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TREATMENT OF CONSTITUTIONAL DELAYED PUBERTY WITH A COMBINATION OF TESTOSTERONE ESTERS*

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SUMMARY: Büyükgebiz A. (Division of Endocrinology, Department of Pediatrics, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey). Treatment of constitutional delayed puberty with a combination of testosterone esters. Turk J Pediatr 1993; 35: 271-275.

Thirteen boys with constitutional delayed puberty (CDP) were treated with a combination of short and long-acting testosterone esters (testosterone propionate, testosterone phenylpropionate, testosterone isocaproate). Mean age at the onset of treatment was 14.9 ± 0.6 years and bone age delay was −2.7 ± 0.9 years. The dose of testosterone used was 200 mg intramuscularly four times at three week intervals, and the treated CDP boys were followed for two years. All the boys with CDP entered puberty after the last dose (testicular volume ≥ 4 ml), and growth rate increased from 4.5 ± 0.5 cm / year, pretreatment, to 8.4 ± 1.6 cm / year, posttreatment, at the two year follow-up. Height for bone age SD score did not change significantly from a mean of −1.1 before treatment to −1.3 after treatment, nor did predicted height before treatment (173.5 ± 6.6 cm) and after treatment (173.3 ± 4.9 cm). Combination of testosterone esters in a given dose and schedule is a safe and effective treatment for prepubertal boys with constitutional delayed puberty. *Key words: constitutional delayed puberty (CDP), testosterone treatment, predicted adult height.*

Constitutional delayed puberty (CDP) is the most common cause of short stature and delayed development in adolescent boys[1]. Boys with CDP have delayed sexual maturation and delayed skeletal bone ages, and are shorter than age-matched controls[1-3]. For psychological reasons, different drugs have been used for pubertal advancement and short-term growth increment in these adolescents with CDP[2-5]. One of drugs used widely for CDP is testosterone enanthate, a long-acting testosterone ester found to be effective and safe especially in small doses[5-7].

A combination of short-and long-acting testosterone esters (20 mg testosterone propionate, 40 mg testosterone phenylpropionate, 40 mg testosterone isocaproate in a 100 mg ampule) was used for our CDP patients, and they were longitudinally followed for two years in an attempt to investigate the physiological responses.

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Material and Methods

Thirteen boys between the ages of 14.2 and 15.4 were referred to our pediatric endocrinology clinic for evaluation of short stature or delayed puberty. They fulfilled the criteria for CDP (no endocrine or systemic disease, height below the 3rd percentile, testicular volume below 4 ml and showing symptoms of psychological disturbance). Two hundred mg of testosterone esters was administered intramuscularly four times at three week intervals, and the patients were then followed up for two years. Clinical data from 13 patients with CDP are shown in Table I. Statistical analyses were performed by *t* test for matched pairs and Wilcoxon signed ranked test where appropriate. P values less than 0.05 were accepted as statistically significant.

Growth was measured by using a Harpenden stadiometer, and bone age was measured by the method of Tanner et al[8]. Testicular volume was assessed by using a Prader orchidometer by the same observer, and predicted adult height was assessed by TW2 method[8,9].

Table I: Data For Subjects Treated with Testosterone

		Posttreatment	
	Pretreatment	3 months	2 Years
Chronological age (years)	14.9 ± 0.6		16.9 ± 0.6
Bone age delay (years)	−2.7 (−3.8 to 0.1)		
Height (cm)	147.6 ± 7.7	150.9 ± 8.8	164.4 ± 7.7
Growth rate (cm / year)	4.5 ± 0.5		8.4 ± 1.6
Predicted adult height (cm)	173.5 ± 6.6		173.3 ± 4.9
Height SDS for BA	−1.1(−2.7 to +1.5)		−1.3(−3.2 to +1.4)
Test. volume (ml)	3.2 ± 0.7	4.3 ± 0.4	11.3 ± 2.5
Pubic hair (Tanner stage)	1	2	4
CA / BA	1.24		1.18

SDS : Standard deviation score.
BA : Bone age.
CA : Chronological age.

Results

After three months of testosterone therapy, all thirteen CDP boys entered puberty (testicular volume 4.3 ± 0.4 ml and pubic hair stage 2) and no regression was detected at their two year follow-up (Fig. 1). Growth rate, which was 4.5 ± 0.5 cm / year, increased to 8.4 ± 1.6 cm / year after two years of follow-up in CDP boys ($p < 0.001$) (Fig. 2).

No significant difference was demonstrated in height SD score for bone age between pretreatment and posttreatment two years ($p > 0.05$). Predicted adult heights, a very important consideration in testosterone treatment, did not vary significantly before testosterone treatment (173.5 ± 6.6) and after treatment (173.3 ± 4.9) ($p > 0.05$). None of the boys experienced adverse reactions during the course of treatment.

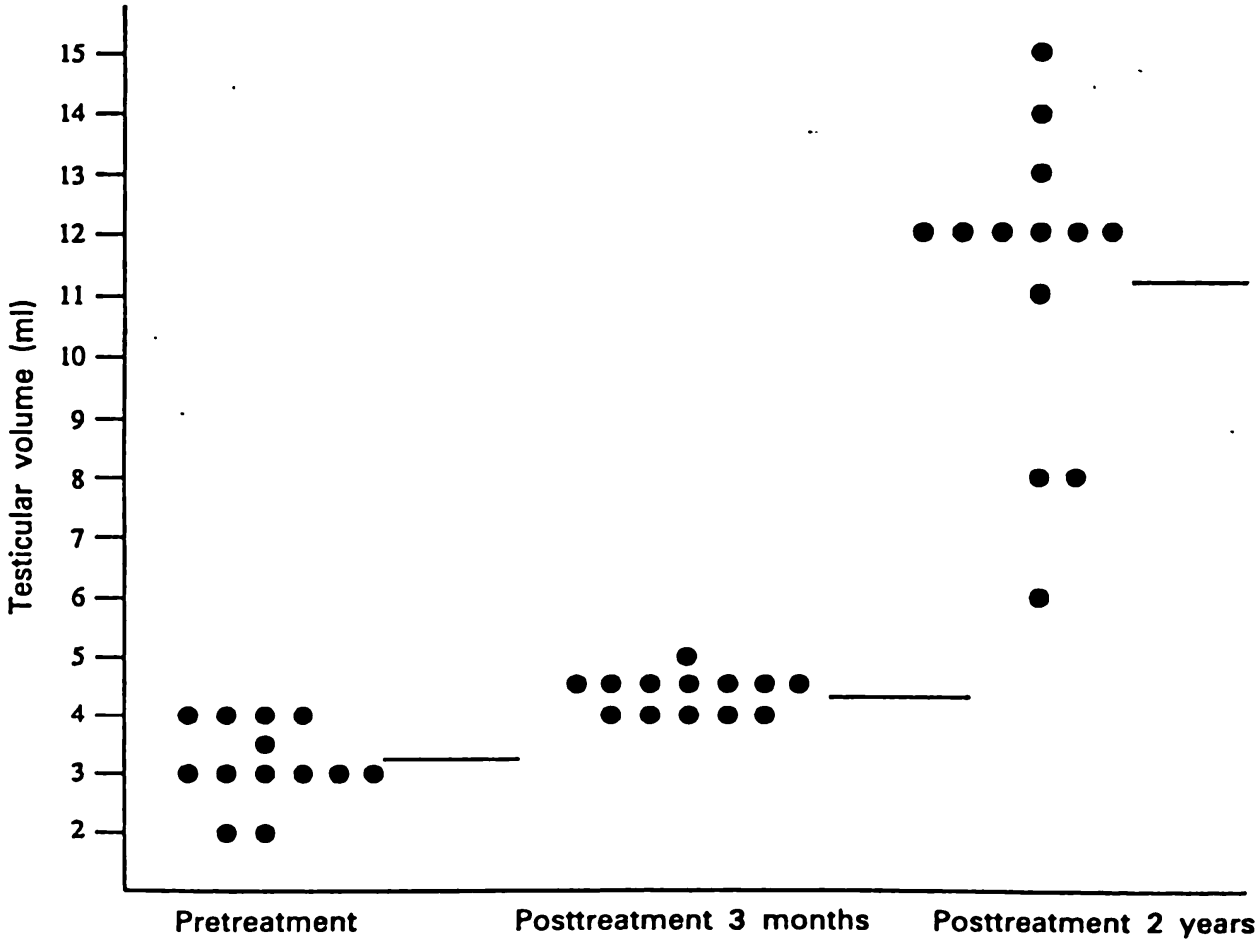

Fig.1: Effect of testosterone therapy on testicular volume in CDP boys. Horizontal line represents the mean value.

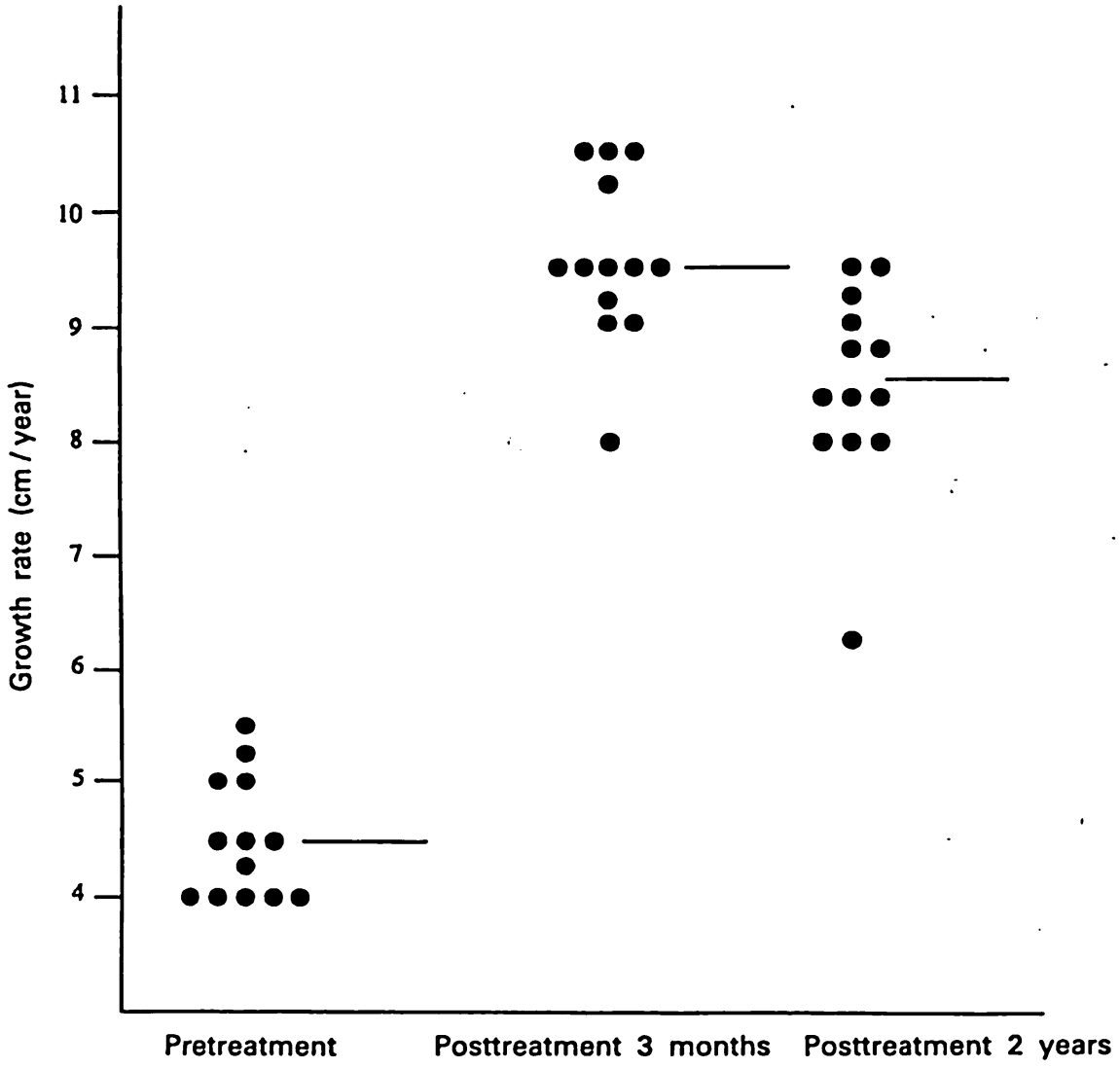

Fig.2: Effect of testosterone therapy on growth rate in CDP boys. Horizontal line represents the mean value.

Discussion

The child with CDP will spontaneously enter puberty between the ages of 14 and 18 years and will ultimately achieve a normal adult height. In this normal growth variant situation, an approach to the patient and his parents with reassurance and a policy of watchful waiting is necessary. There are some situations, however, in which the child is so upset by the combination of short stature and delayed appearance of secondary sexual characteristics that the possibility of intervention needs to be considered seriously[7].

The retardation of growth and delay in sexual maturation exhibited by adolescents has psychological and social consequences. These boys are under the pressure of being short and sexually immature. Some authors have reported that late-maturing boys show greater evidence of negative self-concepts, prolonged dependency needs, and feelings of rejection and rebellion[7,10]. The same authors

claim that after treatment of CDP, the same group of adolescents demonstrated an improvement in both school and extracurricular social activity, suggesting that normalization of growth and sexual maturation may well permit more effective involvement in normal adolescent behavior[7,10].

Although it is shown by several studies that a short course of long-acting testosterone esters promotes puberty in CDP patients without any decrease in predicted adult heights, this is dose-dependent and still a point of investigation.

In our CDP boys treated with a short course of a combination of short-and long-acting testosterone esters, all had entered puberty after the last treatment dose. There was no significant decrease in height for bone age SD scores and predicted heights after two years of follow-up, but growth rates increased significantly. We propose that a combination of testosterone esters (sustanon) at a dose of 200 mg four times at three week intervals is as effective as testosterone enanthate at the same dose and schedule used by several authors for CDP[3,5,7]. Although there was no significant difference in predicted adult heights, final adult height measurements should be determined in order to make the precise decision.

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