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Hormone therapy in hypospadias surgery: a survey on the current practice in Turkey

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Background/aim: Nowadays surgical intervention is possible in smaller phalluses and younger children with hypospadias disease. Different hormone treatments with different doses, modalities, indications, and treatment times come along with some disputes. The aim of this study is to evaluate the management approaches in hypospadias surgery of surgeons in regards to hormone preparations.

Materials and methods: Questionnaires were sent via e-mail to 110 actively working pediatric surgeons and urologists. The answers of 99 surgeons were evaluated (90%). Two surgeons declared that they did not perform hypospadias surgery.

Results: When testosterone usage in penile surgery was questioned, 44.4% of participants (n = 44) answered positively. Small-short penis glans, narrow urethral plate, chordee, disorders of sexual development, buccal mucosa-graft operations, slight tissue, and defective ventral skin were the indications for usage. Forty of forty-four surgeons stated usage in proximal hypospadias, 18 of them in penile hypospadias, and 15 of them in distal hypospadias. The most common form was dihydrotestosterone (62%). According to the respondents, fistulas (83%), infections (78%), and wound dehiscence (77%) were reduced. Fifty-six percent of the surgeons stated that bleeding was increased and 39% stated easier dissection.

Conclusion: As a result of this questionnaire we can understand that there is no standard usage of testosterone in Turkey. Optimal points of usage can be introduced by increasing prospective randomized trials and education programs can ensure similar effective usage.

Key words: Dihydrotestosterone, hormone, hypospadias, testosterone

1. Introduction

Hypospadias is a congenital penile abnormality that is defined as an abnormal proximal location of the urethral meatus on the ventral penis and often includes ventral foreskin deficiency and ventral penile curvature (1,2). Hormone therapy preceding surgical correction is indicated to obtain better surgical conditions. However, there is divergence in the literature regarding the hormone therapy of choice, time of its use before surgery, appropriate dose, and route of application.

In recent years androgen stimulation with testosterone (T) and dihydrotestosterone (DHT) have been proven to have significant effects on favoring better local skin conditions; promoting phallic growth, making surgical correction easier; and resulting in fewer complications and temporarily increasing penile length and glans circumference (3–5), whereas there is controversy with conflicting studies demonstrating negative effects of androgens in hypospadias surgery (6–8). Furthermore, there is considerable variability in clinical practice of the hormone therapy of choice, topical or parenteral usage, time of use, and dose of therapy. We surveyed pediatric surgeons and urologists to determine the current practices for androgen therapy of hypospadias surgery in Turkey.

2. Materials and methods

A multiple-choice questionnaire was emailed to practitioners, inviting them to participate in a survey regarding the use of preoperative androgens, indications for treatment, dosing, administration schedule, and complications. No reminders were sent and a 2-week period was given prior to the closing of the study and beginning of data analysis. Ethical approval was not required for this study.

3. Results

Ninety-nine of 110 (90%) surgeons who received the e-mail invitation completed the survey; 70 were pediatric surgeons and 29 were urologists. The majority of responses came within the first week. Length of time in practice

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with hypospadias surgery varied from 5 to 20 years for the majority of 97 of 99 respondents. Two surgeons declared that they did not perform hypospadias surgery. Of all respondents, 44 (44.4%) used T in daily practice (hypospadias, infertility, etc.). Of the 53 prescribers not using T, 4 cited ineffectiveness, difficulties in obtaining drugs, and high rates of complication previously and abandoned T therapy; 4 stated that such therapy was given by a pediatric endocrinologist and the others reported no previous experience or no need for hormone therapy.

Small or short appearing penis, reduced glans circumference, reduced urethral plate width, chordee, ambiguous genitalia, and grafting of buccal mucosa were the main indications for hormone therapy in hypospadias surgery.

Forty (90.9%) of 44 responders preferred using T in proximal hypospadias, whereas 15 of them used it in distal hypospadias surgery. Of the respondents, 31.9% (31/97) used DHT in practice. Nineteen percent of providers used parenteral T whereas sixty-four of them preferred topical and seventeen used both of them. The administration schedule for testosterone was less than 3 weeks in 11 responders, 4 to 6 weeks in 14, and more than 6 weeks in 17 prior to surgery.

Penile appearance, penile length, glans circumference, increased urethral plate width, and reduced rigidity of buccal mucosa grafts were the effects of T that were mentioned by the responders in the multiple-choice questionnaire. Additionally, practitioners reported that enough growth of the penis, increased glans circumference, increased penile length, end of the predetermined regimen, reduced rigidity in buccal mucosa, and adverse effects (priapism, hirsutism, etc.) were the indications that physicians should stop giving androgens. Demographic data of respondents and T usage parameters are listed in Table 1.

The number of physicians reporting T use by the age of <3 years was 22, at 3 to 5 years was 24, at 6 to 10 years was 14, and at 11 to 17 years was 5. Urethrocutaneous fistula, infection, and wound dehiscence were the long-term complications reported by physicians. Peroperative and postoperative complications were bleeding, edema, ease of dissection, use of tourniquet, use of cauterization, and wound healing. Details of complications are listed in Table 2. Almost all of the physicians in hypospadias surgery did not replace the suture type or suturing technique after T therapy; however, 2 responders replaced the operation technique after hormone therapy.

4. Discussion

Our survey highlights the diversity in types of hormone therapy and especially T, application time, type of application, giving up therapy, age range for therapy, peroperative results, and surgical parameters. Our study demonstrates that hormone therapy in hypospadias surgery reveals a variation among pediatric surgeons and urologists; however, surgeons' experience and habits revealed a weighted spread.

A 97% response rate was obtained from 99 surgeons who had hypospadias surgery in practice, and 44.4% of them reported hormone therapy in hypospadias surgery. In a recent survey by Springer et al., 10.9% of the 377 participants used preoperative androgen regularly (4). In another study, Malik et al. reported a higher T use (78%) among pediatric urologists (9).

Similar to previous reports (10–12), in our study, we have found that T use was common in 40 (90.9%) of 44 applicants when proximal hypospadias was present. However, Ratan et al. reported that not only one anatomical factor, such as meatal location or the severity of chordee, should be considered alone with respect to the hormonal profile of isolated hypospadias. Multiple anatomical factors may improve hormonal supplementation for long-term surgical outcomes (13).

Preoperative androgen stimulation has been reported to increase glans circumference and penile length, and/or improve preputial vascularization before hypospadias surgery.

On the other hand, there are not enough data in the literature about dosing recommendations with various regimens of intramuscular or topical androgens before repair. As there is no established protocol for such evaluations, Snodgrass et al. reported that 63% of patients received preoperative T stimulation based on glans width of <14 mm, which is less than the average normal newborn glans diameter, without previous endocrine testing (14).

Multiple studies with different types of T therapy and with different doses and times of application were reported. Those studies showed an advantage with a statistically significant increase in penile length and glans circumference, as well as induction of neovascularization (3,12,15,16).

In a recent international survey associated with pediatric surgery, pediatric urology, urology, and plastic surgery, it was documented that 108 participants (39.4%) used topical DHT, 120 (43.8%) used intramuscular T, 43 (15.7%) used T cream, and 3 (1.1%) used β-human chorionic gonadotropin (β-hCG) in practice. In the literature different hormones were reported by different authors, such as testosterone enanthate, propionate, DHT cream, and β-hCG (3,9,14,16). In our study, DHT (56.8%), testosterone enanthate (7.8%), β-hCG (15.6%), and testosterone cypionate (5.8%) were the main types of hormones used by physicians.

Two reports compared the use of parenteral and topical T and examined significant penile growth with

Table 1. Demographic data of respondents and testosterone use.

Length of time in practice with hypospadias surgery	n (%)
<5 years	26 (26.2%)
6–10 years	27 (26.2%)
11–15 years	17 (26.2%)
>16 years	27 (26.2%)
Testosterone use in daily practice	n (%)
Yes	44 (44.4%)
No	53 (53.5%)
Indications for testosterone use (multiple answers)	
Small or short appearing penis	36
Reduced glans circumference	21
Reduced urethral plate width	5
Chordee	2
Ambiguous genitalia	18
Prior or after grafting of buccal mucosa	8
Other (thin epidermis)	3
Forms of testosterone (multiple answers)	
Testosterone cypionate	3 (5.8%)
Testosterone enanthate	4 (7.8%)
Dihydrotestosterone	29 (56.8%)
β-hCG	8 (15.6%)
Others	7 (13.7%)
Time for testosterone use prior to surgery	
<3 weeks	11
4 to 6 weeks	14
6 weeks	17
Determination of testosterone effect	
Penile appearance	30
Penile length	13
Glans circumference	28
Increased urethral plate width	11
Reduced rigidity in buccal mucosa graft	6
Indications to stop giving testosterone	
Enough growth of penis	19
Increased glans circumference	13
Increased penile length	7
End of the predetermined regimen	21
Reduced rigidity in buccal mucosa	4
Adverse effects (priapism, hirsutism, etc.)	11

no difference between the two types of administration (17,18). Some studies compared both parenteral and topical T use and found that topical use of T has more side effects of pigmentation of the genitals, appearance of pubic hair, and skin irritation at the site of application (16–18). Similarly, Monfort et al. found that adverse effects were also observed when DHT was used topically, suggesting that intramuscular hormone therapy is preferable to topical therapy (19). Contrarily, in our study we found that the physicians mainly chose topical administration as it is easy to apply and to avoid the systemic effects of parenteral use.

There is no general agreement about the time of application and giving up therapy. In a recent review, intramuscular treatment was reported to be proposed to last 3 months, consisting of a monthly application of T,

Table 2. Complications after testosterone therapy.

Complications (long-term)	
Urethrocutaneous fistula	
Increased	2
Decreased	15
No difference	1
Infection	
Increased	1
Decreased	7
No difference	1
Wound dehiscence	
Increased	2
Decreased	10
No difference	1
Peroperative and postoperative complications	
Bleeding	
Increased	23
Decreased	0
No difference	18
Edema	
Increased	11
Decreased	0
No difference	29
Ease of dissection	
Increased	16
Decreased	5
No difference	20
Use of tourniquet	
Increased	4
Decreased	0
No difference	36
Use of cauterization	
Increased	11
Decreased	0
No difference	28
Wound healing	
Increased	6
Decreased	4
No difference	31

while topical treatment should last on average 3 to 4 weeks, with 2 daily applications (3). In our survey, 50% of the participants answered that the average time of application was 3–4 weeks. On the other hand, the cessation of therapies prior to surgery was reported by 36% within 2 weeks and by 31% within 3 to 4 weeks. Similarly, in a previous report, topical T use was ceased in all patients 1 week prior to surgery, whereas in another study doses of intramuscular T were skipped if penile length and glans circumference had noticeably increased with the first does or first two doses (12,15). Mostly studies failed to report a time of cessation. In another report, monthly intramuscular injections were stopped when penile length was at or above 35 mm (20). In a recent study by Malik et al., the timing of cessation of preoperative T was reported as a risk factor for surgical complications and the predetermined regimen was the major factor for the cessation of therapy (9).

There are not enough data in the literature evaluating the intra- and postoperative effects of hormone therapy. There are some studies reporting that absence of intraoperative complications mainly referred to an absence of important bleeding during surgical time (12,17). Our results show that 56% of physicians experience an increase in bleeding, whereas 44% of them reported no difference. Mostly edema, ease of dissection, use of tourniquet, use of cauterization, and wound healing were reported with no differences. According to responders, long-term complications of urethrocutaneous fistula, infection, and wound dehiscence were reported to decrease in our study. On the other hand, two studies with long-term surgical outcomes reported fewer fistulas and a change in the type of surgery required, avoiding the use of pedicle flaps and tube repairs in 25% of the boys, with a significant reduction in glanular dehiscence and meatal stenosis and a decreased need for reoperation (16,21). However, in our study, none of the physicians reported a change in surgical technique related to the surgical technique for hypospadias repair chosen after the child is under anesthesia and can be evaluated better.

In this survey, we highlighted current national trends in current practice of T therapy. There is no consensus on standardization of T therapy in Turkey, like all over the world. Future prospective studies focusing on standardized dosing and administration of T regimens are needed to compare results. Although many hypospadias surgery techniques are identified and reported to be effective, hormone therapy will be beneficial in some cases of hypospadias surgery as a supportive treatment.

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