

## **THE ROLE OF HUMAN CHORIONIC GONADOTROPIN IN THE TREATMENT OF RETRACTILE TESTIS**

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### **Abstract**

A retractile testis is the testis that can be brought down into the scrotum but then after a period retract upward outside the scrotum by the action of cremasteric muscle.

The aim of this study is to identify the effect of age of the patient, location of the RT, and whether unilateral or bilateral on the response to HCG therapy.

This is a prospective study conducted in the pediatric surgery compartment in Basrah Children Hospital over 3 years (2013-2016). Thirty two boys with a diagnosis of retractile testis (RT) are included in this study. All cases were treated with intramuscular injection of HCG as following: in boys aged 1-4 years: 1000 IU twice weekly for 3 weeks (total 6000 IU) and in those aged more than 4 years: 1500 IU twice weekly for 3 weeks (total 9000 IU). The response to treatment was evaluated in 2 weeks, one month, and 6 months after completing the course of treatment of HCG.

In this study, the diagnosis of retractile testis was confirmed in 32 boys aged (1.25-9.5) years (mean: 5.28 years). Ten boys (31%) were with unilateral retractile testis. Twenty two boys (69%) were with bilateral retractile testis, 15 (27.7%) testes in the prescrotal area, and 39 (72.2%) testes in the inguinal area. From a total 54 retractile testes; 40 (74%) testes respond (descended into the scrotum). The mean age for responder was 5.49 years and the mean age for boys who did not respond was 4.69 years. Six (60%) of 10 unilateral retractile testes and 34 (77.3%) of 44 bilateral retractile testes respond to HCG treatment. Response to HCG occurred in 12 (80%) of the pre-scrotal retractile testes, and in 28 (71.8%) of the inguinal retractile testes. Re-ascending (recurrence) occurred in 6 (15%) testes.

In conclusion, HCG treatment is an effective way of treatment of retractile testis especially in preschool children, bilateral cases, and in those with prescrotal testicular position.

### **Introduction**

A retractile testis is a normally descended testis that move outside of the scrotum but it can be brought down manually into the scrotum during physical examination without pain or tension on the spermatic cord and remain in the scrotum for a while after release<sup>1-3</sup>. This upward movement of the testis is by the action of the cremasteric muscle (cremasteric reflex). The function of cremasteric muscle is to regulate the temperature of the testis in cold weather by elevating the testis to become closer to the body core temperature. The cremasteric muscle is most active in children especially between 2-7 years<sup>4</sup>.

Boys with retractile testis are usually referred to pediatric surgery or pediatric urosurgery outpatient clinic as a cases of cryptorchidism<sup>5</sup>.

Retractile testis is relatively common in pediatric population; the prevalence is recorded as 1.68% in children up to 14 years<sup>6</sup>. The prevalence is also reported to be 3.9% of schoolchildren (7-12) years old<sup>7</sup>. Some regarded retractile testis as a normal variant need only follow up because they often descend at puberty and there is no effect on testicular size or future fertility<sup>8-11</sup>. Others considered retractile testis as a true pathological condition because of the following points:

There is gubernaculum defect in majority of cases; in addition, associated undescended testes are present in 42% of unilateral retractile testes<sup>12</sup>.

Ascending testes (acquired cryptorchidism) can developed in 6%-32% of retractile testis cases carrying the same risk of complications occurring in congenital cryptorchidism<sup>6,13,14</sup>.

Histological changes (tubular degeneration, germ cells maldevelopment) are present in retractile testes and ascending testis in a nearly similar degree as in undescended testis<sup>15-20</sup>.

The size of retractile testes is significantly affected as compared with normal testes<sup>7,21</sup>.

The presence of retractile testis in the inguinal region for prolong period with higher temperature than the scrotal position is the main cause of complications that may affect future fertility especially in bilateral cases<sup>3,15,22,23</sup>.

The proper management of retractile testes still controversial; some prefer surgical correction in form of orchiopexy<sup>20,24</sup>, others prefer conservative management either wait and see<sup>25</sup> or hormonal therapy. Many studies evaluate hormonal therapy using Human chorionic gonadotropin (HCG) to stimulate testicular descent and the results were encouraging<sup>26-29</sup>.

The action of Human chorionic gonadotropin (HCG) is similar to that of luteinizing hormone; it stimulate the leydig cells to produce androgen<sup>1</sup>, in addition it increase vascularity and weight of the testis<sup>30</sup>.

In general; HCG treatment is regarded a safe treatment way; however, it may cause increase in penile size, painful erection, increase in pubic hair, and behavioral changes during the time of treatment and shortly after that<sup>31</sup>.

This study is conducted to identify the effect of age of the patient, location of the retractile testis, and whether unilateral or bilateral on the response to HCG therapy.

## Materials and methods

A prospective study conducted in the pediatric surgery compartment in Basrah Children Hospital over 3 years (2013-2016). Thirty two boys with a diagnosis of retractile testis are included in this study.

The diagnosis of retractile testis is confirmed depending on history and physical examination. The parents of all boys confirmed that the affected testis was in the normal position within the scrotum then started to retract frequently outside the scrotum especially when it exposed to cold environment.

The boys were examined in frog-leg position. The examination was in worm room, started with inspection then palpation with worm hand to avoid cremasteric muscle stimulation, the testis was regarded as a retractile if it can be pushed from the inguinal region to the scrotum without pain or tension and remain there after that for a period at least one minute until cremasteric muscle activation. The examination was repeated two to three times for each boy before the final decision regarding the diagnosis. In some cases continuous pulling of the testis for 30 seconds was required to make the cremasteric muscle in fatigue status to maintain the testis within the scrotum after hand release<sup>1</sup>.

Cases with ipsilateral inguinal hernia in association with retractile testis or those with history of ipsilateral inguinal surgery were excluded from this study.

Data was collected regarding the age of the patient, unilateral or bilateral, and pretreatment and post-treatment location of the testis (prescrotal or inguinal)

All cases were treated with intramuscular injection of HCG, the regimen of treatment was according to the patients age as following:

- 1-4 years: 1000 IU twice weekly for 3 weeks (total 6000 IU)
- More than 4 years: 1500 IU twice weekly for 3 weeks (total 9000 IU)

Two weeks after completing HCG treatment course; each patient was

evaluated for the response to treatment, the position of the testis was recorded again 1 month and 6 months later on. Statistical data analysis was done using SPSS software version 22

## Results

In this study, the diagnosis of retractile testis was confirmed in 32 boys aged (1.25-9.5) years (mean: 5.28 years) Ten boys (31%) were with unilateral retractile testis. Twenty two boys (69%) were with bilateral retractile testis. Of unilateral cases (7) were on the right side

and (3) were left sided.

The distribution of retractile testes according to their location at diagnosis was 15(27.7%) testes in the prescrotal area, and 39(72.2%) testes in the inguinal area.

The response to HCG treatment of a total 54 retractile testes is evaluated, the results was as following:

From a total 54 retractile testes; 40(74%) testes respond (descended into the scrotum). The mean age for responder was 5.49 years and the mean age for boys who did not respond was 4.69 years (Table I) .

**Table I: Response to HCG according to the age of the patients**

Response to HCG	Mean	N
Responded	5.4917	40
Did not responded	4.6905	14
Total	5.2840	54

Six (60%) of 10 unilateral retractile testes and 34 (77.3%) of 44 bilateral retractile testes respond to HCG treatment (Table II) .

**Table II: Response to HCG according to bilaterality**

Response to HCG	Respond	Did not respond	Total
<b>Laterality</b>			
Unilateral	6 (60%)	4 (40%)	10(100%)
Bilateral	34 (77.3%)	10 (22.7%)	44(100%)

According to location of retractile testis, response to HCG occurred in 12(80%) of the pre-scrotal retractile testes, and in 28(71.8%) of the inguinal retractile testes (Table III).

**Table (III): Response to HCG according to the pretreatment location of the testis**

Response to HCG	Respond	Did not respond	Total
<b>Location of the testis</b>			
Prescrotal	12(80%)	3(20%)	15(100%)
Inguinal	28(71.8%)	11(28.2%)	39(100%)

On sixth month follow up examination, Of 40 testes responded to treatment, re-ascending (recurrence) occurred in 6 (15%) testes. One (8%) of 12 pre-scrotal retractile testes and 5(17%) of 28 inguinal retractile testies.

## Discussion

In 1988; Elder JS recommend the usage of HCG in the treatment of retractile testis<sup>32</sup>, also Ashcraft mention that retractile testis can be differentiated from

cryptorchidism by HCG administration meaning that the response of retractile testis to HCG is well established<sup>33</sup>.

According to the Guidelines on Pediatric Urology 2013; the HCG dose 6000-9000 IU h given in four doses over 2-3 weeks<sup>34</sup>, while WHO recommends the following regimen: 250 IU/dose in boys less than one year, 500 IU/dose in those of ages 1-5 years, and 1000 IU/dose in those of ages more than 5 years given biweekly for five weeks<sup>28,35</sup>. In this study the total HCG

dose is 6000 IU and 9000 IU according to the age of the patient, the total dose of HCG is the same of that mentioned in the Guidelines on Pediatric Urology 2013 but divided into six rather than four doses.

In this study the overall response of retractile testis to HCG treatment (success rate) is 74%, which is nearly similar to reported success rate by two previous studies: Ezzat A, et al (76%)<sup>28</sup>, and Metin A, et al (82%)<sup>27</sup>.

Bilateral cases in Ezzat A<sup>28</sup>, et al study were 60% of total case. Our study confirmed the higher prevalence of bilateral cases (69%). The same previous study revealed the mean age of those who respond to HCG was 7.5 years, in our study the mean age was 1 (5.5 years). The least success rate is reported to be in boys less than 2 years (3%-15%)<sup>27,36</sup>.

In this study the success rate of HCG treatment was higher in bilateral cases than in unilateral cases 77.3% and 60% respectively, while in a study by Ezzat et al<sup>28</sup> the response was nearly similar in bilateral and unilateral cases 76.6% and 75% respectively.

Regarding the location of the testes; the response was higher in prescrotal than in

inguinal pretreatment position 80% and 71.8% respectively. This difference in response according to the location of the testis also found in Metin A et al study: 88.8% of prescrotal testes and 75% of inguinal testes responded to HCG treatment<sup>27</sup>.

Recurrence (re-ascending) occurred in 15% of all cases initially responded to treatment, in a study by Metin A et al<sup>27</sup> recurrence occurred in 11 (8.9%) of 123 retractile testes. The increment of recurrence rate in present study may be because more than two third of retractile testes located in the inguinal region, in addition; in the Metin A study; a total HCG dose was 9000 IU used in all cases while in the present study the total dose was (6000-9000) IU according to patient age.

## Conclusion

HCG treatment is an effective way of treatment of retractile testis especially in preschool children, bilateral cases, and in those with prescrotal testicular position. Recurrence rate may reach up to 15% of cases that initially responded to HCG treatment.

## Reference

1. Kurz D, Tasian G. Current Treatment Options in Pediatrics. 2016;2:43-54.
2. Keys C, et al. Retractable testes: A review of the current literature. Journal of Pediatric Urology. 2012; 8:2.
3. Way Goh D, Hutson JM. Is the retractile testis a normal, physiological variant or an anomaly that requires active treatment? *Pediatr Surg Int* 1992 ; 7 :249-52.
4. Caesar RE, Kaplan GW: The incidence of cremasteric reflex in normal boys. *J Urol* 1994 ; 152 :779-80.
5. Goh DW, Hutson JM. The retractile testis: time for a reappraisal. *J Paediatr Child Health*. 1993;29:407-408.
6. Papparella A, Coppola S, Nino F, et al. Epidemiology and treatment of cryptoid and retractile testis: retrospective study in the area of Naples. *Minerva pediatr*. 2013 Feb; 65(1):77-82.
7. Inan M, Aydinler CY, Tokuc B, et al. prevalence of cryptorchidism, retractile testis and orchiopexy in school children. *Urol Int*. 2008; 80(2):166-71.
8. Shapiro E. the risk of retractile testes becoming ascending testes. *Rev Urol*. 2006; 8(4):231-2.
9. La Scala GC and Ein SH: Retractable testes: an outcome analysis on 150 patients. *J Pediatr Surg* 2004; 39: 1014.
10. Hack WW, van der Voort-Doedens LM, Goede J, van Dijk JM, Meijer RW & Sijstermans K. Natural history and long-term testicular growth of acquired undescended testes after spontaneous descent or pubertal orchiopexy. *BJU Int*. 2010 OCT; 106(7):1052-9.
11. Kolon TF, Patel RP, Huff DS. Cryptorchidism: diagnosis, treatment, and long-term prognosis. *Urol Clin North Am*. 2004;31:469-80.
12. Kubota M, Okuyama N, Yamazaki S, et al. is mobile testis a true pathological condition due to a gubernaculum abnormality. *Pediatr Surg Int*. 2007 Jul;23(7):633-6.
13. Stec AA, Thomas JC, DeMarco RT, et al. Incidence of testicular ascent in boys with retractile testes. *J Urol*. 2007 Oct;178(4 Pt 2):1722-4.
14. Agarwal PK, Diaz M, Elder JS. Retractable testis: is it really a normal variant? *J Urol*. 2006;175:1496-9.
15. 3 Han SW, Lee T, Kim JH, et al. Pathological difference between retractile and cryptorchid testes. *J Urol* 1999 Sep ; 162(3 pt1) :878-80.
16. Barthold JS, Gonzalez R. The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy. *J Urol*. 2003 Dec;170(6 Pt 1):2396-401.
17. Rusnack SL1, Wu HY, Huff DS, Snyder HM 3rd, Zderic SA, Carr MC, Canning DA. The ascending testis and the testis undescended since birth share the same histopathology. *J Urol*. 2002 Dec;168(6):2590-1.
18. Gracia, J., Navarro, E., Guirado, F., Pueyo, C. and Ferrández, A. (1997). Spontaneous ascent of the testis. *British Journal of Urology*, 79: 113-115.
19. Lee T, Han SW, Lee MJ, Kim JH, Choi SK, Cho NH, et al. Pathological characteristics in retractile testis comparing cryptorchid testis. *Korean J Urol*. 1999 May; 40(5):617-22.
20. Taghizadeh AK, Thomas DF. Ascent of the testis revisited: fact not fiction. *BJU Int* 2008; 102: 676-8.
21. Goede J, van der Voort-Doedens LM, Sijstermans K, Hack WWM. The Volume of Retractable Testes., *J Urol*. 2011 Nov; 186( 5): 2050-4
22. Caucci M, Barbatelli G, Cinti S : The retractile testis can be a cause of adult infertility. *Fertil Steril* 1997; 68:1051-8.
23. Ito H, Kataumi Z, Yanagi S, Kawamura K, Sumiya H, Fuse H et al. Changes in the volume and histology of retractile testes in prepubertal boys. *Int J Androl* 1986; 9:161-9.
24. Bonney T, Hutson J, Southwell B & Newgreen D. Update on congenital versus acquired undescended testes: incidence, diagnosis and management. *ANZ J Surg*. 2008 Nov; 78 (11), 1010-13
25. Meijer RW, Hack WW, van der Voort-Doedens LM, Haasnoot K, Bos SD. Surgical findings in acquired undescended testes. *J Pediatr Surg* 2004; 39: 1242-4.
26. Job JC. Hormonal therapy of cryptorchidism with human chorionic gonadotropin (HCG). *Urol Clin North America* 1982 ; 9 :405-11.
27. Metin A, Kayigil O, Ahmed SI. The efficacy of human chorionic gonadotropin in retractile testis. *Neuro Endocrinol Lett*. 2005 Feb;26(1):39-42.
28. Ezzat A, Amer W, Abd Elfatah M, et al. Retractable testis: management of 50 boys. *Ann Pediatr Surg*. 2007 Jan;13(1):31-4.
29. Raifer J, Handelsman DJ, Swerdloff RS, et al. Hormonal therapy of cryptorchidism. A randomized, double blind study comparing human chorionic gonadotropin and gonadotropin-releasing hormone. *N Engl J Med* 1986 Feb 20; 314(8):466-70.
30. Hutson JM, Baker M, Terada M, Zhou B, Paxton G. Hormonal control of testicular descent and the cause of cryptorchidism. *Reprod Fertil Dev* 1994 ; 6 :151-6
31. Bertelloni S, Baroncelli GI, Ghirri P, Spinelli C, Saggese G. Hormonal treatment for unilateral inguinal testis: comparison of four different treatments. *Horm Res*. 2001; 55(5):236-9.
32. Elder JS. The undescended testis. Hormonal and surgical management. *Surg Clin North Am*.1988; 68:983-1005.
33. Lee JJ, Shortliffe LMD. Undescended testes and testicular tumors. Holcomb GW, Murphy JP, editors. *Ashcraft's pediatric surgery*. Saunders. 2014. pp. 689-701.
34. Tekgül S, Dogan HS, Hoebek P, et al. Pediatric Urology. European Society for Paediatric Urology, European Association of Urology. Guidelines on Paediatric Urology; 201.
35. Kafer M. Diagnosis and treatment of the undescended testicle. In: Pescovitz O, Eugster E, editors. *Pediatric Endocrinology*. USA: Lipincott Williams & Wilkins; 2004. pp. 255-274.
36. Miller OR, Stock JA, Cilento BG, MaAleer IM, Kaplan GW. Prospective evaluation of human chorionic gonadotropin in the differentiation of undescended testis from retractile testes. *J Urol* 2003; 169: 2328-31.