Cumulative Success Rates Of Testicular Sperm Extraction And Intracytoplasmic Sperm Injection In Non Obstructive Azoospermia

Thesis

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By:

Ashraf Mohamed Selim Zeidan

(M.B.,B.Ch.)

(M.Sc.)

Cairo University

Supervisors

Prof.Dr.Mohamed Farid Roaiah

Professor of Andrology,Sexology & STDs

Faculty of Medicine

Cairo University

Prof.Dr.Medhat Amer

Professor of Andrology,Sexology & STDs

Faculty of Medicine

Cairo University

Assistant Prof.Dr.Mohamed Abbas Eid

Assistant Professor of Andrology,Sexology &STDs

Faculty of Medicine

Cairo University

2006

Cairo University

2006

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ABSTRACT

The objective of this study was to evaluate cumulative success rates of Testicular Sperm Extraction *(TESE*) and Intracytoplasmic Sperm Injection *(ICSI)* in patients with non-obstructive azoospermia *(NOA).*

We selected retrospectively seven hundred and sixty eight (768) patients , who had trial of testicular sperm recovery for ICSI whom were recruited from the Centre of Reproductive Medicine in the *UZ-VUB* hospital in Belgium during the period from 1996 to 2006.

The mean age of the male was 35.6 years (21-62) and for the female was 31.6 years (18-46).

Spermatozoa were found in 364/768 patients (47.4%) during TESE, only 349 patients have undergone ICSI, while the rest (15) patients did not proceed for ICSI.

From total 697 ICSI cycles, fertilization was successful in 550 cycles (79%), while fertilization did not occur in 147 (21%).

From the histopathological point of view, sperms were recovered in 170/380 (45%) patients with *Sertoli cell-only syndrome (SCOS),* 69/148 (46.6%) with *tubular sclerosis,* 111/204 (54.4%) with *maturation arrest,* in 1/1 (100%) patient with *Carcinoma insitu* and in 10/35 (28.6%) patients with no available testicular histopathology, while delivery occurred after ICSI in SCO patients 55/170

(32.3%), *maturation arrest* 34/111 (30.6%), *tubular sclerosis* 23/69 (33.3%) and in 2/10 patients with no available histopathology (0.2%).

Our study showed that the cumulative delivery rate in patients with non-obstructive azoospermia is 33.5% after three cycles.

Testicular Sperm Extraction (TESE) followed by Intracytoplasmic Sperm Injection (ICSI) is an effective treatment in patients with NOA. More than half of the patients undergoing TESE had spermatozoa recovered. Age of men, volume of both testes and serum FSH/ testosterone levels in men were not useful in predicting successful recovery. Fertilization and pregnancy rates were achieved when testicular spermatozoa were used for ICSI.

This study shows that there is a value in performing TESE-ICSI attempts in patients with non-obstructive azoospermia.

Keywords: *Intracytoplasmic Sperm Injection· Non-Obstructive Azoospermia· Testicular Sperm Extraction. Sertoli Cell Only Syndrome. Maturation Arrest. Tubular Sclerosis.*

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INTRODUCTION

The introduction of ICSI has revolutionized the management of male infertility ***(Van Steirteghem et al., 1993).*** If a man has a non-obstructive azoospermia (NOA) and wants to father his own genetic child, the only treatment option available for the couple is ICSI with testicular sperm (TESE) ***(Devroey et al., 1995; Tournaye et al., 1995)*** However, the probability of finding sperm is only approximately 50% in a non-selected population ***(Tournaye et al.,1997)***.

Although the first births of children after ICSI with testicular spermatozoa from patients with non-obstructive azoospermia were reported in the mid-1990s **(*Tournaye et al. 1995)***, success rates after ICSI using testicular sperm from non-obstructive men are still reported per ICSI treatment cycle ***(Devroey et al., 1995 ; Tournaye et al., 1995 ; Silber et al., 1996 ; Schlegel et al., 1997; Vernaeve et al., 2004).*** Only few studies have reported on cumulative success rates of this treatment and these studies only include men in whom TESE has been successful ***(Giorgetti et al.,2005).***

AIM OF WORK

To assess the cumulative chance for men with non obstructive azoospermia to father their own child after testicular sperm extraction and intracytoplasmic sperm injection .

ANATOMY OF THE TESTIS

The testes are the primary reproductive organs of the male. They are ovoid masses that lie in the scrotum. The average testicular volume is 15-20 ml in healthy young men. Average testicular dimensions are 4-5 cm in length, 2.5 cm in breadth and 3 cm in antero-posterior diameter, their weight varies from 10.5 –14 grams. ***(William and Dyson, 1989).***

The ***epididymis*** is a tortuous canal and the first part of the efferent route from the testis, it is much folded and tightly packed to form along, narrow mass attached postero-laterally to the testis. It has a central body, a superior enlarged head and an inferior pointed tail ***(Middleton and Fitzgerald, 1995).***

Testicular coats: The testis is invested by three coats from outside inwards; the tunica vaginalis, tunica albuginea and tunica vasculosa ***(Williams and Dyson,1989).***

The ***tunica vaginalis*** is the lower end of the peritoneal processus vaginalis, which precedes the descent of the fetal testis from abdomen, it has a partial layer and a visceral layer.

The ***tunica albuginea*** is a dense, bluish white covering of the testis, composed mainly of interlacing bundles of collagen fibers, covered externally by the visceral layer of the tunica vaginalis, except at the epididymal head,tail and the posterior testicular aspect, where vessels and nerves enter the testis.

It covers the ***tunica vasculosa*** and, at the posterior border of the testis, projects into as a thick, vertical but incomplete septum, ***the mediastinum testis***. This extends from the upper almost to the lower end of the testis and is wider above than below ***(Williams and Dyson, 1989)***.

Septa radiate from the mediastinum and attach to the inner surface of the tunica albuginea to form 200 to 300 cone shaped lobules, each containing one or more convoluted seminiferous tubules ***(Brooks, 1998).***

The ***tunica vasculosa*** contains a plexus of blood vessels and delicate loose connective, extending over the internal aspect of the tunica albuginea and covering the septa and therefore all lobules ***(Williams and Dyson, 1989).***

The spermatic cord and its coverings

The spermatic cord contains the testicular, deferential and cremasteric arteries, pampiniform plexus of veins, lymphatics, nerves (genital branch of genitofemoral nerve and testicular plexus of the sympathetic trunk) and the vas deferens.

The covering layers of the spermatic cord include the external spermatic fascia (external oblique aponeurosis), the internal spermatic fascia derived from the fascia transversalis, and in between lies the cremasteric fascia which contains fascicule of skeletal muscle united by connective tissue to form the cremaster and is continuous with the internal oblique muscle ***(Rick,Feld and Middleton, 1992).***

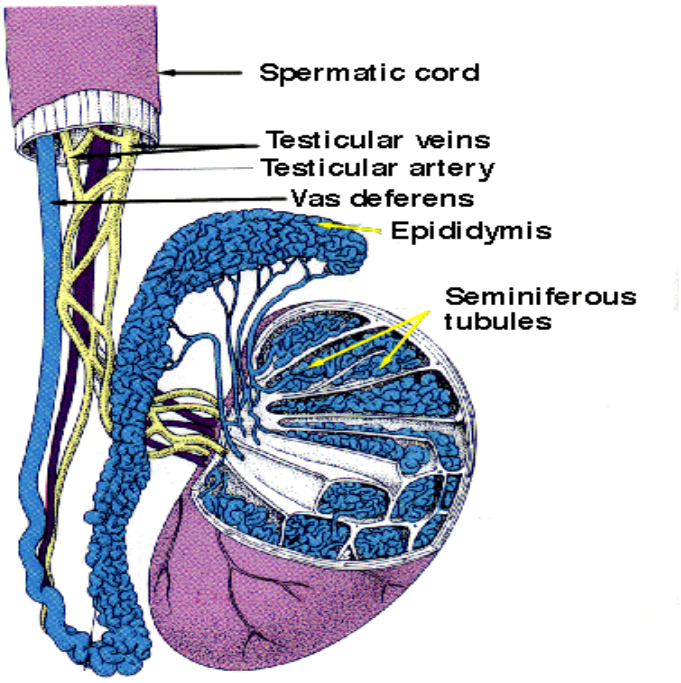

Figure (1): showing testis, spermatic cord and its content.

The arterial supply

Blood supply to the testis is derived from the ***internal spermatic artery*** (testicular) and the vasal (deferential) artery. The ***testicular artery***, the main blood supply to testis, arises from the aorta.

It branches variably along its course to the testis. At the level of the inguinal canal, the testicular artery is usually a solitary artery.

However in 30 percent of men, the spermatic cord will have two arteries, and in approximately 20 percent of spermatic cords, three arteries are found ***(Schlegel and Chang,1991)***.

A single artery enters the testis in 56 percent of cases, two branches enter in 31 percent of cases, and three or more branches enter in 13 percent of cases (***Chang TSK et al.,1992).*** After exiting the inguinal canal, the testicular artery gives off capsular arteries.

These capsular arteries run in the tunica vasculosa, just beneath the tunica albuginea. The capsular arteries, in turn, supply centripetal arteries that run into the substance of the testicular parenchyma towards the mediastinum.

As the centripetal arteries approach the mediastinum, they arborize into recurrent rami branches that course away from the mediastinum. The recurrent rami give rise to a set of arterioles that supply blood to individual intertubular and peritubular capillaries ***(Middleton and Fitzgerald, 1995).***

Studies by ***Jarrow (1990)*** have suggested that injury to the testicular arteries may be minimized during testicular biopsy by avoiding areas likely to contain a significant component of arterial distribution to the testis. The areas least likely to have vessels that could be injured are the medial and lateral upper poles of the testis.

In addition to the capsular arteries, the testicular artery may supply one (or occasionally, more than one) large branch that does pierce the mediastinum of the testis and travels through the testicular parenchyma to the side opposite the mediastinum. These vessels are referred to as transmediastinal arteries, and they can be visualized in approximately one half of the testes ***(Middleton and Bell,1993)***, the testicular artery also supplies epididymal branches.

Transmediastinal arteries always contain blood flowing away from the mediastinum. Once they reach the opposite side of the testis, they enter the tunica vasculosa and supply capsular arteries that subsequently course through the tunica vasculosa and supply centripetal arteries in a normal fashion ***(Middleton and Fitzgerald, 1995).***

The transmediastinal artery is usually single and unilateral, but may be multiple and bilateral. About six percent of transmediastinal arteries branch within the testicular parenchyma ***(Middleton and Bell, 1993).***

Blood supply to the testis may be also derived from the vasal vessels. These small paired arteries branch off the hypogastric artery and travel along the vas deferens, primarily supplying blood to the vas deferens and epididymis.

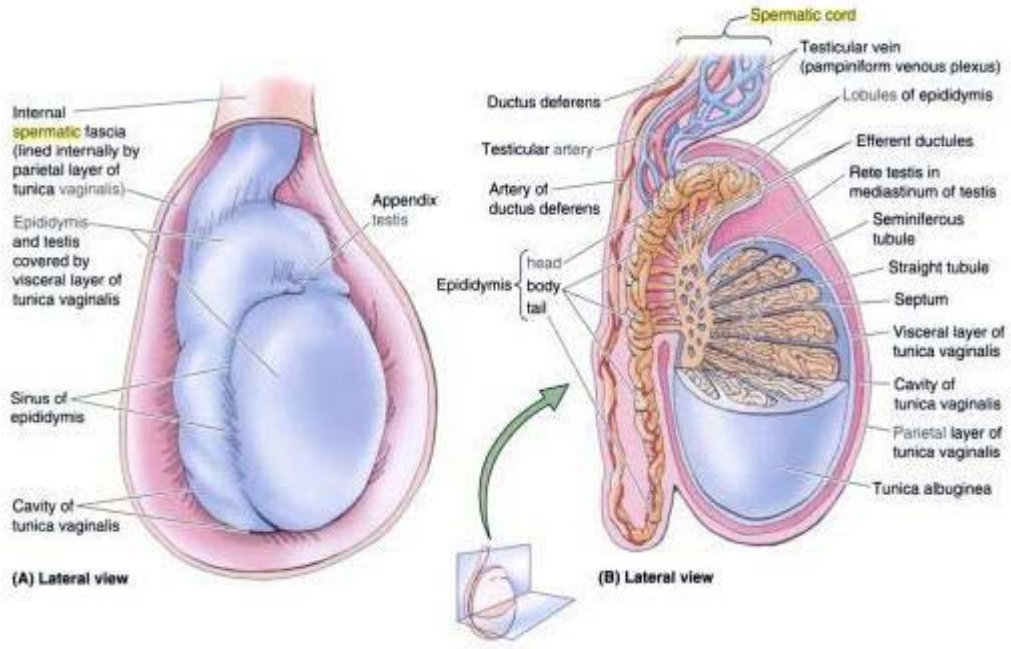

Figure (2) : *Lateral view of testis, spermatic cord and its coverings.*

The venous and lymphatic drainage

The veins within the testis are unusual in that they do not run with the corresponding intratesticular arteries. The small veins in the parenchyma empty into either the veins on the surface of the testis or exit through the mediastinum, ***(Middleton and Fitzgerald ,1995)***.

However, occasionally a transmediastinal vein could be seen in 26 percent of cases. It can be identified running adjacent to a transmediastinal artery in 59 percent of cases, but less frequently, it may be seen isolated in 41 percent of cases ***(Middleton and Bell,1993).***

The veins from several highly anastomotic channels that surround the testicular artery forming the ***pampiniform plexus***. The pampiniform plexus, leaves the posterior border of the testis. As the plexus ascends, it becomes reduced in size, so that at about the level of the deep inguinal ring, a single ***testicular vein*** is formed which runs up on the posterior abdominal wall.

The left testicular vein drains into the left renal vein while the slightly shorter right testicular vein drains directly into the inferior vena cava ***(Middleton and Fitzgerald, 1995).***

The testicular veins may anastmose with the external pudendal, cremasteric, and vasal veins. These connections can allow varicoceles to recur after ablative procedures ***(Brooks,1998).***

Testicular lymphatic vessels ascend through the inguinal canal and pass up over the posterior abdominal wall to reach the lumbar ***(para aortic)*** lymph nodes on the side of the aorta at the level of the first lumbar vertebra ***(Snell, 1986).***

Spermatogenesis and sperm transport

The term ***spermatogenesis*** describes and includes all processes and events involved in the production of gametes and occur within the ***seminiferous tubules*** of the testis.

Normal spermatogenesis is a complex process that depends on many factors. Genetics plays a major role in many of these factors including providing a normal hormonal milieu, the development of the testis and ductal system, and control of the stepwise maturation of sperm in the testis. The Y chromosome plays a key role in testis determination and control of spermatogenesis.

Spermatogenesis starts with the division of stem cells and ends with the formation of mature sperm. The entire process can be divided into three phases: (1) mitotic proliferation and differentiation of spermatogonia, (2) the meiotic division of tetraploid germ cells (spermatocytes), and (3) the transformation of haploid germ cells (spermatids) into testicular sperm (spermiogenesis).

(1) ***Spermatogonia*** are undifferentiated diploid cells that lie in basal part of the seminiferous epithelium and are classified as type A or type B. Spermatogonia divide mitotically.