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Testicular Sperm Extraction: Can we Combat Both Obstructive and Non Obstructive Azoospermia?

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Introduction

The treatment of Azoospermia has undergone a radical change over the past 17 years, evolving from a clinical diagnosis with no direct corrective options to a highly treatable entity. This was the result of Intra-cytoplasmic Sperm Injection [ICSI], which was introduced in 1992, which eliminated many obstacles in the way of fatherhood for men with severe male factor infertility. Today, more than 95% of men can father their own genetic child without the need for donor sperm. It was ICSI which could make this dramatic change in the management of male infertility but only because of the advent of advanced surgical epididymis and testicular sperm retrieval techniques. These two major technical advances changed the treatment for previously untreatable testicular failure or un-reconstructable obstructive azoospermia from "replacement" therapies in the form of donor insemination or adoption for the affected men to have a biologic child of their own.

Sperm Retrieval Techniques

Sperm retrieval techniques are surgical methods that were developed to obtain spermatozoa from the epididymis and testes of azoospermic men seeking paternity. The collected sperm can then be used for intra-cytoplasmic sperm injection in the same cycle or alternatively, can be cryopreserved for use in future sperm injection attempts.

The method of choice for sperm retrieval is primarily based on the type of azoospermia, which can be obstructive or non-obstructive, and the attending surgeon's preferences and experience [1,2]. Spermatozoa can be retrieved from the epididymis or testes in almost all cases of Obstructive Azoospermia [OA], irrespective of the technique used for sperm collection and the cause of obstruction. Non-Obstructive Azoospermia [NOA], on the other hand, is a consequence of spermatogenic failure due to various congenital and acquired causes and is the cause of 10-15% cases of azoospermia [3]. Unlike men with OA, men with NOA have no treatment options other than attempting testicular sperm retrieval. In such cases, spermatogenesis may be focal, thus, spermatozoa can be found and used for ICSI in approximately 30-60% of men with NOA [4]. Thus Testicular Sperm Extraction [TESE] is the technique of choice for NOA, and the use of microsurgery for TESE seems to further increase retrieval rates [4].

Methods of surgical sperm retrieval include:

- PESA: Percutaneous Epididymal Sperm Aspiration.
- MESA: Microsurgical Epididymal Sperm Aspiration.
- TESA: Testicular Sperm Aspiration. This includes testicular fine needle aspiration [TFNA].
- TESE: Testicular Sperm Extraction.

Micro-dissection TESE

The goals of surgical sperm retrieval are: to obtain the best quality sperm, to retrieve an adequate number of sperm for both immediate use and for cryopreservation, to minimize damage to the reproductive tract so as not to jeopardize future attempts at sperm retrieval or surgical reconstruction.

Testicular Sperm Extraction [Tese]

Historically the TESE procedure which was first carried out by Silber et al and Devroey et al in 1993 was applied to men with obstructive azoospermia in whom the epididymis was entirely destroyed or in the case of bilateral absence of the vas deferens [5,6]. More recently testicular sperm extraction and direct sperm aspiration have been described as alternative sperm recovery methods which may be more likely to yield spermatozoa even in patients with NOA who may have focal spermatogenesis. Thus in non-obstructive azoospermic or extreme oligoastheno-terato-zoospermic men who have severe hypo-spermatogenesis, bilateral maturation arrest in spermatogenesis, Sertoli cell-only syndrome or tubular fibrosis, the testes are the only source of sperm cells [1].

The indications of TESE are:

- In obstructive azoospermia where Microsurgical Epididymal Sperm Aspiration [MESA] is impossible because of a totally destroyed epididymis [1]
- In obstructive azoospermia where reconstructive surgical options are not viable
- Failure to retrieve spermatozoa by other surgical sperm retrieval techniques on the day of oocyte recovery in an IVF cycle.

Procedure

For conventional Testicular sperm extraction, a standard open surgical biopsy technique is used to remove the testicular parenchyma without the aid of optical magnification. This procedure is usually carried out without delivering the testis with a 2-cm transverse incision right through the skin to the tunica albuginea [7-14]. A gentle pressure is then applied to the testis and a fragment of approximately 5 x 5 mm is harvested with sharp scissors and placed in sperm culture media (Figure 1). Alternatively, individual albuginea incisions can be made in the upper, middle and lower testicular poles in an organized manner and different areas can be sampled. The testicular specimens are sent to the laboratory for processing and immediate microscopic examination.

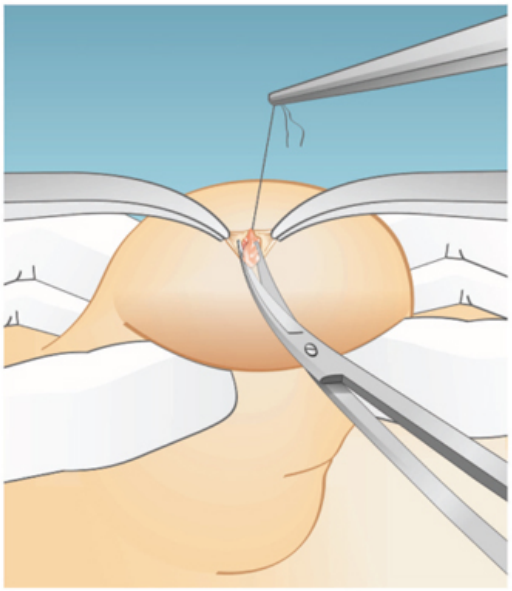

Figure 1 - Conventional testicular sperm extraction (TESE). The illustration depicts TESE using a single open biopsy (see the text for a detailed description). Adapted from: Esteves SC, Agarwal A. Sperm retrieval techniques. In: Gardner DK, Rizk BRMB, Falcone T, Eds. Human assisted reproductive technology: future trends in laboratory and clinical practice. 1st. edition. Cambridge: Cambridge University Press 2011; pp. 41-53.

Figure 1: Conventional TESE depicting a single open biopsy

Microsurgical Testicular Sperm Extraction [Micro-TESE]

Microdissection testicular sperm extraction which was originally described in 1999 incorporates an operating microscope for testicular sperm extraction [8-10]. In contrast to TESE the testes is delivered extravaginally, and the testicular parenchyma is dissected at 16-25x magnification to assist in the isolation of seminiferous tubules that exhibit larger diameters [which are more likely to contain germ cells and eventually normal sperm production] in comparison to non-enlarged or collapsed counterparts. The excised testicular tissue specimens are placed into the Petri dish containing sperm media, and are sent to the laboratory for processing and sperm search [4].

Anesthesia for TESE

Although it is possible to provide efficient anesthesia simply by using local or loco regional anesthesia, the combination of intravenous sedation and local anesthesia offers patients the analgesic effectiveness of local anesthetics combined with the comfort and effective control of anxiety provided by intravenous sedation [2]. In addition it provides the benefit of carrying it out on an outpatient basis too.

Complications

The incidence of complications ranges from 0-70% and mainly includes: persistent pain, swelling, infection, hydrocele, and hematoma [9,10]. Intratesticular hematomas have been reported on follow up ultrasounds performed three months after surgery in most patients [up to 80%] who undergo TESE with single or multiple biopsies, but in most cases resolve spontaneously without compromising testicular function [10]. Large-volume conventional TESE has been associated with a higher risk of a transient or even permanent decrease in serum testosterone levels due to testicular de-vascularization and excessive tissue removal. On the other hand, the incidence of complications is lower following micro-TESE compared to conventional TESE [9-11].

Prognostic Factors for Testicular Sperm Retrieval

Chances for sperm retrieval from TESE in relation to various clinical and endocrine parameters are summarized in Table 1. Higher fertility rates are achieved in OA patients than in NOA patients, with birth rates of approximately 47% and 21%, respectively [12].

Preoperative prognostic factor	Probability
Clinical obstructive azoospermia	100%
Partial disruption of spermatogenesis [AZFc deletion]	75%
History of cryptorchidism	74%
History of hypogonadotrophic Hypogonadism	73%
Klinefelter syndrome	57%
Small testicles [High FSH values]	24%
Complete disruption of spermatogenesis [AZFa, AZFb deletions]	0%

Table 1: Probability of sperm retrieval from testicular sperm extraction in azoospermic males.

Fresh versus Frozen Sperm

The question of whether to use fresh testicular sperm or frozen thawed sperm for ICSI has been the topic of discussion in various studies and forums. However, as most of these studies include both obstructed [who make up most of the patients] and NOA patients clubbed together in the analysis, definitive conclusion cannot be drawn in the management of the males with spermatogenic failure. Although the study population has been small, most of the studies have reported statistically similar pregnancy and live delivery rates between fresh and frozen sperm [14].

Our experience

At our center, which is a part of a Tertiary Care Hospital, both PESA and TESE have been found to be a very efficient method of sperm retrieval in the group of men with both Obstructive and NOA. However, TESE as a sperm retrieval technique has been resorted to, at our center as rescue to PESA when we have not been able to acquire sperms from epididymal retrievals in OA and in all NOA cases. Successful retrieval rates after TESE has been to the tune of 75%.

Conclusions

Testicular sperm retrieval which is a highly feasible and a successful procedure can help in spermatozoa retrieval from the testis in up to

70% of patients, even in cases with testicular azoospermia and severe disorders of spermatogenesis. Thus infertility experts who had very limited options in their repertoire for infertile men can fulfil their dream of fatherhood.

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