



SUCCESS RATE OF UNDESCENDED TESTICLE TREATMENT WITH HUMAN CHORIONIC GONADOTROPIN

USPEŠNOST LEČENJA NESPUŠTENIH TESTISA HUMANIM HORIONSKIM GONADOTROPINOM

Ognjen Ležakov¹, Ivana Vorgučin^{1,2}

¹ Medicinski fakultet, Univerzitet u Novom Sadu, Novi Sad, Srbija

² Institut za zdravstvenu zaštitu dece i omladine Vojvodine, Novi Sad, Srbija

Correspondence: olezakov@gmail.com

Abstract

Introduction: Cryptorchidism is a disorder of the testicles, when during a physical exam, testicles, one or both of them, are not found in the scrotum, but are found either along the inguinal canal or in the abdomen. Two main modalities of treatment are hormonal and surgical treatment.

Aim: The aim of this paper was to determine the success rate of hormonal therapy with human chorionic gonadotropin (hCG) in undescended testicle treatment in patients treated at the Institute for Child and Youth Health Care in Vojvodina, from January 1, 2010, to December 31, 2017.

Material and methods: This research included the patients from the Institute for Child and Youth Health Care in Vojvodina ages 0-18, treated from January 1, 2010, to December 31, 2017. Medical documentation has been analyzed and interpreted using methods of descriptive statistic. The research included boys with undescended testicles, to whom the hormonal therapy was indicated. Patients were divided into 3 groups (<2 years, 2-6 years, >6 years). The therapy was applied twice a week, in the course of 5 weeks (hCG 250-1000 IJ/dose). The position 12 months after therapy was used as a final position.

Results: The hormonal descend was achieved in 63 patients (62.4%) of the total number of patients. The highest success rate was achieved in oldest of our patients (80%).

Conclusion: Hormonal therapy with hCG leads to descent in a high percentage, with very little transitory adverse effects, and it is an important modality in undescended testicles treatment.

Keywords:

hormonal therapy,
human chorionic
gonadotropin,
cryptorchidism,
genital anomalies



Sažetak

Uvod: Kriptorhizam je razvojni poremećaj testisa kod kojeg se testisi, jedan ili oba, prilikom fizikalnog pregleda ne nalaze u skrotumu, odnosno kada se testisi nalaze duž ingvinalnog kanala ili u abdomenu. Dva osnovna modaliteta lečenja ovog poremećaja su hormonsko i hirurško.

Cilj: Cilj rada je bila analiza uspešnosti hormonske terapije humanim horionskim gonadotropinom (hCG) u lečenju nespuštenih testisa kod pacijenata lečenih na Institutu za zdravstvenu zaštitu dece i omladine Vojvodine u periodu 1.1.2010-31.12.2017. godine.

Materijal i metode: Istraživanjem su obuhvaćeni pacijenti Instituta za zdravstvenu zaštitu dece i omladine Vojvodine uzrasta 0-18 godina, lečeni u periodu od 1.1.2010. do 31.12.2017. Analizirana je medicinska dokumentacija 101 deteta, uz korišćenje metoda deskriptivne statistike. Istraživanje je obuhvatilo dečake sa nespuštenim testisima sa indikovanim hormonskom terapijom, koji su podeljeni u tri uzrasne grupe (mlađi od 2 godine, od 2 do 6 godina, stariji od 6 godina). Terapija hCG je primenjivana dva puta nedeljno tokom 5 nedelja (250 IJ/po dozi za mlađe od 2 godine, 500 IJ/po dozi za grupu od 2 do 6 godina i 1000 IJ/po dozi za uzrast starijih od 6 godina). Pozicija testisa nakon dvanaest meseci od primenjene terapije uzimana je kao finalna pozicija.

Rezultati: Od ukupnog broja pacijenata, hormonski descenzus postignut je kod 63 pacijenta (62,4%). Najveća uspešnost bila je u grupi najstarijih pacijenata (80%).

Zaključak: Hormonska terapija hCG dovodi do testikularnog descenzusa u visokom procentu sa vrlo malo tranzitornih nuspojava i značajan je terapijski modalitet u lečenju nespuštenih testisa.

Ključne reči:

hormonska terapija,
humani horionski gonadotropin,
kriptorhizam,
anomalije genitalija

Introduction

Cryptorchidism is a disorder of the testicles, when during a physical exam, testicles, one or both of them, are not found in the scrotum, but are found either along the inguinal canal or in the abdomen. The undescended testicle is one of the most common genital anomalies. Its incidence in preterm children is 30% and in term children it varies from 1.8% to 4% (1). Hormones, such as androgens and insulin like growth factor, affect both transabdominal and in inguinal phase of the testicle's descending (2). Some of the causes include: hormonal disorders, congenital testicle disorders and anatomical barriers that don't allow the testis to descend. It can, also, be iatrogenic after the surgical treatment of hernia (1). The risk factors include prematurity, low birth weight, alcohol and/or nicotine abuse during pregnancy, as well as pesticide exposure, when it has the effect of endocrine disruptors. Cryptorchidism is a part of different syndromes such as: Noonan syndrome, Prader Willi, Dubowitz, CHARGE, Prune belly syndrome, etc. Whether it affects both testicles or just one, undescended testicle can be unilateral (in about 90% of the cases) and bilateral (10% of the cases) (3).

After the physical exam and certain imaging diagnostic methods, a diagnosis can be made. It is important to examine both testicles in a unilateral cryptorchidism, to determine whether there is a compensating hypertrophy of the descended testicle, which can mean that the undescended testicle is atrophic or hypotrophic. If the patient has a bilateral cryptorchidism, karyotype analysis should be done, to exclude pseudohermaphroditism. Imaging methods that can be used in this case are ultrasonography and nuclear magnetic resonance (NMR). Since testicles can be

mistaken for a lymph node during ultrasonography, NMR is usually more conclusive (4).

Undescended testicles require treatment because of the increased risk of malignant tumors of the testes and infertility (5). The testicle that stays outside of the scrotum has an increased risk of tubular degeneration which causes fertility issues. Also, the undescended testicle is often smaller in volume (hypotrophic) than the descended one. Two main modalities of treatment are hormonal and surgical treatment. Hormonal treatment can include either human chorionic gonadotropin (hCG), gonadotropin releasing hormone (GnRH), or both. Human chorionic gonadotropin has a similar effect as the luteinizing hormone (LH). It stimulates testicular steroidogenesis, increases the vascularisation and volume and descends the testicle (5). The main advantage that hormonal treatment has over surgery is avoiding the risks of the anaesthesia and surgical procedure (6).

The aim of this paper was to determine the success rate of hormonal therapy with human chorionic gonadotropin (hCG) in undescended testicle treatment in patients treated at the tertiary level in 8 years.

Material and methods

This research included the patients from the Institute for Child and Youth Health Care in Vojvodina ages 0-18, treated from January 1, 2010, to December 31, 2017. Medical documentation has been retrospectively analyzed and interpreted using methods of descriptive statistics. The research included boys with undescended testicles, to whom the hormonal therapy was indicated. The indication was a supra-scrotal testicular position, in

attempt to achieve hormonal descent. Physical exam was preformed in a warm room, with the warm hands of the examiner. In a standing or a sitting position, inguinal palpation was done. Patients were divided into 3 groups (<2 years, 2-6 years, >6 years). The youngest patient was 14 months old and the oldest was 13 4/12 years old. Intramuscular injections of hCG were applied twice a week, in the course of 5 weeks. The doses were: 250 IJ/dose for the children younger than 2, 500 IJ/dose for the children between 2 and 6, and 1000 IJ/dose for the oldest group (older than 6). Volume and position were examined 1, 6 and 12 months after therapy using Prader's orchidometer. The position 12 months after therapy was used as a final position.

Results

The total number of patients in the eight years period was 101. A number of 17 patients were younger than 2, 24 aged between 2 and 6 and 60 were older than 6. There were 56 patients out of total number of patients who had unilateral cryptorchidism (9 patients younger than 2, 13 patients between 2 and 6 and 34 older than 6). The number of patients had bilateral cryptorchidism was 45 (8 patients younger than 2, 11 patients between 2 and 6 and 26 older than 6) (**Table 1**).

Out of total number of patients, the hormonal descent was achieved in 63 patients (62.4%). In patients with unilateral cryptorchidism (56 boys), the success rate was 67.9% and in patients with bilateral cryptorchidism (45 boys) it was 55.6%. In patients younger than 2, the descent was achieved in 17.6%. Patients between 2 and 6 had the success rate of 50%, and in patients older than 6 it was 80%, as shown in **Table 2**. During the administration, side effects were monitored. Occasional erections, penile and scrotal enlargements were noticed in all patients, and all of them were transitory. Testicular hypotrophy wasn't noticed in any of the patients.

Table 1. The age of patients with undescended testicles

| Patients' age | Unilateral cryptorchidism | Bilateral cryptorchidism | Total |
|-----------------|---------------------------|--------------------------|------------|
| <2 years | 9 | 8 | 17 (16.8%) |
| od 2 do 6 years | 13 | 11 | 24 (23.8%) |
| >6 years | 34 | 26 | 60 (59.4%) |
| Total | 56 (55.4%) | 45 (44.6%) | 101 (100%) |

Table 2. The success of hormonal descent

| Patient's age | All patients | | | Unilateral cryptorchidism | | | Bilateral cryptorchidism | | |
|---------------|--------------|----|------|---------------------------|----|------|--------------------------|----|------|
| | n | R | R% | n | R | R% | n | R | R% |
| <2 years | 17 | 3 | 17.6 | 9 | 0 | 0 | 8 | 3 | 37.5 |
| 2-6 years | 24 | 12 | 50 | 13 | 8 | 61.5 | 11 | 4 | 36.4 |
| >6 years | 60 | 48 | 80 | 34 | 30 | 88.2 | 26 | 18 | 69.2 |

n - number of patients treated with hormonal therapy; R - patients that achieved descent; R% - percent of the patients who achieved descent

Discussion

Cryptorchidism, or the undescended testicle is one of the most common genital disorders. Some of more serious consequences are infertility and increased risk of seminoma in situ. Regardless of the therapeutic choice, the main goal is to achieve descent in scrotum (1). Two main modalities are surgical and hormonal treatment. The answer to which therapy the advantage should be given is controversial and the topic of many papers. The consensus of Nordic countries states that the surgical therapy has an advantage over hormonal therapy. Its success rate is 95% and should be done in children between 6 and 12 months of age. Their opinion is that the hCG treatment damages the spermatogenesis, because of increased germinative cell apoptosis (7). Other researchers also agree that the surgical treatment is preferred, pointing out the side effects of the hormonal therapy on a cellular level (8), the risk that the prolongation of the surgical treatment carries and the hormonal treatment's price (9). One of the complications of the surgical treatment is testicular atrophy. It happens when the testicular blood vessels are damaged, which leads to testicular ischemia (4).

In hormonal treatment, hCG and GnRH are used. These hormones stimulate Leydig cells in producing testosterone, which stimulates the process of "mini puberty" that leads to descent and spermatogonia production stimulation (10). Hormonal treatment can, also, be used as neoadjuvant treatment, because it is shown that it increases vascularisation, improves fertility index and the histological quality of testicles (11). Described side effects are: decrease in testicular volume, increased transitory intratesticular pressure and a potential negative influence on spermatogenesis (7).

After the applying of human chorionic gonadotropin in our patients, the descent was achieved in a

significant percent - 62.4%. The efficiency was highest amongst the oldest group, in boys older than 6 (80%), in both unilateral and bilateral cryptorchidism. Lower, but still significant percent was achieved in younger age groups (17.6% and 50%). Different authors suggest that the success rate is between 20 and 25%; others say it reaches 81.8% (1). Also, it is noticed that, like in our case, the highest descent success rate was achieved in older boys (12). In a Turkish study, 123 patients with retractile testicles were given hormonal hCG therapy. The success of hormone therapy was higher than 80% in both unilateral and bilateral retractile testicles. In this study, the highest number of patients (109, which is 88.6% out of total number) and the highest success rate (88.5%) was achieved in patient ages 2 – 6. In our case, the success in this group is lower (50%), which may be due to small number of patients in this age group (24, which is 23.8% of total number). Both our (17.6%) and Turkish study (33.3%) have shown the lowest success rate in youngest groups. Also, both studies found similar results, regarding side effects of the hormonal therapy (transitory penile and scrotal growth, and occasional erections in all patients) (13).

Currently, there are not enough studies that would speak in favour of hormonal therapy (not enough patients included, inadequate or non-existent control groups). This is one of the reasons why deciding on a modality of treatment is still controversial, since there is a need for further researching, and a need for a unique treatment guide.

In our case, none of the patients had reduced testicular volume one year after the therapy, and other side effects, such as penile and scrotal enlargement, occasional erections, pubic and scrotal hairiness - all were transitory.

The effects of the therapy and potential side effects will be regularly observed by both urologist and paediatric endocrinologist. When patients turn 18, they will be forwarded to an adult endocrinologist and an adult urologist in order for fertility to be evaluated and side effects to be monitored.

Hormonal treatment may be considered as an important modality in undescended testicle treatment, as the first line therapy and as preparation for an easier orchidopexy, because of high success rate in our case, and in other cases as well, with very little transitory side effects.

Conclusion

Hormonal descent was achieved in a high percent, in 62.4% cases. The highest efficiency was accomplished in patients older than 6 (80%) in both unilateral (88.2%) and bilateral (69.2%) undescended testicles. Lower, but still significant success rate was achieved in younger age groups (17.6% and 50%). Hormonal treatment leads to the testicular descent in a high percentage of cases, with very little transitory side effects, and it could be considered as an important modality of undescended testicles treatment.

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