Role of preoperative versus post-operative HCG therapy in bilateral nonpalpable undescended testis

A. N. Gangopadhyay, Shilpa Sharma, V. Bhushan¹, R. C. Shukla²

Departments of Pediatric Surgery, ¹General Surgery and ²Radiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India
Correspondence: AN Gangopadhyay, Department of Pediatric Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi – 221 005, Uttar Pradesh, India. E-mail: gangulybhu@rediffmail.com

ABSTRACT

To evaluate the role of human chronic gonadotropin (HCG) and compare the results when it is given preoperatively and postoperatively in bilateral nonpalpable undescended testes (BNUDT) to facilitate the surgical outcome. Sixty-six cases of BNUDT, from January 1997 to January 2004, were divided equally into two groups on a random basis: Group A – control group received HCG doses which were completed 7–10 days preoperatively and Group B – test group received postoperative HCG doses started 7–10 days after surgery. The HCG was given as per WHO recommendation. The results were assessed clinically, by color Doppler ultrasound and HCG stimulated testosterone assay. Standard orchidopexy was done in all cases. Both groups were comparable in terms of age, testicular size, and vascularity as assessed by the Doppler ultrasonographic study. The mean basal serum testosterone and the HCG stimulation were also comparable in both the groups. At the sixth week follow up, the difference in the serum testosterone level was statistically significant, Group A 60.50 ± 7.19 ng/dl vs Group B 81.17 ± 5.88 ng/dl. The testicular vascularity at the sixth week follow up was more in Group B (74% normal vs 55% normal). Sixteen (24%) testis were retracted in Group A, while none were in Group B. Postoperative HCG therapy has been proved to be more effective than conventional preoperative therapy for better surgical outcome in BNUDT.

KEY WORDS: Cryptorchidism, Human chorionic gonadotropin, Nonpalpable testes

A prevalence rate of 3.68% of cryptorchidism at birth, which decreases to 1% by 3 months of life, has been noted.[¹] Scorer observed the same to be 0.8% of normal children at 1 year of age.[²] Human chronic gonadotrophin (HCG) produced by the human placenta with a α-subunit that is almost identical to the α-subunits of pituitary gonadotrophin has been shown to induce testicular descent, presumably by stimulating testosterone or by stimulating dihydrotestosterone production. The stimulatory effect of this polypeptide hormone on testicular steroidogenesis has enabled it to be widely used for evaluating male Leydig cell function.[³] The general goal of an HCG stimulation test is to increase serum testosterone levels. More than 10-20-fold baseline HCG has been used extensively in the preoperative period both as a stimulating test for identification of testicular presence in cryptorchidism and as a therapeutic measure to induce descent.[⁴][⁵] The HCG induces a significant increase in the volume density of both interstitial tissue and blood vessels. In normally descended and undescended testis, there appears to be no permanent damage.[⁷]

We have made an attempt to study its role in the postoperative management of bilateral nonpalpable cryptorchidism and to compare the result with that of conventional preoperative use of hormonal therapy as an adjuvant to orchidopexy.

MATERIALS AND METHODS

Over a 7-year period (January 1997–January 2004), 66 cases of bilateral, nonpalpable, undescended testis diagnosed clinically and detected by color Doppler ultrasound were treated by systemic randomization and by dividing them into two nearly identical groups [Tables 1, 2]. Group A – control consisted of 33 subjects who were given preoperative HCG therapy, which was completed 7–10 days before surgery. In Group B, 33 subjects of the test group were given postoperative HCG therapy which commenced 7–10 days after surgery [Table 3].

The HCG was given as per the WHO protocol [Table 4]. The treatment schedule as per WHO recommendation is
1. 250 IU twice weekly for 5 weeks in boys up to 1 year of age.
2. 500 IU twice weekly in 1-5-year-old boys.
3. 1000 IU twice weekly for 5 weeks for boys >5 years.

Standard orchidopexy was done in all cases. Testicular size was measured clinically by orchidometer with slide calipers. The volume (ml) was calculated by

\[ V = L \times B \times D \times 0.523 \]

Color Doppler ultrasound was done in all cases to localize the testes, measure its size and note its vascularity. The HCG stimulation test was done in all cases with 1500 – 2000 IU of HCG daily for 3 days and measurement of serum testosterone on the sixth day by radio immunoassay (using RIA kit).

Results
In Group A, 8 (24%) cases were < 2 years, 11 (34%) cases were between 2 and 5 years and 14 (42%) cases were < 5 years. In Group B, the same was 7 (21%), 16 (49%), and 10 (30%) cases, respectively. The site of the tests was at the inguinal canal, deep ring, and undetectable in 43 (33%), 59 (44%), and 30 (23%) cases, respectively, taking both the groups together (132 testes).

The testicular size as measured by color Doppler ultrasonography was comparable in both the groups 0.70 ± 0.16 ml \((n = 51)\) in Group A and 0.60 ± 0.21 ml \((n = 51)\) in Group B. The vascularity was poor in 30 testes (45%) in Group A and 19 testes (29%) in Group B, and normal in 21 testes (32%) in Group A and 32 testes (48%) in Group B. It was not detectable in 15 testes in each group. The basal serum testosterone level was 4.21 ± 0.49 ng/dl in Group A and 4.38 ± 0.76 ng/dl in Group B. The testosterone level was comparable in both the groups after the HCG stimulation test [Table 3]. The difference between the serum testosterone, 6 weeks and 6 months after HCG treatment was statistically significant in both the groups at \(P < 0.001\) [Table 3].

The testicular vascularity at 6 weeks follow up was more in Group B [98 (74%) – normal, 34 (26%) poor] than in Group A [72 (55%) – normal, 60 (45%) poor]. The difference in testicular size, 6 weeks after treatment between both the groups was statistically significant [Figure 1]. In three testes (16%) of Group A, there was decrease in testicular size. Testicular retraction was not encountered in Group B although it occurred in 16 testes (24%) in Group A.

DISCUSSION
Out of 256 patients of undescended testis attending the pediatric surgery out-patient department of the University Hospital, Varanasi, 100 (39%) patients had bilateral

### Table 1: Initial Doppler ultrasonographic study of two groups of bilateral nonpalpable testes

<table>
<thead>
<tr>
<th></th>
<th>Control group ((n = 33))</th>
<th>Test group ((n = 33))</th>
<th>Statistical value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size of testis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(volume in ml)</td>
<td>0.70 ± 0.16 (ml)</td>
<td>0.60 ± 0.21 (ml)</td>
<td>(t = 1.65) ((P = NS))</td>
</tr>
<tr>
<td><strong>Size of testis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep ring</td>
<td>15 (45.45%)</td>
<td>16 (48.48%)</td>
<td>(X^2 = 0.62) ((P = NS))</td>
</tr>
<tr>
<td>Inguinal canal</td>
<td>13 (39.39%)</td>
<td>12 (36.36%)</td>
<td></td>
</tr>
<tr>
<td>Not detectable</td>
<td>5 (15.16%)</td>
<td>5 (15.16%)</td>
<td></td>
</tr>
<tr>
<td><strong>Vascularity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>14 (42.42%)</td>
<td>13 (39.39%)</td>
<td>(X^2 = 0.56) ((P = NS))</td>
</tr>
<tr>
<td>Normal</td>
<td>12 (36.36%)</td>
<td>13 (39.39%)</td>
<td></td>
</tr>
<tr>
<td>Not detected</td>
<td>7 (21.22%)</td>
<td>7 (21.22%)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2: Age distribution of patients

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Control group</th>
<th>Test group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2</td>
<td>8</td>
<td>7</td>
<td>15 (22.8%)</td>
</tr>
<tr>
<td>2 – 5</td>
<td>12</td>
<td>15</td>
<td>27 (40.8%)</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>13</td>
<td>11</td>
<td>24 (36.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>33</td>
<td>66 (100%)</td>
</tr>
<tr>
<td>Mean ± SD (years)</td>
<td>4.5 ± 2.33</td>
<td>4.49 ± 2.48</td>
<td>(t = 0.007) ((P\text{ value not significant}))</td>
</tr>
</tbody>
</table>

### Table 3: Serum testosterone levels during the study

<table>
<thead>
<tr>
<th>Serum testosterone level (ng/dl)</th>
<th>Control</th>
<th>Study</th>
<th>Statistical value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>4.21 ± 0.49 ((n = 33))</td>
<td>4.38 ± 0.76 ((n = 33))</td>
<td>NS</td>
</tr>
<tr>
<td>After HCG stimulation test</td>
<td>98.68 ± 4.33 ((n = 16))</td>
<td>91.60 ± 7.8 ((n = 16))</td>
<td>NS</td>
</tr>
<tr>
<td>After 6 weeks</td>
<td>60.50 ± 7.19 ((n = 33))</td>
<td>81.17 ± 5.88 ((n = 33))</td>
<td>(P &lt; 0.001) (significant)</td>
</tr>
<tr>
<td>After 6 months</td>
<td>58.40 ± 6.21 ((n = 12))</td>
<td>79.40 ± 8.32 ((n = 10))</td>
<td>(P &lt; 0.001) (significant)</td>
</tr>
</tbody>
</table>

### Table 4: WHO protocol for HCG stimulation test

<table>
<thead>
<tr>
<th>Dose</th>
<th>Schedule</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 IU</td>
<td>Twice weekly x 5 weeks</td>
<td>&lt; 1 year</td>
</tr>
<tr>
<td>500 IU</td>
<td>Twice weekly x 5 weeks</td>
<td>1 – 5 years</td>
</tr>
<tr>
<td>1000 IU</td>
<td>Twice weekly x 5 weeks</td>
<td>&gt; 5 years</td>
</tr>
</tbody>
</table>

Gangopadhyay AN, et al: hCG therapy in undescended testis
undescended testis and 66 (26%) of them had bilateral nonpalpable testes. Cendron et al observed 15.5% cases of bilateral undescended testes and 27.6% of nonpalpable gonad. This discrepancy would be explained by the fact that majority of unilateral palpable undescended testis are managed at the primary and secondary level hospitals.

Hormonal treatment has been widely used in the treatment of cryptorchidism.[7]-[9] Preoperative use of HCG has been shown to be efficacious in causing nonpalpable testis to become palpable.[10] The HCG test will permit the determination of the presence or absence of testosterone production, and in some cases it results in testicular descent. In cases of failure that require surgery, the HCG will stimulate tissue growth enhancing the success of orchidopexy. That HCG is useful in testicular descent is also verified by another study carried out by Zucchini and Cacciari.[11] The rationale for giving HCG is that it stimulates Leydig cells that results in an increase in plasma testosterone, which promote testicular descent. A number of studies have been done in which HCG has been given.[11],[12] The HCG has also been found to improve surgical outcome when given preoperatively.[5] Increase in testicular size and vascularity as observed by us after HCG therapy has also been reported earlier.[5]

On the contrary, others have found the testicular size to be statistically significantly smaller in patients receiving preoperative HCG therapy than those treated by surgery only (9 ± 5 vs 12 ± 6 ml, P < 0.05).[13] Thus, postoperative use of HCG may prove beneficial because the increase in vascularity caused by HCG therapy is not subjected to surgical trauma.

Fertility has been reported to be better among patients who have responded to HCG therapy alone than among those who subsequently required orchidopexy.[14] Postoperative use of HCG might also improve fertility as and when given after the surgical trauma is over and its effects may last longer.

In our study, all the testes treated by postoperative HCG remained in their scrotal sacs without any retraction, 6 weeks after treatment. Hadiselimovic suggested that HCG stimulates testicular secretion, increases the size and vascularity of scrotum, testes, and vas deference, enlarges the inguinal canal, and causes differentiation of the epididymis.[15]

We have assessed the serum testosterone level 6 weeks after HCG therapy as the effect of HCG stimulation has been shown to remain up to a 4-6-week period.[16] In conclusion, our hypothesis for superiority of postsurgical hormone therapy over conventional presurgical hormone therapy is based on the following presumptions.

- The effect of presurgical hormone therapy is completely neutralized by the surgical insult of mobilization of testes and its pedicle, thereby causing further ischemic insult to the testes while doing orchidopexy.
- On the contrary, post surgical hormonal therapy counteracts this ischemic insult of surgery by increasing vascularity through hormonal mediation, and thereby tides over this crises period. Hence we recommend that postoperative hormonal therapy is a better option than preoperative therapy in such cases for better results.

REFERENCES


JIAPS on Web

http://www.journalonweb.com/jiaps

JIAPS now accepts articles electronically.
It is easy, convenient and fast. Check following steps:

1. **Registration**
   - Register from [http://www.journalonweb.com/jiaps](http://www.journalonweb.com/jiaps) as a new author
   - Two-step self-explanatory process

2. **New article submission**
   - Prepare your files (Article file, First page file and Images, if any)
   - Login into your area
   - Click on ‘Online Submission’ under ‘New Article’
   - Follow the steps (three steps for article without images and five for with images)
   - On successful submission you will receive an acknowledgement quoting the manuscript numbers

3. **Tracking the progress**
   - Click on ‘In Review Process’ under ‘Submitted Articles’
   - The table gives status of the article and its due date to move to next phase
   - More details can be obtained by clicking on the ManuscriptID
   - Comments sent by the editor and referee will be available from these pages

4. **Submitting a revised article**
   - Click on ‘In Review Process’ under ‘Submitted Articles’
   - Click on ‘Modify/Add Files’
   - Submit revised copy of your article in area ‘New Article File’
   - Click on ‘Revision Done’
   - You can also modify Article Title, Article Type and Images from this area

**Facilities**
- Submission of new articles with images
- Submission of revised articles
- Checking of proofs
- Track the progress of article in review process

**Advantages**
- Any-time, any-where access
- Faster review
- Cost saving on postage
- No need for hard-copy submission (except on acceptance images should be sent)
- Ability to track the progress
- Ease of contacting the journal

**Requirements for usage**
- Computer and internet connection
- Web-browser (preferably newer versions - IE 5.0 or NS 4.7 and above)
- Cookies and javascript to be enabled in web-browser

**Online submission checklist**
- **First Page File** (text/rtf/doc/pdf file) with title page, covering letter, acknowledgement, etc.
- **Article File** (text/rtf/doc/pdf file) with text of the article, beginning from Abstract till References (including tables). Limit the file size to 400 kb
- **Images** (jpeg, tiff, gif, bmp, png, eps, etc.): Submit good quality colour images. Each image should be less than 100 kb in size