

## Effect of Human Chorionic Gonadotropin (hCG) on Palpable Undescended Testis Position: A Prospective Study

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### ABSTRACT

**Background:** The difference of undescended testis initial position has significant effect on expected surgical results. The authors evaluate effect of HCG injection on testicular position in palpable undescended testis. **Methods:** Sixty patients with 77 palpable undescended testes were clinically examined and underwent ultrasonographic examination followed by intramuscular HCG injection according to WHO recommended dosage system; 250 IU in age <1year, 500 IU in age 1-5years, 1000 IU in age >5 years, twice a week for 5 weeks for all age groups. Another clinical and ultrasonographic examination was done 1 week and 2 months after last injection of HCG. **Results:** From total 77 testes of patients injected with HCG; 14 testes failed to improve in position (18.2%), 62 testes showed 1 degree of improvement (from inguinal to prescrotal or from prescrotal to scrotal location) (80.5%) and 1 testis showed 2 degrees of improvement (from inguinal to scrotal location) (1.3%). 35 testes reached a scrotal position and did not need to undergo surgery (45.5 %). **Conclusion:** Intramuscular injection of HCG as neoadjuvant therapy in cryptorchid boys induced testicular descend to scrotum in 45.5% of cases and improved position of testis prior to orchidopexy in 36.3% of study group. Total 81.8% of the injected study group gained benefit from suggested therapy

**Key words:** undescended testis - HCG - orchidopexy

### INTRODUCTION

Undescended testis is one of the most common congenital anomalies in which one or both testes fail to descend into the scrotum. The testes may be found in the abdomen or inguinal canal [1, 2]. The incidence of undescended testis is about 1 - 4.5% of newborns with a higher incidence in pre-terms (30-45%) [3, 4]. The testes may descend into the scrotum in 75% of full-term neonates and in 90% of premature newborn neonates during infancy. This incidence drops to 0.8-1.2% by the age of one year [5-7].

The main goal of therapy in undescended testis cases is to place the testes in the scrotum and improve future fertility index. This therapy may be hormonal and/or surgical [8, 9]. A common consensus about the surgical treatment of undescended testis can not be argued, though there is debate about the hormonal treatment regarding its influence on both testicles position and future function and fertility [10-12].

Human chorionic gonadotropin (hCG), Gonadotropin-releasing hormone (GnRH),

testosterone, and GnRH analogues are used in many centers preceding surgical management in a number of cases, particularly in Europe [13]. Studies showed that hCG induces testicular descent and improves the histopathology of the testis without harming germ cells. Its effectiveness is estimated to be about 20-25% [14, 15].

There are only few reports about the effect of hormonal treatment on the position of the testicle. In our study, we aim for evaluation of the effect of hCG injection on the position and size of the testis.

### PATIENTS AND METHODS

A prospective study of 60 children with undescended testes was conveniently sampled from Cairo University Specialized Pediatric Hospital (CUSPH) clinic. The study lasted for eight months, from January 2015 to August 2015.

The study only included male children between the age of 6 months and 10 years with unilateral or bilateral undescended testis located

either in the inguinal canal or at the scrotal neck by the clinical examination.

The study excluded male with age under 6 months or over 10 years, with ectopic or retractile undescended testis, impalpable undescended testis, previous surgical intervention for undescended testis or a history of previous hormonal therapy for undescended testis.

The study population got injected with hCG intramuscularly according to the WHO recommended dose. hCG injections, brand name (chorionom), are available in 2 concentrations (1500 IU and 5000 IU) in a 2 ml vial. WHO recommended doses are 250 IU in boys <1 year of age twice a week for five weeks, 500 IU in those of ages 1-5 years twice a week for five weeks and 1000 IU in those of ages >5 years twice a week for five weeks<sup>[16]</sup>.

Prior to the beginning of the study, all study participants were assessed by taking a full history, doing a full clinical examination and ultrasonographic examination by an experienced sonographer. Evaluation of the injection effect was done by full clinical examination and ultrasonography one week and two months after the last injected dose.

Statistical Analysis of data was done by IBM computer using SPSS (statistical program for social science version 16) as follows: description of quantitative variables as mean, standard deviation (SD) and range, description of qualitative variables as number and percentage, Chi-square test was used to compare qualitative variables between groups, and paired t-test was used to compare quantitative variables before and after among the same group.

## RESULTS

Study population included 60 male children with a total number of 77 palpable undescended testes. Their age ranged from 7 months to 10 years with a mean of 3.5 years.

Fourty-two of them had unilateral palpable undescended testes; 19 on the right side and 23 on the left side. Meanwhile, 17 children had bilateral palpable undescended testes and only one had bilateral undescended testes with left impalpable

testis (the impalpable testis was excluded from the study). Their age at presentation varied; 43 male presented since birth, 11 presented during the first 6 months of life and 6 presented after the age of 6 months.

Based on the clinical and ultrasonographic assessment, the testes of the patients were classified into two subgroups according to the initial position of the palpable undescended testes. The first subgroup included testes which have inguinal location and the second subgroup included testes which have prescrotal location. The first subgroup had 39 testes in 34 patients, while the second subgroup had 38 testes in 29 patients.

Cases were classified into three groups according to the response to treatment; the first group is the failure of treatment group; there is no change in the position of the testis and the patient needs surgical intervention. The second group is the one-degree improvement group; there is a change of position of the testis either from inguinal location to prescrotal location or from prescrotal location to scrotal location and according to the final position of the testes the patient either needs surgical intervention or not. The third group is the two-degree improvement group; there is a change of position of the testis from inguinal location to scrotal location and the patient did not need any surgical intervention.

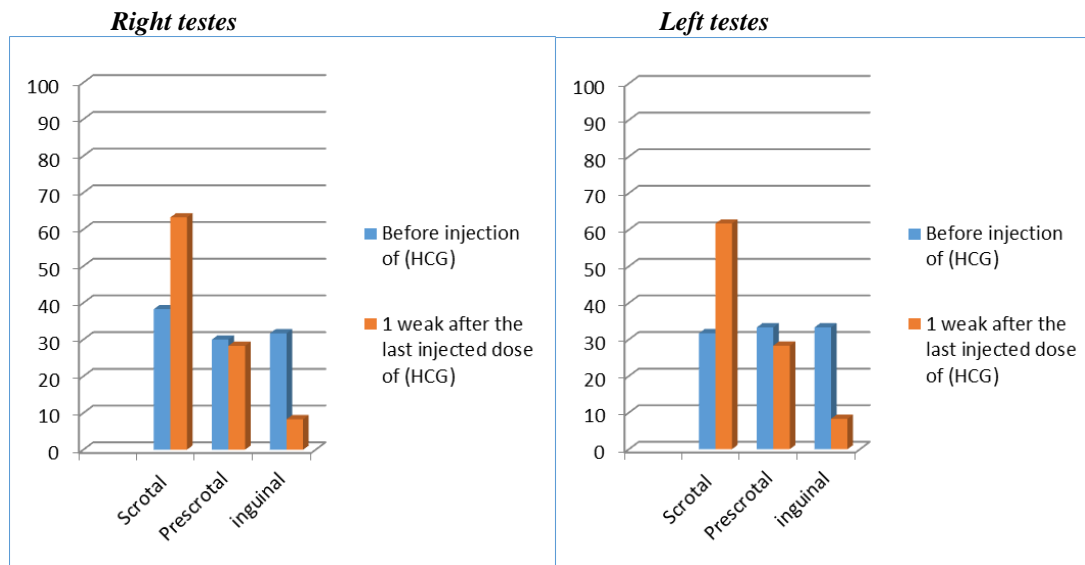
From the total 77 testes included in our study; 14 testes failed to improve its position (18.2%), 62 testes showed one-degree improvement (80.5%) while one testis showed two-degree improvement (1.3 %). Thirty-five testes reached a scrotal position and did not need to undergo surgery (45.5 %).

From a total number of 60 patients only two patients showed side effects from the hCG injection in the form of slight growth of the pubic hair and slight penile enlargement with percentage of 3.33%. Both patients turned normal in the follow up at the end of the study.

Using chi-square test to compare between the position of the testes before injection of hCG and one week after the last injected dose of hCG showed statistically significant difference with a P value <0.05. (Table 1 & Fig. 1)

**Table (1):** Comparison between the position of the testes before injection of (HCG) and 1 weak after the last injected dose of (HCG) among cases.

<b>Tables and figures</b>	Before injection of (HCG)	1 weak after the last injected dose of (HCG)	P Value
<b>Right testes</b>			
Scrotal	23 (38.3%)	38 (63.3%)	<b>0.000</b>
Prescrotal	18 (30%)	17 (28.3%)	
Inguinal	19 (31.7%)	5 (8.3%)	
<b>Left testes</b>			
Scrotal	19 (31.7%)	37 (61.7%)	<b>0.002</b>
Prescrotal	20 (33.3%)	17 (28.3%)	
Inguinal	20 (33.3%)	5 (8.3%)	



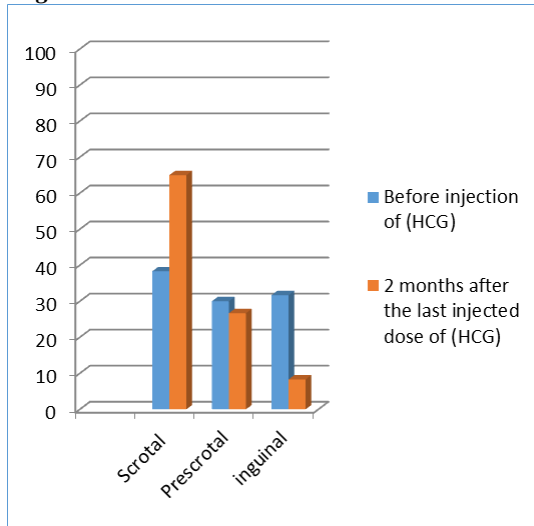
**Figure (1):** Comparison between the position of the testes before injection of (HCG) and 1 weak after the last injected dose of (HCG) among cases.

Using chi-square test to compare between the position of the testes before injection of hCG and two-month after the last injected dose of hCG showed statistically significant difference with a P value <0.05. (Table 2 & Fig. 2)

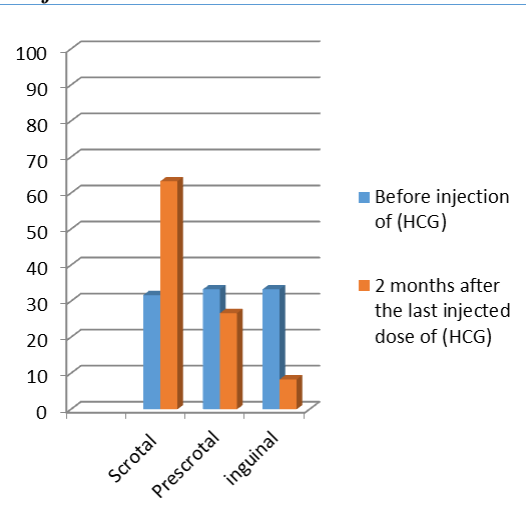
**Table (2):** Comparison between the position of the testes before injection of (HCG) and two months after the last injected dose of (HCG) among cases.

	Before injection of (HCG)	2 months after the last injected dose of (HCG)	P Value
<b>Right testis</b>			<b>0.000</b>
Scrotal	23 (38.3%)	39 (65%)	
Prescrotal	18 (30%)	16 (26.7%)	
Inguinal	19 (31.7 %)	5 (8.3%)	
<b>Left testis</b>			<b>0.000</b>
Scrotal	19 (31.7%)	38 (63.3%)	
Prescrotal	20 (33.3%)	16 (26.7%)	
Inguinal	20 (33.3%)	5 (8.3 %)	

**Right testes**



**Left testes**



**Figure (2):** Comparison between the position of the testes before injection of (HCG) and two months after the last injected dose of (HCG) among cases.

The initial position of the undescended testes was found to have a statistically significant effect on the final result after HCG injection ( $p = 0.00$ ). Out of 39 testes located in the inguinal canal, 10 testes failed to improve their position with percentage of 25.6%, while 29 testes showed improvement of their position with percentage of 74.4% but only one testes of them reached scrotal position with percentage of 2.56%.

On the other hand, out of 38 testes located in the prescrotal position, only 4 of them failed to

improve their position with percentage of 10.53%, while 34 testes improved their position with percentage of 89.47% and all of them reached scrotal position and did not need to undergo surgery.

Using paired t-test to compare the mean testicular size before and after injection of hCG at one-week and two-month showed statistically significant difference with a P value  $< 0.05$ . (Table 3, 4)

**Table (3):** Comparison between mean testicular size before injection of (HCG) and 1 week after the last injected dose of (HCG) among cases.

	Before injection of (HCG)	1 week after the last injected dose of (HCG)	Percentage of Change	P Value
Right testis	116.9±53 mm <sup>3</sup>	161±75 mm <sup>3</sup>	34%	<b>0.000</b>
Left testis	105±47 mm <sup>3</sup>	147±60 mm <sup>3</sup>	38%	<b>0.000</b>

**Table (4):** Comparison between mean testicular size before injection of (HCG) and two months after the last injected dose of (HCG) among cases.

	Before injection of (HCG)	Two months after the last injected dose of (HCG)	Percentage of Change	P Value
Right testis	116.9±53 mm <sup>3</sup>	185±90 mm <sup>3</sup>	17%	<b>0.000</b>
Left testis	105±47 mm <sup>3</sup>	135±35 mm <sup>3</sup>	22%	<b>0.000</b>

## DISCUSSION

Since 1930s, hormonal therapy has been used in Europe, though there are controversies over using it [8]. In 2013, a questionnaire about the management of undescended testes was given to pediatric endocrinologists in Turkey. 58.3% of the participants favored medical treatment, while 41.7% preferred surgical treatment for the management of undescended testes [16].

In a meta-analysis assessing the efficacy of hormonal therapy (1985-1990), the success rates of LHRH and hCG were detected to be 47% and 33% in 22 nonrandomized studies, 21% and 19% in 11 randomized studies, respectively, whereas the success rate of placebo was 4%. There was no significant difference in the success rates of treatments among patients younger or older than 4 years [17].

From the total 77 testes included in our study, 62 testes showed one-degree improvement (80.5%) while one testis showed two-degree improvement (1.3 %). Thirty-five testes reached scrotal position and did not need to undergo surgery (45.5 %). Our results are comparable to Kucharski et al. who studied 101 boys with 110 undescended testes after hCG-therapy and reported that 49 testicles (44.5%) descended to the scrotum and these 44 patients were not qualified for orchiopexy. Gonadotropin induced the descent of 90 out of 110 testicles at least one

level down, so the overall effectiveness of hCG treatment was 81.8% [13]. Also, our results are similar to what reported by Giannopoulos et al. who studied 2,467 boys with 2,962 palpable undescended testes between 1987 and 1999 and found that 1,762 ( 59.48% ) cases of cryptorchid testes were in the scrotum after combined hormonal therapy [18].

In this study, we found that the initial position of the undescended testes before HCG injection had a statistically significant effect on the final position of the testis as the improvement was more frequent among cases with prescrotal location compared to those with inguinal location ( $p = 0.000$ ), accordingly, hCG may be more successful in the treatment of the undescended testes with prescrotal location than those with inguinal location. Also, the mean testicular size increased significantly before and at one-week and two-month after injection of hCG.

Only 2 cases (3.33%) out of 60 showed side effects from the hCG injection in the form of slight growth of the pubic hair and slight penile enlargement. Both patients turned completely normal in the follow up visit at the end of the study.

Hormonal therapy is often a safe treatment modality; however, it may lead to penile growth, painful erection, and behavioral changes while on treatment [8]. Some authors have also pointed out the paucity of randomized controlled studies with

adequate sample sizes and adequate statistical power in the literature; thus, there is insufficient evidence showing the efficacy of hormonal treatment on undescended testes [19]. The 2007 Consensus Report of Nordic countries recommended that surgery is the first-line treatment modality. Surgery should be performed by pediatric surgeons and urologists at age 6-12 months [20].

A more in depth long term studies investigating the short and long term effects of hormonal therapy in undescended testis treatment are needed.

## CONCLUSION

Intramuscular injections of hCG given as neoadjuvant therapy in boys with undescended testis induced testicular descent to the scrotum in 45.5% of cases and improved position of testis before orchidopexy in further 36.3% of patients. More randomized clinical trials are recommended to prove the efficacy and side effects of the hormonal modality of treatment.

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