

The efficacy of human chorionic gonadotropin in retractile testis

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Abstract

OBJECTIVES: To evaluate the efficacy of hCG therapy on retractile testis in various testicular locations and age groups.

SETTING AND DESIGN: This study comprised 123 boys whose diagnosis were retractile testis with scrotal base, high scrotal and superficial inguinal localizations with an average age of 4,2 (1-8) years.

METHODS: 123 boys with retractile testes were given a total dose of 9000 hCG and its effect on scrotal base, high scrotal and superficial inguinal located testes were evaluated after 2 weeks and 6 months of completing hCG course. The patients were evaluated in four age groups such as less than 2 years of age, between 2-4, 4-6 years and more than 6 years of age and the response rates were also noted in these age groups.

RESULTS: In unilateral cases, the response in base, high scrotal and superficial inguinal levels were found as 100%, 83,3%, 72,7% respectively where as these rates were found as 100%, 92,6%, 76,3% respectively in bilateral cases after 2 weeks of hCG therapy. The response rates in less than 2 year old group, 2-4, 4-6 and more than 6 years group were found as 0%, 80%, 78,7%, 100% respectively in unilateral cases and 33,3%, 90%, 86,9% and 83,3% respectively in bilateral cases. After 6 months, reascend was observed in 12,4% in unilateral group and 6,7% in bilateral group.

MAIN FINDINGS: 72,7-100% of retractile testes respond to hCG administration with the highest response in the age of more than six year group.

CONCLUSION: High response rates observed in retractile testes after hCG therapy in more than 2 years old age group indicate that hCG must be given as a primary treatment in retractile testes and orchiopexy for the failures. Also patients must be followed up closely for reascend cases.

Abbreviations:

hCG – Human Chorionic Gonadotropin
FSH – Follicle Stimulating Hormone

Introduction

Retractile testis is a frequently observed condition consisting of the ascent of one or both testis towards the superficial inguinal pouch after an active cremasteric reflex. From this extrascrotal position, the retractile testis is manipulated easily into its natural seat, but it may ascend again after a variable period of time [1]. Thus, the prolonged presence of the retractile testis in this extrascrotal position may affect the germinal epithelium, even though a primary testicular dysfunction cannot be ruled out [2]. Although retractile testis is believed as a benign entity descending at puberty and needing no further treatment, there are many reports showing tubular degenerations both in retractile and cryptorchid testes causing future infertility problems [3,4,5].

The observation that a retractile testis is frequently hypotrophic compared with the normally descended contralateral testis leads to test the hypothesis that retraction and permanence in the extrascrotal position can affect fertility [5]. To find a solution to this problem, hormonal therapy is suggested in undescended and retractile testis before surgery is attempted. Optimal age for hormonal therapy is 5 years of age and it can be effective at age 3 years [6]. The action of hCG is similar to that of luteinizing hormone, leading to a stimulatory effect on testicular steroidogenesis and in response to hCG injection, the testis increases in weight and vascularity and may then descent [7]. In this study the efficacy of hCG therapy on various locations of retractile testes were investigated and its efficacy due to age groups were evaluated.

Material and methods

The study comprised 123 boys whose diagnosis was confirmed as retractile testis from the 560 cases referred as undescended testis to the outpatient clinics of TCDD Ankara Hospital which is a second level hospital in a 12 year period (1990–2002). These 560 cases also include 15 retractile testis cases who did not participate the hCG treatment and so unfollowed. In the examination we tried to make the child feel relaxed in a warm room. Before touching the child, the genitalia and inguinal region was first visually examined since the first touch may stimulate a cremasteric reflex and then by placing the child in the frog-leg position and by gently milking from the inguinal canal to the scrotum we tried to bring the high retractile testis downwards. We repeated the inspection and palpation at least three times before confirmation of final spontaneous position. If the testis can be brought down in this way and remains in the scrotal base for 1–2 minutes without tension, the diagnosis of a retractile testis was made.

Patient demographics were recorded for age, unilaterality or bilaterality and testicular final localization such as base, high scrotal and superficial inguinal

pouch levels. When the testis was visible in the scrotum on initial inspection and retracted into higher levels on attempted palpation and could be then manipulated back to scrotal base remaining there for 1–2 minutes is noted as basal level. This classification was made due to the position of testis after manipulation. Non of the patients have prior treatment for cryptorchidism or inguinal hernia.

hCG treatment consisted of 1500 IU intramuscular injections 3 times per week for a total of 2 week period in every patient. No blood samples for testosterone or inhibin B were taken before treatment. Each patient was reevaluated 2 weeks and 6 months after completing hCG course for the final position and any reascend afterwards. In the initial examination, if the testis was found in high scrotal or superficial inguinal levels and descended to the bottom of the scrotum and persisted in its localization after hCG administration was accepted as responder. If the testis was found in the base level in the initial examination and persisted in its base level despite any attempted palpation was also accepted as responder. If the final location of the testis was not the bottom of the scrotum and if it didn't persist in its location, it was accepted as non responder. After initial response if the testis goes back to an upper localization, it is accepted as reassensus. In the nonresponders after 2 week period, surgery was offered to correct the problem. At surgery processus vaginalis patency was categorized as closed or patent due to operative findings and no testicular biopsies were taken during orchiopexies. The patients were also evaluated in 4 age groups such as less than 2 years of age, between 2–4 and 4–6 years and more than 6 years of age and the response and reascent rates were also calculated in these age groups.

Results

In this study 123 patients with retractile testis who accepted hCG treatment were evaluated. Mean patient age was 4,2 (1–8) years and 75 (60,9 %) of the cases were bilateral and 48 (39,2%) unilateral. 36 (75 %) of the unilateral cases were on the right side while 12 (25%) were on the left. In unilateral cases the testis found in base, high scrotal and superficial inguinal pouch levels were 16,7%, 37,5% and 45,8% respectively. In bilateral cases these levels were found as 13,3%, 36% and 50,7% respectively (Table I).

39 (81,9%) of unilateral cases and 64 (85,3%) of bilateral cases respond hCG treatment. In unilateral cases, the response in base, high scrotal and superficial inguinal pouch levels were 100%, 83,3% and 72,7% respectively whereas the response in base, high scrotal and superficial inguinal pouch levels in bilateral group were 100%, 92,6% and 76,3% respectively. From the failures, 9 patients in unilateral group and 8 patients in bilateral group accepted orchiopexy. Processus vaginalis was found closed in 5 (62,5%) patients in unilateral group and in 3 (37,5%) in bilateral group peroperatively and no testicular size difference was observed. Testicular volumes were not measured at initial examination or there-

Table I: hCG response in retractile testis of various localizations

	Unilateral		Bilateral			
	n	%	n	%		
	48	39,1	75	60,9		
	Orchiopexy			Orchiopexy		
Localisation (testis)						
Base	8	16,7	10	13,3		
High scrotal	18	37,5	27	36		
Sup.ing pouch	22	45,8	38	50,7		
% response after hCG	39	81,9	65	85,3		
Base	8	100	–	10	100	–
High scrotal	15	83,3	3	25	92,6	2
Sup.ing pouch	16	72,7	6	29	76,3	9
Reascent after hCG						
High scrotalSup.ing pouch	6	12,4	4	5	6,7	3

Table II: hCG response due to patient age groups

Age	Total		Unilateral		Response		Bilateral		Response	
	n	%	n	%	nR	% R	n	%	nR	%R
2<	4	3,3	1	2,1	–	–	3	4	1	33,3
2–4	40	32,5	20	41,7	16	80	20	26,7	18	90
4–6	69	56,1	23	47,9	18	78,7	46	61,3	40	86,9
>6	10	8,1	4	8,3	4	100	6	8	5	83,3
	123	100	48		38		75		64	

nR: number of responders
%R: percent of responders

after, but on comparative palpations no major size differences were observed.

The patients who responded to hCG administration were reexamined after 6 months and reascensus was observed in 6 (12,4%) patients in unilateral group and 5 patients (6,7%) in bilateral group. 4 patients in the unilateral group and 3 in bilateral group accepted orchiopexy for treatment. Processus vaginalis was found closed in 1 (25%) in unilateral group and in 1 (33,3%) in bilateral group with no testicular size difference.

When the patients were evaluated in age groups such as, less than 2 years, between 2–4, 4–6 years and more than 6 years and the responses in unilateral group were 0%, 80%, 78,7% and 100% respectively whereas in bilateral group 33,3%, 90%, 86,9% and 83,3% respectively (Table 2).

Side effects of hCG treatment were also questioned. Erections and growth of penis was observed in all patients, pain in genital region in 7 (5,6%) and hair growth in suprapubic region in 26 (21,1%) patients. After 6 months of hCG course, pain in the genital region and suprapubic hair growth disappeared in all cases but penile growth and erections remained the same in 42 (34,1%) of the patients. No investigation regarding premature epiphyseal closure was done.

Discussion

Undescended testis is a common condition which occurs in 3,4% of nine month gestation birth and 30% of premature infants. Half of such testicles descent spontaneously in the first month of life and the incidence at

year 1 of age is 0,8%. An undescended testis is defined as a testis that has become arrested in its descent through the normal pathway. This must be distinguished from the ectopic testis that has derived from the normal pathway of descent and from the retractile testis which is believed to be a normal variant produced by an exaggerated cremasteric response [8,9]. A true undescended testis is often associated with a poorly developed hemiscrotum on the ipsilateral side.

Various dosages of hCG have been used ranging from a total dose of from 3000 IU to 40 000 IU divided daily or weekly injections, for days or months. The World Health Organization recommends biweekly injections of 250 IU for young infants, 500 IU in patients up to 6 years of age and 1000 IU in boys thereafter for 5 consecutive weeks [10]. Our protocol was different from WHO guidelines which needs biweekly injections for five consecutive weeks. In many studies different hcg protocols were used, some of them giving 3300 IU hCG weekly for four weeks having a dose higher than our protocol given to cryptorchid cases of one to five years old [11]. The side effects of hCG when used in large doses include premature epiphyseal closure; accelerated development of secondary sexual characteristics, such as pubic hair, genital enlargement which usually recedes following cessation of treatment [12,13]. There are indications that treatment with hCG induces inflammation like changes in the testicular microcirculation and that these changes regress 6–9 months after treatment [14,15]. It has also been shown that hCG treatment is followed by an increase in germ cell apoptosis, which in turn is associated with smaller testis volume and higher FSH levels in

adulthood. Apoptotic loss of spermatogonia after hCG treatment of cryptorchidism warrants reevaluation of the safety of this treatment. Therefore, whether or not hCG-induced testicular descent is a completely safe treatment remains open for debate [16]. In our study no blood samples were taken to evaluate the potential impact of hCG on Sertoli cell function such as inhibin B measures. When the results were evaluated due to testicular localisation, 100% of base localised testes, 83,3–92,6% of high scrotal and 72,7–76,3% superficial inguinal localised testes respond to our standard treatment. When the percentage of respond for age groups are reviewed, before age of 24 months only 15% of patients receiving hCG respond and this response increases up to age 6 years with a peak of 75% between ages 2 and 6 and there after decreases [20]. In our patients a response rate of 3,3% under 2 year age group and higher descent rates in the older age groups may indicate the limited role of hCG in under 2 year age group.

A large hernia sac leading to testicular adhesion and an obliterated fibrous string have been blamed as a cause of ascending testis [17]. The predominance of a closed processus vaginalis without a fibrous band in series suggest that, like low lying undescended testis, an ascending testis tends to be associated with a closed processus whereas a higher undescended testis is associated with large patent processus [18–19]. Failure to respond hCG treatment of an undescended testis may be accounted for by anatomical abnormalities such as a patent or abnormal processus vaginalis or mechanical obstruction such as gubernacular remnant. In our group processus vaginalis was found patent in 37,5% of the unilateral cases and 62,5% of bilateral cases peroperatively supporting this statement.

Although retractile testis is believed to be a normal variant produced by an exaggerated cremasteric response and doesn't affect fertility, there are some reports showing histological changes in the retractile testis needing some form of therapy or surgery to correct the situation [4,5]. Alenxandre was the first reporting the occurrence of poor spermiograms and histologic lesions in 22 infertile adults with small and soft retractile testes, which supported the possibility of a correlation between retractile testis and infertility [21]. Later there were many reports published showing similar tubular degenerations both in retractile and undescended testes necessitating orchiopexy in both conditions [3,4,5]. Our high response rates in retractile testes by hCG administration leads us to start with hCG as primary treatment and orchiopexy for the failures, with a close follow-up in order not to miss the ascending cases.

Conclusions

hCG was given in base, high scrotaland superficial inguinal located retractile testes with response rates of 100%, 83,3%, 72,7% respectively in unilateral cases and 100%, 92,6%, 76,3% respectively in bilateral cases. When the results were evaluated due to age groups,

better results obtained in more than 2 year age groups indicates the limited role of hCG in under 2 year age group.

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