

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA
DOCTORAL SCHOOL

PHD THESIS
UNDESCENDED TESTICLE IN CHILD
CLINICAL AND THERAPEUTIC ASPECTS

- Abstract -

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Introduction

The demographic decline of the European population, which is foreseen in almost all existing forecasts, is more strongly expressed for our country than for the most countries on the continent. Thus, for over 20 years, Romania's population is continuously decreasing and the cease of this situation is still quite a distant goal.

A couple is considered infertile if after unprotected sex for a year, she is unable to become pregnant. Worldwide it is estimated that a woman is responsible for about 35% of all cases, a man of about 35%, and both partners in approximately 20%. In 10% of cases of infertility of couples, the cause is unknown.

Testicular migration disorders are the leading cause of male infertility and their correct and timely resolution lead to a future increase in the chances of procreation in adult life.

The undescended testis is a vast chapter of pediatric urology and carries more clinical aspects:

- Testicular criptorchidy
- Testicular ectopy
- Oscilant testicle
- Anorchidy

The theme of testicular migration disorders is still an issue of great interest and concern in the medical world because, in terms of taking charge of these patients concur many different medical specialties such as family medicine, pediatrics, pediatric surgery, endocrinology, pathology, clinical laboratory, medical genetics, psychiatry, etc. Considering these aspects, the therapeutic approach of this malformation varied greatly from one era to another, trying to respond as closely as possible to the following questions:

- What would be the optimal age at surgery to carry out the testicular descent?
- What is the role and the place of the endocrine treatment
- What would be the optimal surgical procedure to perform the orchidopexy?

Testiculul necoborât la copil - Aspecte clinico-terapeutice

- In the case of the unilateral testicular migration disorders are the pathological and morphological lesions also occurring in the contralateral testicle?
- - What is the therapeutic approach to the impalpable testis? Are we dealing with a real anorchidism or is it an ectopic intraabdominal testis?
- - What is the therapeutic approach regarding the dysplastic testicle? Orchidopexy - hoping at least to maintain the endocrine function or orchiectomy to prevent malignant degeneration?
- - In the case of orchiectomy at an early age what would be the benefit of a testicular prosthesis fitted to prevent atrophy of the scrotum?
- - Testicular migration disorders are single pathological manifestations or are they often associated with other birth defects?
- What would be the most effective methods of clinical and laboratory exploration to quantify fertility after orchidopexy?
- - What are the complications that can occur in the case of testicular migration disorders and how frequently they occur so as to require surgery as early as possible after diagnosis?
- What would be the psychological consequences of the future adult who presented this disease in childhood?

Knowledge stage

Known since the ancient times, the testicular migration disorders were first described in 1786 by Hunter and the orchidopexy was first tested in 1820 by Rosenmerkal. However, only in 1877, Annandale performed the first successful orchidopexy.

Gonadal differentiation – starts at week 6, and ends at the 12-th week. It involves triggering a cascade of complex mechanisms which are the expression of multiple genes in a timeline and a well-defined concentration.

Gonadal differentiation mechanism could be understood better after 1990 when it was discovered the SRY gene - encoding a transcription factor that plays the role of Testis Determining Factor.

The testicular descent takes place in two stages:

- Transabdominal phase (8-15 weeks) is controlled by the expansion of the genito-inguinal ligament caudal portion (gubernaculum) and cranial portion regression. Insulin like three factor secreted by Leydig cells appears to be a first growth stimulator gubernacular growth seconded by the anti-Mullerian hormone. Testosterone is what determines regression of the cranial portion of the genito-inguinal ligament.

- Inghino-scrotal phase (25-35 weeks) primarily involves migration of the gubernaculum from groin into the scrotum; this migration is guided by the genito-femoral nerve by releasing calcitonin gene-related peptide under the influence of androgens.

Congenital cryptorchidism is caused by failure to migrate into the scrotum (1% - 2%), but has been shown that there is another 1% -2% of boys showing failure secondary cryptorchidism spermatic cord lengthening with increasing.

From the point of view of certainty of diagnosis, testicle migration disorders are evident in most cases since the inspection patient when the doctor examining the patient may notice a scrotal asymmetry.

The undescended testes preoperative localization is particularly useful for the efficient management of migration disorders of the testicles from the point of view of the proper choice of surgical approach and in terms of subsequent fertility prognosis.

Both clinical examination and ultrasound are non-invasive, widely available and no side effects and were considered very useful where material resources are poor and where laparoscopy is not available. However, some authors are skeptical about their accuracy in locating the undescended testicles especially for the intra-abdominal ones.

Currently, the Department of Health and Human Services of the US states that its guidelines regarding migration disorders testicle ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) does not provide information in addition to physical examination.

Given that conventional imaging explorations either have a low reliability, too high costs and are more difficult to perform (require sedation and anesthesia often) and hormonal dosages can not specify the exact location of the testicle, exploratory laparoscopy has increasingly imposed in the recent years, both for diagnostic and therapeutic purposes.

Testiculul necoborât la copil - Aspecte clinico-terapeutice

The ultimate goal of treatment of testicular disorders migration is to bring down and fix in the scrotal pouch the undescended testis either on the normal route of descent or outside of it in order to obtain a normal fertility or at least an improved one.

Personal contributions

Purpose, objectives and research premises

The study undertaken started from the observation that the issue of migration disorders of testis is a topic of great interest at present not only in the context of a low birth rate, but also of a very high infant mortality phenomena that seem to lead to a substantial reduction the population of our country in the coming years.

This study is a continuation of the some older concerns of the Pediatric Surgery Department of the Emergency County Hospital of Craiova communicated and translated into numerous papers published in journals and specialized treaties.

This dissertation proposes a study by retrospective analysis of the testicular migration disorders found in children, whilst also bringing some new elements regarding the treatment of this genitourinary malformations and also some experimental study regarding the testicular sufferance in ischemia conditions.

Research Methodology

This paper evaluates the experience gained over a period of 20 years (1994-2013) in treating the migration disorders of the testis, during which it was recorded in the Pediatric Surgery Department of the Emergency County Hospital of Craiova a number of 1536 cases.

The study material was extracted from case report forms and their operator's protocols of the Pediatric Surgery department of the Emergency County Hospital of Craiova.

The study included only patients who have been diagnosed with testicular migration disorders at any age. The study included the patients with palpable testis in the groin as well as the ones with impalpable testicles.

There were excluded from the study the cases of acquired cryptorchidism - usually of iatrogenic origin. Also were excluded the cases of floating testis.

After the retrospective examination of the clinical sheets of the patients diagnosed, apart from the clinical status and treatment aspects with testicular migration disorders we have collected data on: the occupation of both parents, any pre-conception parental exposures to toxic substances; use of drugs by the mother during pregnancy.

I have extracted this data in order to detect a possible causal correlation between the exposure of the parents to certain teratogenic agents with potential adverse effects on human reproduction and migration disorders of the testicle.

Results

Epidemiological aspects

In terms of incidence per year in the studied group we have seen that there is a random distribution of the cases of testicular migration disorders, most cases being recorded in 1999 and 2013 (81 and 82 cases respectively) and the fewer of them were found in 2000 and 2001 (74 and 73 cases respectively).

Regarding issues related to the age of patients who were hospitalized in the Pediatric Surgery Department of the Emergency County Hospital of Craiova in the period 1994 to 2013 with the diagnosis of disorders of testis and migration the mean age of those patients was 5.9 years.

The average age at which it was practiced the orchidopexy dropped from a decade to another, although it is still above recommendations in the literature, but given medical addressing in our area and sometimes even socio-economic conditions of patients we believe that this represents progress in terms of preserving fertility for the operated patients.

Regarding the undescended testicle types of patients hospitalized in the Pediatric Surgery Department of the Emergency County Hospital of Craiova during 1994-2013 were mostly unilateral forms predominantly on the right side (611 cases - representing

39.78 % of all cases of abnormal migration of the testicle which constituted the study group). Another important clinical aspect which was of concern in the analysis of patients with disorders of the testicle migration was the association with other congenital malformations.

Within the group of 1536 patients with testicular migration disorders hospitalized in Pediatric Surgery Department of the Emergency County Hospital of Craiova during 1994-2013 have met a total of 515 cases of congenital malformations associated representing a percentage of 34.18% of undescended testis batch of patients whom I have studied.

Regarding the types of congenital malformations associated with the cases of testicular migration disorders most of them were uro-genital malformations, followed in order of frequency by the cardiovascular malformations and genetic syndromes.

Undescended testicle complications

Testicular torsion is one of the acute complications with severe consequences in particular by the fact that it may occur more frequently on a testicle undescended whose attachment means are insufficient. In an experimental study on porcine models we tried to determine the resistance to ischemia of the torsioned testicle according to the time elapsed and the degree of torsion, and the effects it has on the controlateral testicle.

The histopathological aspects drawn from this experiment tend to show that the time from onset torsion is an important factor in saving the twisted testicle necrosis, but also the torsion degree plays a key role, for irreversible pathological changes such as necrosis is installed at a greater speed as the degree of torsion is higher.

In the 1536 cases admitted in Pediatric Surgery Department of the Emergency County Hospital of Craiova in the period 1994 to 2013 we have recorded a total of 49 cases of testicular torsion on undescended testicle representing 3.19% of the total study group.

The analysis of the studied group according to parental occupations

An important role in the genesis of malformations and also of the testicular migration disorders plays the external teratogenic factors chemical, physical or biological found in both domestic environment and especially in the professional one where both partners of the couple enter into contact during pre- and post-conception period.

Regarding the parental occupation of the patients in our study a major impediment was the fact that complete data was not available in the observation charts of the patients. Thus from all cases of testicular migration disorders hospitalized in Pediatric Surgery Department of the Emergency County Hospital of Craiova in the period 1994-2013 that made up the group that I have studied I could collect comprehensive data on parental occupation in a total of 1233 cases.

The undescended testicle treatment

The undescended testicle is one of the most common abnormality identified at birth. The main reasons for the treatment of undescended testicle are the increased risk of infertility and the risk of testicular malignisation or twisting.

The medical treatment

With regard to the hormonal therapy in the 1536 patients hospitalized in the Pediatric Surgery Department of the Emergency County Hospital of Craiova during 1994-2013 with testicular migration disorders most of the patients 59.96% (925 cases) received only orchidopexy and only a percentage of 40.04 have received also hormonal therapy. In all the cases we have used hormone therapy we used human chorionic gonadotropin (HCG) at a dose of 500 microns per week for a month.

The surgical treatment

Surgery - is currently the best method to prevent relapses and to secure the testis into the scrotal pouch regarding the management of the testicular migration disorders of the child.

Age at which we have practiced the orchidopexy has dropped from a decade to another so that the average age of the patients who composed the group that I have studied was 5.9 years.

Not only the recommendations regarding the optimal age for practicing the orchidopexy have changed over the years, but also the types of surgical interventions that we have used.

A new element in the treatment of undescended testicle has emerged with the introduction of the minimally invasive surgery in the Pediatric Surgery Department of the Emergency County Hospital of Craiova in 2012 since when we have used the laparoscopic approach for the Fowler-Stephens procedure for the undescended testicles.

Within the group of 1,536 patients admitted Pediatric Surgery Department of the Emergency County Hospital of Craiova in the period 1994-2013 surgery Fowler-Stephens type was practiced in a number of 14 patients, all operated after May 2012 when laparoscopic surgery was introduced in the clinic.

Of the total laparoscopic interventions performed in this period 5 cases were operated in one-stage and the remaining 9 cases were operated in two stages at a mean of 7.2 months between the two interventions (the section of the testicular vessels and the orchidopexy).

Conclusions

- This paper evaluates the experience gained over a period of 20 years (1994-2013) in treating the migration disorders of the testis, during which it was recorded in the Pediatric Surgery Department of the Emergency County Hospital of Craiova a number of 1536 cases
- The incidence per year shows that there is a random distribution of the cases of testicular migration disorders along the studied period.
- The average age at which it was practiced orchidopexy dropped from a decade to another
- Regarding the undescended testicle types of the patients hospitalized in for testicular migration disorders they were mostly unilateral forms
- Within the group of 1536 patients hospitalized for testicle migration disorders we have encountered a number of 525 cases with associated congenital malformations
- Regarding the parental occupations that we have encountered in association with testicular migration disorders hospitalized in the Pediatric Surgery Department of the Emergency County Hospital of Craiova during 1994-2013 the majority of them belonged to the occupational group of agriculture
- With regard to the hormonal therapy use in the 1536 patients batch most of the patients 59.96% (925 cases) received only orchidopexy and only a percentage of 40.04% received also additional hormonal therapy.
- Comparing the two decades of the studied period (1994 - 2013) we have seen also a change of the surgical approach tactics for the testicular migration disorders in the Pediatric Surgery Department of the Emergency County Hospital of Craiova
- A new element in the treatment of undescended testicle that has emerged with the introduction of minimally invasive surgery in the Pediatric Surgery Department of the Emergency County Hospital of Craiova in 2012 since when we have used the laparoscopic approach for the Fowler-Stephens procedure for the impalpable undescended testicles.