Evaluation of low-dose hCG treatment for cryptorchidism

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SUMMARY: Aycan Z, Üstünsalih-İnan Y, Çetinkaya E, Vidinlisan S, Örnek A. Evaluation of low-dose hCG treatment for cryptorchidism. Turk J Pediatr 2006; 48: 228-231.

The aim of this study was to evaluate the efficiency of low-dose hCG (human chorionic gonadotropin) (500 IU/week for 3 weeks) in the treatment of cryptorchidism and in the assessment of Leydig cell functions. We included 35 male patients who had been diagnosed with cryptorchidism by the pediatric endocrinology specialist in the study. Twenty-one cases (Group I) received 500 IU/week of hCG while 14 patients (Group II) received 1500 IU/m^2 three times a week, both for three weeks. The percentage of testis descent was calculated for both groups for the right and left testes. Leydig cell functions were evaluated by the pre- and post-treatment measurement of plasma testosterone level in all cases. A delta testosterone greater than 100 was considered to be a sufficient response. Among our patients, 77% had unilateral and 23% bilateral cryptorchidism. Unilateral cryptorchidism was detected in 80.9% of Group I patients and 71.4% of Group II patients. The pre-treatment percentages for Group I of right- and left-sided cryptorchidism were 81% and 38.1%, respectively, which decreased to 23.8% and 9.5% after treatment. The pre-treatment percentages for Group II of right- and left-sided cryptorchidism were 57.1% and 71.4%, respectively, which decreased to 14.3% and 35.7% after treatment. The success rate of hCG treatment, as defined by the testis descending into the scrotum, was 66.7% for Group I and 57.1% for Group II ($p>0.05$). There was no significant difference between the two groups when Leydig cell functions were assessed. In conclusion, it is possible to use low-dose hCG for the treatment of cryptorchidism and the assessment of Leydig cell functions.

Key words: *low-dose hCG treatment, cryptorchidism.*

Undescended testis is a frequent genitourinary anomaly in infants[1-3]. Possible causes of undescended testis include testicular dysgenesis, developmental abnormality of the testis, short vas deferens, short testicular vessels and human chorionic gonadotropin (hCG) deficiency[2]. Human chorionic gonadotropin stimulates testicular steroid hormone synthesis, similar to the luteinizing hormone, and enables the testis to descend to the scrotum while increasing the size and vascularity of the testis[1,4]. Human chorionic gonadotropin treatment has therefore been used for the treatment of cryptorchidism with various protocols for several years[5-7].

It is stressed that histological changes in Leydig cells begin in the 6th month when the testis is not present in the scrotum. It is therefore suggested to begin cryptorchidism treatment after the 6th month with luteinizing hormone releasing hormone (LH-RH) agonist, as hCG treatment can be a cause of infertility in adult life by increasing germ cell apoptosis. If the patient does not respond, low-dose hCG treatment is recommended[8].

The aim of this study was to investigate the effect of low-dose hCG (500 U/week for 3 weeks) in the treatment of cryptorchidism and in assessment of Leydig cell function.

Material and Methods

We included 35 male cases with an average age of 5.5±3.4 years who had received a diagnosis of cryptorchidism from the pediatric endocrinology specialist. Both testes were defined as scrotal, prescrotal, inguinal or

nonpalpable according to their location. Twenty-one cases (Group I) received hCG at a dose of 500 IU/week and 14 cases (Group II) received a dose of 1500 IU/m^2 (min 500 IU/dose - max 1500 IU/dose) three times a week, both for three weeks. The average ages for the two groups was similar at 5.2±3.1 (0.5-10.8) years for Group I patients and 5.9±3.9 (0.6-13.9) years for Group II patients. The age distribution of the groups was similar. In Group I, 19% were 0-2 years old, 24% were 2-4 years old and 57% were above 5 years old, while in Group II, the same distribution was 21%, 29%, and 50%, respectively. At the end of the three-week treatment, testis examination of the cases was carried out by the same pediatric endocrinology specialist. The percentage of descent of the right and left testis was calculated for both groups. The pre- and post-treatment difference between the two groups was calculated with Fisher's exact test.

Human chorionic gonadotropin stimulation test was made to evaluate Leydig cell function. Among 35 cases, 30 completed the three-week hCG treatment and were then evaluated regarding their Leydig functions. The test is based on the principle that samples for testosterone are taken basally and the 1st and 4th day after the last hCG injection. Delta testosterone levels were found by subtracting the basal levels of plasma testosterone levels from the peak levels of plasma testosterone levels after the treatment (either the 1st or 4th day). Leydig cell response was considered to be sufficient if delta testosterone increment was 100 ng/dl or more[9]. The difference between the delta testosterone levels of Group I and Group II was determined with the Mann-Whitney U test. P<0.05 was considered to be statistically significant.

Results

Table I presents the pre- and post-treatment testis location of the 35 cases included in our study. Seventy-seven percent of our cases had unilateral and 23% bilateral cryptorchidism. Among the unilateral undescended testis cases, 63% were on the right side and 37% on the left side. There was no significant difference as to testis location between Group I and Group II. In Group I, the pre-treatment right cryptorchidism rate was 81% and left cryptorchidism 38.1%, while the post-treatment rates decreased to 23.8% and 9.5%, respectively (Fig. 1). For Group II, the pre-treatment cryptorchidism rates were 57.1% for the right and 71.4% for the left, while the post-treatment rates were 14.3% and 35.7%, respectively (Fig. 2). The success rate with the testis descending into the scrotum with treatment was 76.2% for the right testis and 90.5% for the left testis in Group I versus 85.7% and 64.3%, respectively, for Group II patients. No significant difference was found between the groups regarding the success rate of right and left testis descent into the scrotum (p>0.05). When the total treatment success rate was determined without classifying into right or left testis, this rate was 66.7% for Group I and 57.1% for Group II (Fig. 3). Although response to low-dose hCG treatment was better in Group I (66.7%), there was no statistically significant difference between the two groups regarding the success rate of the treatment (p>0.05). In addition, there was no

Table I. Pre- and Post-Treatment Testis Location of the Cases and Treatment Success

	GROUP I (n=21)				GROUP II (n=14)			
	Pre-treatment		Post-treatment		Pre-treatment		Post-treatment	
Pre- and post-treatment testis location	Right testis	Left testis	Right testis	Left testis	Right testis	Left testis	Right testis	Left testis
Scrotal	4	13	16	19	6	4	12	9
Prescrotal	2	2	3	2	1	2	0	1
Inguinal	14	6	2	0	5	5	2	4
Nonpalpable	1	0	0	0	2	3	0	0
Undescended testis (%)	81	38.1	23.8	9.5	57.1	71.4	14.3	35.7
Descent into scrotum (%)			76.2	90.5			85.7	64.3
Total success rate (%)			66.7				57.1	

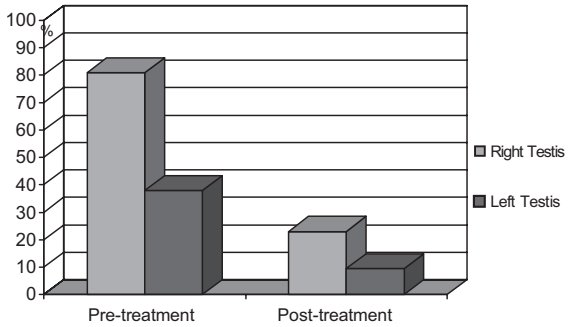

Fig. 1. Pre- and post-treatment cryptorchidism in Group I patients.

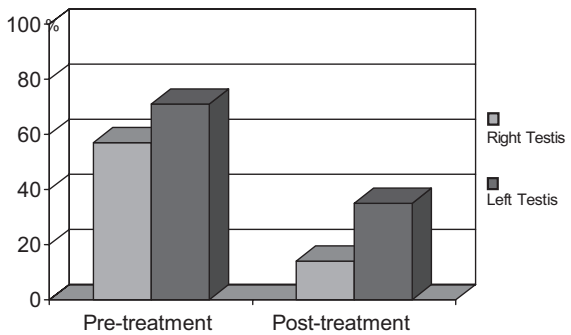

Fig. 2. Pre- and post-treatment cryptorchidism in Group II patients.

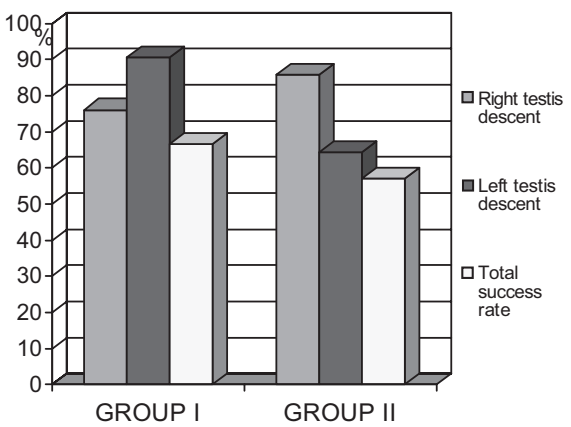

Fig. 3. Success rate of the hCG treatment in Group I and Group II patients.

difference in testis volume between the testis descending into the scrotum with treatment and the scrotal testis.

Evaluation of Leydig cell function could be carried out in 16 patients from Group I and in all patients from Group II. The Leydig cell functions of 13 of 16 cases in Group I (81.2%) and of 13 of 14 cases in Group II (92.8%) were assessed as adequate. There was no statistically significant difference between the two groups ($p>0.05$).

Discussion

We determined that in our patients with cryptorchidism, which we believe is a public health problem for our country, despite diagnosis at a late age, most responded well to low-dose hCG treatment.

The incidence of cryptorchidism is 1-4.5% of newborns[1,2,5,6], but increases to 30% in preterm babies[2]. The spontaneous descent of a testis not located in the scrotum in the newborn period usually takes place within the first three to six months, but is infrequent after the first year[5,6]. It is therefore now suggested that treatment should begin at six months. It is believed that when hormonal treatment is started at the end of the 6th month, the gonadotropin and testosterone deficiency will also be treated efficiently and in time[10]. There are many protocols for the hormonal treatment of cryptorchidism[2,4,11]. It is suggested that hCG be used by itself or together with LH-RH analogues for hormonal treatment[12]. The World Health Organization suggests treatment with 250 IU hCG twice a week for five weeks for children up to 12 months old, 500 IU hCG twice a week for five weeks for children 1 to 5 years of age and 1000 IU hCG twice a week for five weeks in older children, and recommends a total optimal dose of 10,000 IU[2]. Some studies report a higher treatment success rate when an LH-RH agonist is used together with hCG, but other studies do not support this[11,13-15]. The location of the testis and the age hormonal treatment is administered are reported as important factors that influence the treatment result, with the best results observed in prescrotal cryptorchidism[14]. In our study, inguinally-located testes descended into the scrotum in 90% of the patients receiving low-dose hCG treatment (Group I), but in only 40% of the patients receiving high-dose hCG. The success rate varies greatly at 6-80% in patients who receive only hCG[2,6], but is higher, at 20-50%, in patients receiving only LH-RH[2], and 57-82% for patients receiving combined treatment[15]. It is experimentally postulated that hCG can increase germ cell apoptosis and cause adult infertility[8]. A study by Taskinen et al.[16] reported a significantly

lower adult testis volume in cryptorchidism cases who received 10 doses of hCG treatment with 500 U up to 7 years of age or 1000 U for older children, compared to patients who did not receive preoperative hCG. It is therefore suggested to begin cryptorchidism treatment after the 6th month with an LH-RH agonist (1-1.2 μg/day for 4 weeks), to add low-dose hCG (500 U/week for 3 weeks) if the patient does not respond, and to treat surgically if there is still no response (14). In our study, we were more successful with low-dose hCG treatment (66.7%) than with high-dose hCG treatment, but there was no statistically significant difference between the two groups.

It is known that patients with cryptorchidism may have deficiencies in Leydig cell function and that this function should therefore be evaluated with an hCG stimulation test[9]. However, there are many different protocols for the hCG stimulation test with no standardization[17-19]. We thought that the hCG used for treatment in this study could also be used to evaluate Leydig cell function. We found adequate Leydig cell function at a rate of 81.2% with the low-dose hCG used in Group I and of 92.8% with the high-dose hCG used in Group II. We did not detect a significant difference between the groups ($p>0.05$).

In conclusion, we have demonstrated that low-dose hCG treatment (500 IU/week for 3 weeks) is sufficient to treat cryptorchidism and evaluate Leydig cell function.

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