ORIGINAL SCIENTIFIC ARTICLE

FERTILITY AFTER THE OPERATION OF CRYPTORCHISM IN CHILDHOOD

Veroljub Vucic

Department of Urology, Medical Center Krusevac, Serbia

Received: 20.12.2018.
Accepted: 08.06.2019.

Corresponding author:

Veroljub M. Vucic

Department of Urology, Medical Center Krusevac, Serbia

E-mail: vlade66@hotmail.rs

UDK: 616.68-007.2-089
616.699
Ser J Exp Clin Res 2022; 23(2):121-125
DOI: 10.2478/sjecr-2019-0030

ABSTRACT

Cryptorchism is a congenital anomaly of male genitalia, and is defined as a disorder of lowering testicles into the scrotum. In our study, the quality of sperm and fertility of men who were operated from unilateral or bilateral cryptorchism in childhood were analyzed. According to the age in which they were operated, patients were classified into different time groups, subjected to clinical examination and sperm analysis. A normal sperm count was found: 36.9% of the total number of patients operated from unilateral to bilateral cryptorchism. The highest percentage of normal sperm counts was 73.97%: the data which was found in the group that was operated from one-sided cryptorchism to the end of the second year of life. Regardless of the age of the cryptorchism operation, it is possible to expect a disorder of spermatogenesis.

Keywords: *cryptorchism, sperm count, fertility, orchidopexy.*

INTRODUCTION

Cryptorchism is defined as the incomplete descent of one or both testicles from the abdominal cavity through the inguinal channel into the scrotum. It is a multifactorial etiological abnormality that affects 1-1.8% of male neonates (1). It can be considered to be associated with infertility and testicular cancer (2). In order to reduce these correlations, it is necessary to set and correct testicles in the scrotum (2, 3). [Supplementary Concept], Estrogen Replacement Therapy, Orchiopexy

It is not known when the ideal age of surgical treatment is and which the ideal therapy is (4). However, several studies have shown that as soon as possible, patients should start treatment because they have an improved spermatogenesis (3, 5).

Damage to the cells may be of secondary origin due to abnormal testicular position. These lesions are basically characterized by a progressive decrease in the number of cells and in the size of the tubular space with peritubular fibrosis and hyalinization, resulting in a reduction in the number of Leydig cells. These changes can affect the production of sex hormones that cause testicles atrophy with subsequent infertility (6, 7, 8). Therefore, the level of testicles and hormone levels is associated with maintaining spermatogenesis, and is considered indirect consequences for fertility (9, 10, 11). But, it is possible that the undescended testicle in the scrotum is indirectly related to atrophy (12, 13, 14, 15).

The surgery is recommended to be performed within 15-18 months, since cell loss is very rare and loss of germinal cells is associated with a subsequent risk of infertility (16, 17, 18).

MATERIALS AND METHODS

In our research, we analyzed a total of 84 men who had the operation of unilateral or bilateral cryptorchism at different times of their youth. Of the total of 84 patients, 46 were unilateral and 38 subjects had bilateral cryptorchism. We grouped them into three groups: a group of patients operated by the end of the second year of life (1), a group of patients operated from the second to the end of the seventh year (2), and a group operated seven years after (3). All patients gave three samples of spermograms, and all samples were made in the same laboratory.

In the period from February 2016 to the end of April 2017 the sperm analyses were carried out at the Institute for Health Care of the Medical Center in Krusevac. In all patients, three samples of sperm counts were taken, and a sample of the highest quality was analyzed. All samples were made in the same laboratory. Seed samples of patients tested for cryptorchism were taken by masturbation after 3 to 5 days of sexual abstinence and tested for 30 minutes at 37S. The concentration and mobility of the number of sperm counts are estimated according to the WHO recommendation. Samples are grouped into four groups: Normal finding, oligospermia (<20x106/ml), severe oligospermia (<5 x106/ml) and azoospermia.

Only a case of unilateral and bilateral cryptorchism is analyzed without analysis of family history (anomalies of the urogenital tract in the family, diseases and specific conditions of parents that can have an effect, for example, on mothers with diabetes, premature birth, weight of preoperative testis status such as atrophic testicles, use of hormonal gonadotropins, hernias, hypospadias, postoperative complications that may affect the number of spermatozoa and fertility estimation in men after operated cryptorchism). The test was conducted in accordance with the ethical principles of clinical trial on humans under the Helsinki Declaration and approved by the local ethics committee.

The obtained results are expressed as the mean±SD. In order to test the statistical significance of the results, we used Student's t-test and Pearson's correlation coefficient. Data processing is done using the Microsoft Office Excel 2003 software package in the Windows XP Professional Professional environment.

REZULTS

A normal finding of sperm count was found in 31 (36.9%) patients of a total of 84. The largest number of normal sperm count findings was found in patients operated from one-sided cryptorchism in the period up to the end of the second year of life. Oligospermia was found in 23 (28.5%) subjects, while heavy oligospermia was found in 14 (21.4%) patients operated by cryptorchism.

Azoospermia was found out in 11(13.09%) of a total of 84 subjects. In terms of age groups and cryptorchid side, a normal finding of sperm count is the most common in patients operated from one-sided cryptorchism until the end of the second year of life (73.9%) (Table 1).

Table 1. Normal sperm count

Age group	Nº cryptorchism			Normal sprmogram			% normal			Spermogram		
	U	B	∑	U	B	∑	U	B	∑	U	B	∑
0-2	23	16	39	17	7	24	73.9	43.7	61.5	36.9	18.4	28.5
2-7	14	14	28	3	2	5	21.4	14.2	17.8	6.52	5.26	5.9
< 7	9	8	17	2	0	2	22.2	0	11.7	4.34	0	2.38
Total	**46**	**38**	**84**	**22**	**9**	**31**	**47.8**	**32.6**	**36.9**	**47.8**	**23.6**	**36.9**

U-unilateral; **B-** bilateral; ∑-total

Table 2. Test variables in the first step (Step 1): year; one-sided-both sided

Step 1	B	S.E.	Wald	df	Sig.	Exp(B)
Year	.038	.012	10.208	1	.001	1.039
Unilateral		.542	4.923	1	.026	3.325
Bilateral	1.202					
Constant	2.578	.901	8.195	1	.004	.076

B= coefficients; **S.E.-** standard error coefficients;
Wald (the significance of the coefficient in the model); **Sig. (**p=**)**; **Exp (B)**= eB

Using the t-test, there is a statistically significant difference between the first and second groups (p=0.001), between the first and third groups (p=0.008), and between the first and fourth groups (p=0.014).

The highest percentage of normal sperm was 73.9% in an age group operated by one-sided cryptorchism until the end of the second year of life. In the case of surgeries with one-sided cryptorchism, we have twice more normal findings than in both cases (22 to 9).

The normal finding of sperm count is the most common in the age group operated by the end of the second year of life. It amounts to 43.77%, while in other age groups we have a very declining percentage of normal sperm finding in patients operated by bilateral cryptorchism (14.2% 0%).

There is a statistically significant difference (p=0.018) in the appearance of normal levels of spermatozoa in patients treated with single or double cryptorchism. Binary Logistic Regression examines the dependence of the findings (normal-abnormal) from the time when the operation of a single-sided or double cryptorchism was performed. Finding depends on age (p=0.001), and whether cryptorchism is one-sided or double-sided (p=0.026) (Table 2).

If the age is increased by one month, the risk that the finding does not occur normally increases by 3.9%. If cryptorchism is two-sided, the risk of finding outcomes increases by 3.32 times in relation to unilateral cryptorchism.

DISCUSSION

Infertility, due to its frequency, is not only the problem of marital partners, but of the entire society (19, 20). Looking at the age groups and the side of cryptorchism, the normal finding of spermograms is most common in patients with unilateral cryptorchism by the end of the second year of life (73.9%) (Table 1) (21, 22, 23).

On the 46 operations 22 (47.8%) of the subjects had a normal spermogram. On the 38 operations on both sides of cryptorchism 9 of the subjects (23.6%) had a normal spermogram. Cryptorchism occurs in about 4% of boys, which leads to a fall of testis from the abdominal cavity to the scrotum.

Infertility is due to damage of the epithelial epithelium caused by elevated temperature in the abdominal cavity. In cryptorchism, the disturbed function of the testicle can cause hormonal disorders. The level of hormone disorder is an indicator of damaged testes and can be used as a prognostic factor (24, 25, 26, 27).

The disorder of spermatogenesis is much more severe in patients with bilateral cryptorchidism compared to one-sided (24). The reason is the poor quality of sperm as well as permanent tubular damage in infertile men who have probably been operated in correlation with the time in which the surgical correction was performed (28).

Sperm parameters are often disrupted in patients with a history of cryptorchism (29). Boys older than 8 months have a low spermatogenic index, which indicates that surgery should be done before that time (22).

CONCLUSION

Cryptorchism leads to damage of spermatogenesis, as the loss of Leydig cells leads to sterility. The damage of spermatogenesis is more pronounced in patients with bilateral than in one-sided cryptorchism. Therefore, surgical treatment should be done earlier.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2013. Voluntary written and informed consent was obtained from each participant prior to enrollment in the study.

COMPETING INTERESTS

There are no conflicts of interest.

FUNDING

None.

REFERENCES

1. Hutson J.M, Thorup J. Evaluation and management of the infant with cryptorchidism. Curr Opin Pediatr 2015; 26(4): 520-4.
2. Kolon T.F, Herndon C.D., Baker L.A., et al. Evaluation and treatment of cryptorchidism: AUA guideline. J Urol 2014;192(2): 337-45.
3. Pastuszak A.W, Lipshultz L.I. AUA guideline on the diagnosis and treatment of cryptorchidism. J Urol 2014; 192(2): 346-9.
4. Steinbrecher H. The undescended testis: working towards a unified care pathway for 2014. Archives of Disease in Childhood 2014; 99(5): 397-8.
5. Tsai MC, Cheng YS, Lin TS, et al. Clinical characteristics and reproductive outcomes in infertile men with testicular early and late maturation arrest. Urology 2012; 80(4): 826.
6. Molokwu, CN, Somani, BK, Goodman, CK. Outcomes of scrotal exploration for acute scrotal pain suspicious of testicular torsion: A consecutive case series of 173 patients. Brit J Urol Int 2011; 107: 990-993.
7. Hanerhoff BL, Welliver C. Does early orchidopexy improve fertility? Transl Androl Urol 2014; 3(4): 370-376.
8. Ashley RA, Barthold JS, Kolon TF. Cryptorchidism: pathogenesis, diagnosis, treatment and prognosis. Urol Clin North Am. 2013; 37:183 – 193.
9. Thorup J., Clasen-Linde E., Thorup S.C., et al., Pre-and postoperative status of gonadotropins (FSH and LH) and inhibin-B in relation to testicular histopathology at orchiopexy in infant boys with unilateral undescended testes. J Pediatr Urol 2015; 11(1): p. 25 e1-5.
10. Rao PK, Burnett AL. Development of the male reproductive system. In: Kavoussi PK, Costabile RA, Salonia A, editors. Clinical Urologic Endocrinology. Principles for Men's Health. London: Springer-Verlag; 2013. pp. 11-24.
11. Kollin C., Ritzen E.M. Cryptorchidism: a clinical perspective. Pediatric endocrinology reviews: PER. 2014;11 Suppl 2: 240-50.
12. Hunter W. State of the testis in the foetus and on the hernia congenita. William Hunter's Medical Commentaries 1762: 75-89.
13. Ivell R, Wade JD, Anand-Ivell R. INSL3 as a biomarker of Leydig cell functionality. Biol Reprod 2013; 88(6):147.
14. Toppari J, Virtanen HE, Main KM, Skakkebaek NE. Cryptorchidism and hypospadias as a sign of testicular dysgenesis syndrome (TDS): environmental connection. Birth Defects Res A Clin Mol Teratol 2012; 88: 910-919.
15. Mano R, Livne PM, Nevo A, Sivan B, Ben-Meir D. Testicular torsion in the first year of life – characteristics and treatment outcome. Urology 2013; 82: 1132-7.
16. Kollin C, Stukenborg JB, Nurmio M et al: Boys with undescended testes: endocrine, volumetric and morphometric studies on testicular function before and

after orchidopexy at nine months or three years of age. J Clin Endocrinol Metab 2012; 97: 4588.
17. Moursy EE, Gamal W and Hussein MM: Laparoscopic orchiopexy for non-palpable testes: Outcome of two echniques. J Pediatr Urol 2011; **7**: 178.
18. Hanerhoff BL, Welliver C. Does early orchidopexy improve fertility? Transl Androl Urol 2014; 3(4): 370-376.
19. Serrano T, Chevrier C, Multigner L, Cordier S, Jégou B. International geographic correlation study of the prevalence of disorders of male reproductive health. Hum Reprod 2013; 28(7): 1974-1986.
20. Robin G, Boitrelle F, Marcelli F, et al. Cryptorchidism: from physiopathology to infertility. Gynecol Obstet Fertil 2014; 38(10): 588-599.
21. Kobayashi H, Nagao K, Nakajima K. Advanced Studies in Medical Sciences. 1. Vol. 1. HIKARI Ltd; 2013. Therapeutic Advances in the Field of Male Infertility: Stem Cell Research; pp. 39-54.
22. Hanerhoff BL, Welliver C. Does early orchidopexy improve fertility? Transl Androl Urol 2014; 3(4): 370-376.
23. Hadziselimovic F, Hocht B, Herzog B, Buser MW. Infertility in cryptorchidism is linked to the stage of germ cell development at orchidopexy. Horm Res 2007; 68:46-52.
24. Thorup J, Kvist K, Clasen-Linde E, Petersen BL, Cortes D. The relation between adult dark spermatogonia and other parameters of fertility potential in cryptorchid testes. J Urol 2013;190(4 suppl): 1566-1571.
25. Cobellis G, Noviello C, Nino F, et al. Spermatogenesis and cryptorchidism. Front Endocrinol (Lausanne) 2014; 5: 63.
26. Ivell R, Wade JD, Anand-Ivell R. INSL3 as a biomarker of Leydig cell functionality. Biol Reprod 2013; 88(6): 147.
27. Hakonsen LB, Ernst A, Ramlau-Hansen CH. Maternal cigarette smoking during pregnancy and reproductive health in children: a review of epidemiological studies. Asian J Andol 2014;16: 39-49. doi: 10.4103/1008-682X.122351.
28. Hadziselimovic F, Hadziselimovic NO, Demougin P, Oakeley EJ. Testicular gene expression in cryptorchid boys at risk of azoospermia. Sex Dev 2011; 5: 49-59. doi: 10.1159/000323955.
29. Bilius V, Verkauskas G, Dasevicius D, Kazlauskas V, Malcius D, Hadziselimovic F. Incidence of high infertility risk among unilateral cryptorchid boys. UrolInt 2015; 95:142-145. doi: 10.1159/000369476.