Testicular Sperm Extraction and Intracytoplasmic Sperm Injection: Outcomes in a specialist fertility centre

Abstract:
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Introduction
Azoospermia is defined as the absence of sperm in ejaculated semen and is the most severe form of male factor infertility. It is currently defined as 0% sperm in total ejaculate (WHO, 2010). Azoospermia is classified as obstructive (OA) or non-obstructive (NOA) (3). In OA, spermatogenesis is normal but post-testicular obstruction is present. In NOA, spermatogenesis is impaired such as maturation arrest, disorganised tubules, immature germ cells, or absence of germ cells (3). Due to the severe pathologies, surgical management of NOA is less successful compared to OA (4).

Methods
A retrospective review was performed on 136 consecutive men undergoing TESE (August 2003-October 2014) in the Assisted Conception Unit of Clane General Hospital. A single urologist performed all cases using a standard open surgical technique on the right testis. Patients with severe oligospermia or azoospermia were initially investigated with routine blood tests and semen analysis. Male hormone profile and ultrasonography was in keeping with testis tumour. He proceeded to left radical orchidectomy and concomitant right vasectomy. Histopathology confirmed stage 1 seminoma and maturation arrest on the TESE specimen. Forty six percent (n=67) of procedures involved bilateral testicular biopsies. Thirty five percent (n=51) were from right testes and 19% (n=29) from the left. The mean number of biopsies taken was two.

In assisted reproduction, intracytoplasmic sperm injection (ICSI) is now routinely used in conjunction with in vitro fertilisation in oligospermic/azoospermic men. A single spermatozoon is injected centrally into the cytoplasm of an oocyte. This contrasts to conventional IVF cycles where oocytes are inseminated in vitro with approximately 50,000 spermatozoa. In OA or NOA men an adequate number of sperm invariably will not be retrieved. Recovered sperm can be either used on the day of retrieval for ICSI or cryopreserved for future use. The aim of the present study was to evaluate the effectiveness of ICSI cycles in severe oligospermic (i.e. fresh prepared sample inadequate for ICSI) or azoospermic men following TESE as part of assisted reproduction in a specialist fertility centre in Ireland. Our centre was established in 1985 and fertility treatments have been part of the services since its inception. The primary outcome variables were: sperm retrieval rates, clinical pregnancy rates and miscarriage rates per cycle.

Results
Patient demographics
A total of 146 TESE procedures in 136 men were performed. All cases had documented azoospermia or severe oligospermia (Table 1). The indication for TESE was OA in 59 (n=80) and NOA in 41% (n=56). Mean male age at TESE was 40.3 years. For men with OA, 64% (n=53/80) had a history of varicocele, with or without varicocele reversal (53%; n=27/51). The mean interval between vasectomy and vasectomy reversal was 11 years (range: 3-32 years). The mean interval between vasectomy and TESE was 13.8 years (range: 3-32 years). Overall, 158 (n=20) of patients had a history of undescended testes. One patient with NOA and an atrophic right testis presented with an incidental palpable left testis swelling on day 35 to 40 after embryo transfer. Sperm retrieval rates were 99% (n=79/80) and 33% (n=18/56) for OA and NOA men respectively. Four men had a history of varicocele reversal and persistent infertility (i.e. duration from initial varicocele to reversal and/or increased female age). Twelve of the 13 men successfully had sperm retrieved but only 3 proceeded to ICSI because vas reversal was successful or else the couple had not yet proceeded to ICSI at the time of preparation of this manuscript.

Histopathology
Seventy-two percent (98/136) of men had testicular specimens sent for routine histopathology, of which 58% (n=47/80) had a history of OA. All specimens in the OA group showed normal spermatogenesis. Ninety-one percent (n=51/56) of men had a history of OA. All specimens in the OA group showed normal spermatogenesis. Ninety-one percent (n=51/56) of men was successful or else the couple had not yet proceeded to ICSI at the time of preparation of this manuscript.
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with NOA or oligospermia had testicular tissue sent for histopathology. The frequency of different histopathological patterns for the NOA and oligospermia subgroups are shown in Table 1.

ICSI

The relevant ICSI data is shown in table 2. Of the 98 couples who had sperm stored, 40 have not used the sperm to date and 58 couples have proceeded to ICSI. Seventy-eight percent (n=45/58) of the couples who proceeded to ICSI had a diagnosis of OA. Overall, 114 ICSI cycles were performed and 33 cycles resulted in fertilisation (29%). The clinical pregnancy rate, i.e. detection of a fetal heart beat after day 35 was 23/68 (34%) with no couples lost (4% n=7/114 cycles) (Table 2). The average female age at ICSI was 37 years (range: 27 - 44). Of the couples that proceeded to ICSI, the fertilisation rate per cycle was 34% with OA (n=28/83 cycles) compared to 16% per cycle with NOA (n=5/31 cycles) and the average attempt per couple consisted of 2 cycles (range: 1 - 5).

Discussion

The combination of TESE with ICSI for the treatment of NOA and OA is now performed more frequently as Assisted Reproductive Techniques (ARTs) continue to evolve. Percutaneous methods for sperm retrieval yield success rates in the range of 90-100% for OA and 30-50% for NOA. Reproductive Techniques (ARTs) continue to evolve. Percutaneous methods for sperm retrieval yield success rates in the range of 90-100% for OA and 30-50% for NOA. Congenital causes of OA include cystic fibrosis (CF), congenital absence of the vas deferens (CBAVD), Young's syndrome and prostatic/ ejaculatory duct cysts. CBAVD is caused by an abnormality in the CFTR gene. All males are routinely screened for CF. Their initial testing also includes endocrine, infective, genetic and traumatic abnormalities. Clinical pregnancy rates with ICSI range from 20-44% internationally after sperm is retrieved from men with azospermia. In Ireland, access to ARTs is limited, as these facilities are generally not available in the public sector. Many private clinics are performing a number of ARTs that incur considerable costs for patients. Although private clinics are monitored by the Irish Medicines Board (IMB) and must follow European guidelines, it is important that their results are published in peer-reviewed journals, particularly in this era of media and Internet advertising. The main findings of the present study are that sperm retrieval rates for azoospermia, fertilisation rates with ICSI, and pregnancy and miscarriage rates are in keeping with international results. These findings demonstrate that TESE can be safely and successfully performed to retrieve sperm for ICSI in men with oligo- or azoospermia in specialist centres in Ireland.

Different surgical techniques have been described for TESE procedure, our unit performs the window technique initially described by Devroey et al. in 1995. Alternatively, individual incisions can be made into the upper, middle and lower pole if multiple testicular biopsies are indicated. The advantages of TESE in this setting are that the technique is repeatable, quick to perform and no microsurgical experience is required. The disadvantages include a relatively low rate of retrieved sperm in NOA (17-60%) and the risk of testicular atrophy if multiple biopsies are taken. In micro-dissection TESE, the testicular parenchyma is dissected at 16-25x magnification to search for enlarged islets of seminiferous tubules. It is not performed in our unit as it is costly, micro-surgical expertise is required and our results are satisfactory. Importantly, TESE is contraindicated in the setting of hypopopandrotrophic hypogonadism secondary to pituitary tumours. In these patients oligospermia and azoospermia are successfully managed with medical therapy. An area of controversy relates to the role of TESE in males with primary testis failure (as evidenced by atrophic testes and raised serum FSH) where success rates are low as in this study. A number of studies have investigated adverse factors for predicting pregnancy rates in couples with oligo-/azoospermia. These include increasing male age, aetiology of the azoospermia, testicular histopathology, type of sperm used (i.e. fresh versus frozen), and the use of pentoxysphrine on the ICSI cycle. None of these significantly affect fertilisation, embryo cleavage, clinical pregnancy, live birth and miscarriage rates. However, female age has been repeatedly shown to affect fertilisation, with a female partner less than 37 years of age consistently demonstrating improved fertility rates. Increasing female age is an adverse predictor due to the gradual depletion of ovarian reserve. We counsel couples that are considering ARTs that fertilisation correlates adversely with an increasing female age and may therefore be less likely with repeated ICSI cycles.

Sperm retrieval is successful in approximately 30-50% of men with NOA; our findings are consistent with these international studies. Other predictive factors for sperm retrieval in NOA include testicular histopathology and elevated serum FSH levels. The presence of tubules with spermatozoa on testicular biopsy is the best predictor of positive surgical sperm retrieval in patients with NOA. TESE offers male patients with severe oligo- or azoospermia an opportunity for sperm retrieval for ICSI. We have demonstrated sperm retrieval rates and pregnancy rates that are comparable with international studies in other specialist assisted reproduction centres. These findings support the ongoing role for TESE and ICSI as assisted reproductive techniques for male factor infertility in Ireland.

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References


