was significantly associated with therapy duration (x=12.5, y=44,5, r 0.42, p<0.001). Time duration between therapy withdrawal and menarche was 14.0 months (range 3–42). This time interval negatively correlated with both CA (x=15.6, y=7.5, r −0.56, p<0.001) and BA (x=15.6, y=9.9, r −0.30, p<0.01) at the time of therapy withdrawal and also with treatment duration (x=15.6, y=44.5, r −0.34, p<0.01).

The history of MC patterns showed both a progressive decrease of OM prevalence (χ^2 47.8, p<0.0001) and a concomitant progressive increase of RMC and IMC (χ^2 54.5, p<0.0001) by increasing GA (Table 1). No cases of secondary amenorrhea were recorded during the entire follow-up and only a few cases of polymenorrhea were found during the first two gynaecological years (Table 1).

Although Depot preparations of GnRHa have been the choice treatment for CPP since the mid 1980s, their long-term effects on gonadal function are controversial: one study reported an increased prevalence of polycystic ovaries (PCO) in GnRHa treated girls [2], whereas PCO-like ovaries were seen only rarely or not at all in a more recent study [3]. According to our results MC abnormalities are observed only during the first gynaecological years and their prevalence decreases with increasing GA, a pattern which is also frequently found in normal adolescents [5]. These data confirm that GnRHa therapy has no long-term detrimental effects on MC of girls with CPP even though prolonged over time [4]. On the contrary, in our patients time to menarche following GnRHa withdrawal inversely correlated with treatment duration. An unexpected finding of our study is that MA of our patients was higher than MA of the respective mothers and unrelated to it, contrary to what is generally reported in various other conditions [3]. The relationship between MA of the girls and their mothers, in fact, is known to persist under all circumstances, with few exceptions [3]. This confirms that GnRHa therapy is able to modify the natural course of puberty events in girls with CPP.

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