

## Role of pre-operative gonadotropin in orchidopexy

*El-sayed H. Abdallah, MD<sup>a</sup>; Mohammed A. Abdelkhalekb, MD<sup>b</sup>; Guindy, MD<sup>c</sup>;  
Amr A. Mostafa, MD<sup>d</sup>*

- a) Departments of General Surgery (Pediatric Surgery Unit), Al-Azhar University.*
- b) Departments of Urology, Al-Azhar University.*
- c) Department of Paediatrics, Al-Azhar University.*
- d) Department of Radiology, Al-Azhar University.*

**Background:** To evaluate the role of human chorionic gonadotropin (HCG) in cryptorchid boys regarding testis position and size in treatment of palpable undescended testis (UDT).

**Patients and methods:** One hundred children presented with unilateral palpable UDT were studied in the period from May 2007 to May 2010. Their ages ranged from 2-12 years with mean age 6.4 years SD  $\pm 2.1$  and were divided into two equal groups: Group A – (control group) in which surgical orchidopexy was done without preoperative hormonal preparation and Group B – (studied group) in which the patients received preoperative intramuscular injection of HCG 30-50IU (Pregnyl) per kilogram of bodyweight, two times a week for five succeeding weeks. The patients were subjected to clinical examination, laboratory investigations including testosterone level pre- and post- HCG therapy, ultrasound (U/S) and color Doppler ultrasound (CDUS). The results were assessed clinically, hormonal level, and CDUS. Standard orchidopexy was done in all cases. Both groups were assessed in terms of testicular size and vascularity by CDUS. The mean basal and post-HCG stimulation serum testosterone level were also compared in both groups. Both groups were also followed up postoperatively, clinically and by U/S.

**Results:** We found sizable testis, long cord with good vascularity, easily dissectible associated hernial sac and more capacious scrotum with good post-operative results in group B patients.

**Conclusion:** Preoperative HCG treatment is a safe effective tool to increase testicular size and viability which improve the results of orchiopexy.

**Key words:** Undescended testis, orchiopexy, human chorionic gonadotropin (HCG).

### Introduction:

Cryptorchidism is the most common urogenital birth defect in males necessitating surgery. The importance of cryptorchidism treatment concerns with the possibility of diminishing risk of malignant degeneration and improving fertility.<sup>1</sup> Malignant changes and degeneration in UDT is 4-40% higher than normal testes.<sup>3</sup> Testicular descent occurs late in fetal life and is regulated by many factors including intra-abdominal pressure, hormonal, neurologic influence and presence of gubernaculum. The absence of any of these elements may contribute to cryptorchidism. The incidence of undescend depends on fetal age, up to 30% of premature boys have

either one or both undescended testes. In boys born at term the incidence is between 3-4%.<sup>4</sup> Approximately at the age of 3 months, transient increase in serum gonadotropin and testosterone occurs which is responsible for spontaneous descent in more than one half of boys with cryptorchidism. The incidence of cryptorchidism in untreated adults is approximately 1%.<sup>5</sup>

Success rate of hormonal treatment varies from 0-55% with human chorionic gonadotropin (HCG) and 9-87% with gonadotropin releasing hormone (Gn-RH). Surgical interference for undescended testes still is the main way for treatment to avoid complications. Shortening of the

spermatic cord and under-development of the scrotum are still the main problem in surgical treatment of UDT. The use of HCG as a preoperative preparation for orchidopexy helps the surgeon by increasing the length and the vascularity of the cord and increase size of the testis and the scrotum becomes more capacious and well developed in addition to help the dissection of hernia sac.<sup>7</sup> The proper treatment of cryptorchidism is still controversial. In the past, it has been dictated by experts in hormonal therapy. By ascertaining the cause of UDT, the action of gonadotropin factor and the efficacy of surgical procedures, the surgeon is enabled to reconstruct a rationale form of treatment. Currently, most pediatric urologists suggest treatment of cryptorchidism before the child is 2 years old, preferably when he is between 6-18 months.<sup>8</sup> The surgeon is able to place the UDT into the scrotum however, surgical treatment is difficult and complications range from 1.5% to 12.2%. Certain outstanding difficulties are encountered in surgical procedures when the scrotum is under-developed and the testis is malformed, small and associated with short vessels.<sup>9</sup> The modalities available for surgical or hormonal therapy are performed on an outpatient basis. Hormonal manipulation is based on the observation that increased testosterone may encourage testicular descent.<sup>12</sup> Human chorionic gonadotropin HCG produced by human placenta with a  $\alpha$ -subunit that is almost identical to the  $\alpha$ -subunit of pituitary gonadotropin has been shown to induce testicular descent presumably by stimulating either testosterone or dihydrotestosterone production by Leydig's cells.<sup>13</sup> Immediately after treatment with HCG, there was a large increase in the conversion of 3-(OH) progesterone and 3-(OH)pregnenolone by 17-alpha-hydroxylase and 3-beta-hydroxysteroid dehydrogenase. Considerable amount of testosterone was formed especially from pregnenolone within 2 weeks of last HCG injection and steroidogenic activity has decreased. These observations indicated that HCG treatment of boys with UDT does

not result in irreversible or even long lasting stimulation of their steroidogenic activity.<sup>14</sup> Hawkin's in 1995 stated that no long term ill effects have been in association with this short term hormonal therapy. The mean goal of HCG therapy is to increase serum testosterone level. More than 10-20-fold baseline HCG has been used extensively in the preoperative period as a therapeutic measure to induce testicular descent.<sup>15</sup> HCG induces a significant increase in the volume and density of both interstitial tissue and blood vessels.<sup>11</sup>

### **Patients and methods:**

The study included one hundred children who suffered from unilateral palpable UDT attending outpatient clinics of Al-Hussein and Bab El-sha'ria Hospitals, Al-Azhar University, in the period from May 2007 to May 2010. Their ages ranged from 2-12 years with mean age 6.4 years SD  $\pm$ 2.1 years. All patients subjected to full history taking & clinical examination, complete laboratory investigations and Doppler U/S examination for evaluation of size, site and vascularity of the UDT. Those children were genotypically and phenotypically normal.

Exclusion criteria: Non-palpable undescended testes, bilateral palpable undescended testes and abnormal genotype and phenotype (ambiguous genitalia).

These patients were grouped into two groups:

Group A: 50 patients operated without hormonal therapy and

Group B: 50 patients prepared by hormonal therapy (HCG) pre-operatively.

The HCG was given according to the body weight as shown in **Table (1)**.

Preoperatively, testicular size was measured clinically by orchidometer with slide calipers. The volume V (ml) was calculated by  $V = \text{length } L \text{ (cm)} \times \text{breadth } B \text{ (cm)} \times \text{diameter } D \text{ (cm)} \times 0.523$ . Color Doppler ultrasound was done in all cases to localize the testes, measure its size and note its vascularity. Re-measurement was done for both groups. Standard orchidopexy was done in all cases.

## Results:

This study was done on 100 patients who suffered from unilateral palpable UDT. The left side is more commonly affected as shown in **Table (2)**.

The patient ages range from 1-12 years with mean age 6.6/12 years. **Table (3)** show age at presentation of UDT.

In our study, we measured serum testosterone level in both groups and after HCG therapy for group B only and we found that serum testosterone level was at the low normal value before HCG therapy and increased significantly in group B after HCG therapy as shown in **Table (4)**.

In our study, as regard U/S findings, we found that the site of the undescended testis was the inguinal canal (30%), external inguinal ring (50%) and at the neck of scrotum (20%). After hormonal therapy in group B, we found increased size of testes by about 10-15% based on the first U/S examination, increased vascularity by Doppler U/S and scrotal development by clinical observation in addition to increased activity and increased appetite as observed by parents. As regard the site of the testis, in 8 out of 15 cases of group B (16%) with testicles at the site of inguinal canal, the testicles reached the site of external inguinal ring.

In 10 out of 25 cases of group B (20%) with testicles at the site of external inguinal ring, the testicles reached the site of scrotal neck.

In 7 out of 10 cases of group B (10%) with testicle at the scrotal neck, the testicles reached at the bottom of scrotum.

In 25 cases of group B (50%) the site of the testes did not change after HCG therapy but their size increased by 10-15% of the first U/S measure with increased vascularity by Doppler U/S. On surgical orchidopexy, the surgery was more easy, the testis was sizable, the cord was longer, the hernia sac was thicker and easier dissectible from the cord, tissue plane was good and the scrotum was well developed and capacious as shown in **Figure (1)**.

Follow up after orchidopexy, the testicular size was good.

## Discussion:

One hundred children suffering from unilateral palpable UDT attending the outpatient clinics of Al-Hussein and Bab El-sha'ria Hospitals, Al-Azhar University, in the period from May 2007 to May 2010, their ages ranged from 1-12 years with mean age 6.6/12 years with 60 cases presented with left unilateral palpable UDT and 40 cases presented with right unilateral palpable UDT. Serum testosterone level was measured in all patients and we found that basal level was at the low normal value (4.2-4.3 ng/dl) [Normal value: 3-10 ng/dl] (Nicholson and Pesce 2000). After HCG therapy for group B we re-estimate hormonal level and we found significant increase in testosterone level (91ng/dl) and this coincided with Gangopadhyay et al. 2005. The testicular site and size were measured by Doppler U/S for all cases at the start of the study and we found that the site of the undescended testis was at the inguinal canal in (30%), external inguinal ring in (50%) and at the neck of scrotum in (20%) and the testicular volume ranged from 0.8-0.9 cm<sup>3</sup>. After HCG therapy in group B as regard the site of the testis we found a change in the site in 50% as follows: 16% in whom testicles at the inguinal canal, the testicles reached the external inguinal ring, (20%) in whom testicles at the external inguinal ring, the testicles reached the scrotal neck and (14%) in whom testicle at the scrotal neck, the testicles reached at the bottom of scrotum. However, in 50% the site of the testes did not change after HCG therapy by Doppler U/S but the size of testis increased by 10-15% of the first U/S measure with increased vascularity by Doppler U/S. On surgical orchidopexy, the surgery was more easy, the testis was sizable, the cord was longer, the hernia sac was thicker and easier dissectible from the cord, tissue plane was good and the scrotum was well developed and capacious. We hypothesized that HCG may prevent ischemic damage during orchidopexy by increasing collateral flow and this is in agreement with Geesman et al. 1992. The ultimate aim of all therapeutic approaches to UDT is to achieve intrascrotal fertile testis. This can

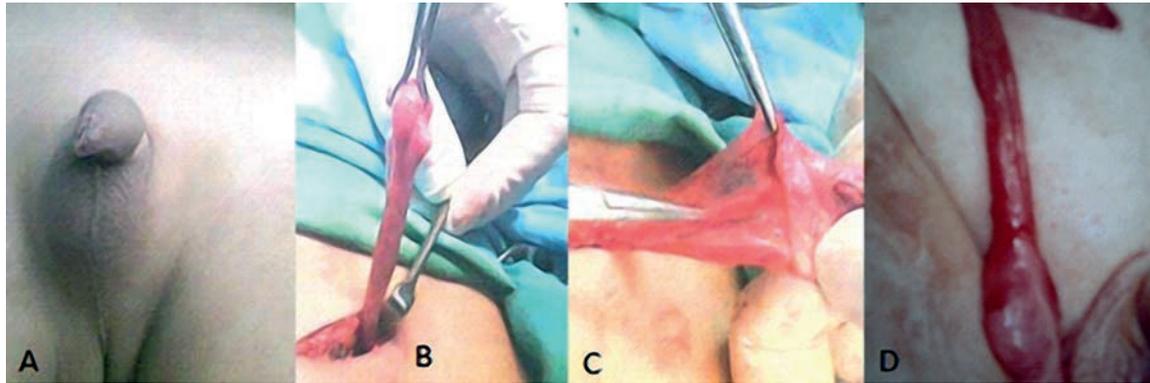


Figure (1): A: The scrotum is well developed and capacious. B: the cord is longer. C: the hernia sac is thicker and easier dissectible from the cord. D: the testis easily reaches the scrotum.

Table (1): Doses of HCG therapy for UDT

Dose	Schedule	Age
30-50 IU/KGbodyweight im	Twice weekly x 5 weeks	1-5 years
30-50 IU/Kg bodyweight im	Twice weekly x 5 weeks	> 5 years

Table (2): Distribution of unilateral palpable UDT as regard the affected side

Distribution \ Side	Right side	Left side
	Number of cases	40
Percent	40%	60%

Table (3): Age distribution of the patients

Age in years \ Item	Number of cases	Percent
<2	16	16%
2-6	48	48%
6-12	36	36%
Total	100	100%

Table (4): Serum testosterone level during the study

Hormonal level (ng/dl) \ Group	Control group (A)	Studied group (B)
Basal level	4.21±0.49	4.25±0.53
After HCG therapy	Not measured	91.60±7.8

be achieved either by hormonal therapy only (HCG or Gn-RH), or hormonal therapy as a preoperative preparation. In our study, success rate of hormonal-induced intrascrotal descent 14%. The most striking result of

our work is the evidence of the efficacy of early hormonal treatment in improving the trophism of cryptorchid testes. Hormonal treatment, when administered at the end of the first 6 months of life, can be considered

an effective and timely substitution of the gonadotropin and testosterone insufficiency of the cryptorchid infant. Therefore, we propose this therapeutic procedure combined with surgery. LHRH nasal treatment was not difficult to administer, even in very young infants, and did not cause any distinct adverse events with the exception of increased excitability in about 25% of cases. Treatment with (Gn-RH) as nasal spray was introduced in Europe in 1975 and proved successful although the pathophysiologic background has been questioned and success rate has been variable.<sup>21</sup> HCG caused mild signs of androgenization (hyperpigmentation of genital skin, erections, moderate penile growth) in almost all patients. Orchidopexy in the 1<sup>st</sup> year of life does not pose any significant problem to a competent pediatric surgeon and there are important anatomic advantages: the inguinal channel is shorter and it is easier to place a very high intra-abdominal testis into the scrotum. Many data in the literature indicate a good correlation between germ-cell count in childhood and semen quality as an adult.<sup>7</sup> In our study, HCG as an intramuscular injection was used with slight psychologic side effect instead of Gn-RH as the last drug is not available and is more expensive. Lala study in Switzerland 1993 with HCG 500 I.U. I.M. three times weekly for three weeks showed that 37.8% of testes descended into scrotum. Lala study showed also testicular descent occurred more often in patients with testes were located in lower position.<sup>12</sup> In our study, the results are less than Lala 14% as the regimen of HCG is different. Nowadays, there must not be debate on the choice of medical or surgical approach for the management of UDT and on their efficacy in preventing long term complications. It must be a matter of synergism of both hormonal HCG and/or followed by surgical orchidopexy to help and improve the surgical orchidopexy. In cases of failure that require surgery, the HCG will stimulate tissue growth enhancing the success of orchidopexy. The result that HCG is useful in testicular descent is also verified by another study carried out by Zucchini and Cacciari in 1982. The rationale for giving HCG is

that it stimulates Leydig cells that results in an increase in plasma testosterone, which promote testicular descent. In our study, we found that HCG therapy stimulates testicular secretion, increases the size & vascularity of scrotum, testes and vas deference, enlarges the inguinal canal, and causes differentiation of the epididymis and this coincided with Hadiselimovic and Gangopadhyay et al.<sup>23</sup>

### Conclusion :

Preoperative HCG treatment is a safe effective tool to increase testicular size and viability which improves the results of orchidopexy.

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