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Overview of Epidemiology and Management of Undescended Testis (Cryptorchidism)

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Cryptorchidism (undescended testis, maldescendus testis) is a disorder in which one or together testes miscarry to slope into the bottommost of the scrotum. The study aimed to summarize the updated evidence regards, epidemiology, etiology, classification, diagnosis, and treatments of Cryptorchidism or undescended testis. Several causes can result in developing cryptorchidism. Disruption of any phase of testicular prolapse due to genetic hormonal, structural, ecological, or social issues can lead to cryptorchidism. The diagnosis of undescended testes is clinical. The test should be performed by an experienced person and should always be performed using a two-way technique. In some cases, imaging diagnostics for cryptorchidism may be helpful. The rationale for treating cryptorchidism is to reduce the risk of its long-term consequences. Current treatments for undescended testes include hormone therapy, orchopexy, and surgical correction.

Keywords: Cryptorchidism; undescended testis; maldescendus testis; orchiopexy; long term sequelae.

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1. INTRODUCTION

Cryptorchidism (*Maldescendus testis*) is a condition in which one or two testicles do not fall to the bottom of the scrotum [1]. Alternatively, the testicle is located somewhere on the normal path of testicular descent. It can be in the abdominal cavity, groin, scrotum, or upper part of the scrotum. Congenital cryptorchidism is one of the most common birth defects in children. In children with a birth weight of more than 2,500 grams, there is a prevalence at birth of 1.8% to 8.4% [2]. The prevalence of male babies at birth with premature delivery and / or low birth weight varies between 1.1 and 45.3%, at the age of 3 months and 1 year it is 0.9-1.6 and 1.0 -1, respectively 5%.

Cryptorchidism is associated with a future risk of poor semen quality and an increased incidence of testicular germ cell tumors (TGCT). The risk of TGCT is 2 to 5 times greater than that of the general population. Prompt treatment for cryptorchidism does not automatically reduce the risk of TGCT in later life [3].

Cryptorchidism can occur on one or both sides, but primarily affects the right testicle. The testicle is positioned somewhere on the "descent path", for example: at the level of the abdomen from the retroperitoneum to the inguinal ring; in the inguinal canal; ectopic downward trajectory; Dysplasia; genetic disorder; absent or absent; unilateral (three points out of two). Undescended testicles can usually be felt in the inguinal canal. In a small number of patients, the missing testicle may be located in the abdomen or it may be absent [4]

Cryptorchidism is associated with reduced levels of hormones in the testes. On the other hand, congenital hypogonadism can be one of the indicators of cryptorchidism [5]

Approximately 4% of term newborns have cryptorchidism with premature birth and / or low birth weight between 1.1 and 45.3%. In general, the prevalence rate is 4 to 5% at birth, 1% to 1.5% after three months, and 1% to 2.5% after nine months [6].

1.1 Objectives

The study aims to summarize the updated evidence regards, epidemiology, etiology, classification, diagnosis, and treatments of Cryptorchidism or undescended testis.

2. MATERIALS AND METHODS

2.1 Study Duration

Data was collected during the period from 1– 29 May, 2021.

2.2 Data Collection

PubMed and EBSCO Information Services was chosen as the search databases for the publications used within the study, as they are high-quality sources. Topics concerning the updated evidence regard, epidemiology, etiology, classification, diagnosis, and treatments of Cryptorchidism or undescended testis, published in English around the world. The keyword search headings included “Cryptorchidism, undescended testis, maldescendus testis, Orchiopexy, long term sequelae", and a combination of these was used. References tilt of all involved study was searched for additional helpful data. Double revision of each member’s outcomes was applied to ensure the validity.

2.3 Statistical Analysis

No need for software to analyze the files. The data was extracted based on the study objective. These data was reviewed by the group members to determine the initial findings. Dual review of every member’s products will be functional to guarantee the rationality and abate the errors.

2.3.1 Epidemiology of undescended testis

About 4% of newborns have cryptorchidism, with premature delivery and / or low birth weight varies between 1.1 and 45.3%. Internationally, the prevalence ranges from 4% to 5% at birth, around 1% to 1.5% at three months of age, and 1% to 2.5% at nine months of age [6].

2.3.2 Etiology of undescended testis

A normal hypothalamic-pituitary-gonadal axis is a prerequisite for normal testicular descent [7]. A disorder in any phase of testicular descent caused by inherited hormonal, anatomical, environmental, or social factors can cause cryptorchidism. One of the main risk factors for cryptorchidism is low birth weight [8], which indicates intrauterine growth retardation, including premature babies born before the descent of the testes, sporadic, idiopathic congenital defects, other causes are: low placental weight, maternal obesity, alcohol

consumption during pregnancy, family history and congenital malformation syndromes, Down syndrome, Prader-Willi syndrome, and Noonan syndrome [9].

Androgen receptor (AR) gene mutations can cause androgen resistance and prevent inguino-scrotal descent of the testes [10]. If there is some form of androgen resistance or estrogen exposure during inguinoscrotal descent, bilateral testicular migration may be hampered, resulting in intersex abnormalities, gastroschisis, and omphalocele, also more common with cryptorchidism [11].

2.3.3 Risk factors of undescended testis

Factors that might increase the risk of an undescended testicle in a newborn include low birth weight, premature birth, family history of undescended testicles or other problems of genital development, conditions of the fetus that can restrict growth, such as down syndrome or an abdominal wall defect, alcohol use by the mother during pregnancy, cigarette smoking by the mother or exposure to secondhand smoke, parents' exposure to some pesticides [12].

Fetal exposure to high levels of endogenous estrogens can be associated with testicular maldescence; Testosterone is also crucial for successful testicular descent: for example, cryptorchidism can be achieved in animal models by exposing the animal to pure antiandrogens [13]. Therefore, it was hypothesized that low maternal testosterone levels may be related to the development of cryptorchidism in the child. However, studies that directly measured maternal serum testosterone levels have reported little or nothing [14]. The low human chorionic gonadotropin observed in the placenta of boys with cryptorchidism may reflect decreased testosterone production, which in turn leads to impaired testicular descent, but this relationship remains unclear. Like testosterone, the protein hormone InsulinLike 3 is crucial for testicular descent: cryptorchidism can be achieved in animal models by switching off the gene that codes for this hormone [15]. In recent years, levels of InsulinLike 3 in umbilical cord blood have been reported to be lower in children born with cryptorchidism.

2.3.4 Classification

The majority of cryptorchid cases are detected at birth. This condition is known as congenital cryptorchidism. However, some boys born with testicles in the scrotum may later develop testicular subluxation, known as acquired testicular stenosis or ascending testis [16]. In contrast, recurrent foreskin stenosis is a condition in which the testicles do not descend at birth, but undergo spontaneous descent, and then ascend to a higher position.

Cryptography can also be classified as “palpable” or “non-palpable”. On examination, the testicles can be palpated under the skin. An invisible testicle cannot be felt. About 70% of all undescended testicles are palpable [17].

An unreduced testicle may be palpable during normal descent. Perhaps the testicles have grown in the wrong place and are outside the scrotum (ectopic). It is possible that a muscle reflex moves the testicle between the scrotum and abdomen (contracture) [18].

A testicle that is not descending, palpable, or intra-abdominal, or even absent. It may be located above the genitals (inguinal ring), near the kidneys, between the rectum and bladder, or near the muscular wall that covers the stomach. [18,19].

2.3.5 Diagnosis of Undescended Testis

The diagnosis of testicles is not clinical. Testing should be performed by an experienced person and should always be performed using the two-handed technique [20]. Palpation should take place in a non-anxious environment and with a warm hand, as cold or anxiety may cause the testicle to contract in a cremasteric reflex.

The patient should be examined in the supine position with the legs in the initial abduction position. Examination should begin with probing the testicle at the level of the anterior iliac spine and using the non-dominant and non-dominant hand to sweep the groin from side to side. After palpating the testicle, the examiner should grasp it with the dominant hand and continue scanning the testicle toward the scrotum with the other hand [21]. Testicular mobility, size, consistency, and tension should be assessed. The position of the testicles in the scrotum should be maintained for one minute, so that the cremaster muscle fatigues [22]. The testicle is then released, and if it stays in place for a short time but then retracts, it is considered retractable [23]. In all patients, the size, location, and texture of the descending testis should also be examined. Laboratory tests, including karyotype, should be ordered, along

with measurements of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). After three months of age, a human chorionic gonadotropin (hCG) stimulation test can be performed to assess testicular response by measuring testosterone levels [24]. If LH and FSH are elevated, but testosterone levels are undetectable, the diagnosis of anorchia can be suspected. In some contexts this can be confirmed by aligning the MIS levels.

Diagnostic imaging in cryptographic studies can be useful in some cases, with ultrasonography being the most widely used imaging modality to evaluate non-opacified testes. Ultrasound has a variety of capabilities for detecting palpable testicles and has an estimated sensitivity and specificity of 45% and 78%, respectively, for accurate localization of an undescended testicle. Because of the poor ability to locate the testes without palpation, ultrasound has no role in the routine evaluation of boys with stenosis [25].

MRI is a useful technique especially for intra-abdominal testes that cannot be detected by laparoscopy or open surgery. Because of its superior differentiation potential, MRI is the most commonly used method to differentiate testicular tissue from adjacent tissue in obese patients. However, unlike the USG, it is not sensitive for detecting intra-abdominal testes [26]. MRI can be used as one of the diagnostic tools for undescended testes if the patient's parents are reluctant to perform diagnostic and therapeutic laparoscopy. More precisely, it is MRA (Magnetic Resonance Angio) to look for hypoplastic testicular vessels [27]. In surgical exploration of the undescended testicle, the use of minimally invasive laparoscopy is often the gold standard for diagnosis. If testicular imaging is available, testicular surgery (also called lanopexy), which is surgery to relocate the testicle into the scrotum. If the testicular vessels are blind, a diagnosis of absent or endangered testicles is made. In this way, diagnosis and treatment can be performed in a single facility [27, 28].

2.3.6 Treatment and management of undescended testis

The rationale for the treatment of cryptorchidism is to reduce the risk of its long-term sequelae, including secondary/progressive infertility, testicular tumors, torsion, and cosmetic problems. Regarding fertility, it has long been observed that spermatogenesis is impaired during spermatogenesis, which can lead to infertility or subfertility [28]. There is a small temperature difference between the abdomen and the scrotum (23°C), but this warmer environment impairs normal spermatogenesis. These underdeveloped testes were suppressed germinal epithelium development, with a decrease in the total number of germ cells from the first year of life [28].

Regarding testicular malignancy, testicular pathology is one of the few well-defined risk factors for testicular malignancy. The possible pathogenesis is that undifferentiated sex cells remain in cryptorchid testes after birth. They can then progress to carcinoma in situ (CIS) and possibly germ cell tumors (GCT) [29].

Current methods of management of undamaged testicles include: hormone therapy, testicular correction, and surgery. Primary hormone therapy is a treatment modality that has been used to induce undescended testicles, although it is more widely practiced outside of the United States [30]. Human chorionic gonadotropin (hCG) and gonadotropin-releasing hormone (GnRH) have been used individually and together for this purpose, citing endocrine factors, and in particular disorders of the gastrointestinal tract. hypothalamic-pituitary-gonadal axis, may play a role in cryptogenicism. [31]. HCG works to stimulate androgen production by Leydig cells, mimicking the effects of pituitary LH (luteinizing hormone). Likewise, GnRH triggers the release of gonadotropins LH and FSH (follicle-stimulating hormone) by the pituitary gland, causing a transient increase in gonadal steroidogenesis. The success rates of hormone therapy vary widely [32].

The primary treatment of testicular pathology is surgical repositioning of the testicle into the scrotum, a technique known as lanopexy.

In infants with cryptanalysis, the procedure should be performed within one year of birth, and cases of 'acquired' cryptopathy, detected in childhood, should be administered as soon as possible [33]. Orchidopexy performed before puberty (or before age 12) reduces the risk of testicular malignancy later in life compared with subsequent revision by 2 to 6 times compared with those who received surgical correction after 12 years of age [34].

In a palpable testicle, location can often determine which surgical method is to be used. [35]. Examination under anesthesia provides the

opportunity to better assess or confirm the position of the testicle. If it is in the inguinal region, a transverse inguinal incision is used to divide the connective tissue, separate the spermatic cord from the spermatic cord, isolate and line the seminal vesicles, and maneuver the testicle into the scrotum in a subcutaneous sac or bottom pocket. If the testicle can be palpable near the scrotum, or if it can readily return to the dependent scrotal position, scrotal dilation may be used. This method uses a antenatal incision to perform the above steps, sometimes an inguinal incision is also used if a closer dissection is needed for greater mobility than the scrotal incision allows [36].

Surgical treatment of undescended testis is indicated when the testis is in a non-scrotal position, especially after unsuccessful hormone therapy. If testicles can be palpable preoperatively, the classical orchiectomy should always be performed first, followed by orchiectomy [37]. At Sophia Children's Hospital, mitosis and orchitis are still performed using techniques developed by Schoemaker. If the testicle is not palpable, laparoscopy should be performed to determine whether the testis may be in the abdominal cavity. If the dissociation and testes are not sufficient to immobilize the scrotum due to short vas deferens, automated implantation by microsurgery can be performed [38,39].

3. CONCLUSION

Foreskin stenosis (non-descending orchitis) is a condition in which one or both testicles fail to descend to the bottom of the scrotum. The study aims to summarize the up-to-date evidence regarding the epidemiology, etiology, classification, diagnosis, and treatment of testicular or undescended testicles. There are several possible causes for the development of cryptography. Disruption of any stage of testicular prolapse triggered by genetic hormonal, anatomical, environmental or social factors can lead to testicular dysplasia. The diagnosis of testicles is not clinical. Testing must be performed by an experienced person and should always be performed using a two-handed technique. Diagnostic imaging in demyelinating pathology can be useful in some cases, ultrasound is the most used imaging modality to evaluate unruptured testicles, MRI is a particularly useful technique. for testes located in the abdomen. The rationale for the treatment of cryptorchidism is to reduce the risk of its long-term sequelae, including infertility/progressive infertility, testicular tumors, torsion, and cosmetic problems. Current management of an undamaged testicle includes hormone therapy, orchiectomy, and corrective surgery.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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