

Surgery for azoospermia in the Indian patient: Why is it different?

Rajeev Kumar

Department of Urology, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Obstructive azoospermia is one of the few surgically correctable causes of male infertility. The outcomes of surgery in these patients are variable and often dependent upon the diagnosis and surgical expertise. We aimed to review the reported outcomes in Indian patients and evaluate potential reasons why these outcomes may be different from those reported from other regions. A search was performed on Medline/Pubmed using relevant keywords to identify publications from India on surgical management of azoospermia. The same search was repeated on Google and on the website of the Indian Journal of Urology. Personal emails were sent to prominent urologists performing surgery for azoospermia in India to obtain their opinions and reprints of their published articles. These were then reviewed. Very few articles were identified that pertained to the original search. A large majority of patients are diagnosed with idiopathic infertility. The outcomes of surgery where a clear diagnosis can be made are generally good and often comparable with the published literature. Infections are probably an under-diagnosed etiology. More research and publications are required to determine the etiology of obstructive azoospermia in the Indian men. These would help appropriate patient counseling and treatment.

Key words: Azoospermia, India, infertility, male, vasoepidymostomy

INTRODUCTION

There are few diagnoses in infertile, azoospermic men that are amenable to surgical correction. The most common among these are epididymal obstruction, vasectomy and obstruction of the ejaculatory ducts (EDO). The importance of diagnosing these conditions and treating them appropriately lies in the fact that they can be cured. Surgical treatment of azoospermia has generally been associated with poor outcomes such that few infertility specialists, particularly in India, feel it worthwhile to evaluate these men or counsel them for a surgical correction. The widespread availability of assisted reproduction techniques has further decreased the initiative to seek such treatment over *in vitro* fertilization (IVF). In

2007, the Urological Society of India initiated an effort to develop guidelines for the management of male infertility in India. This stemmed from the perceived differences in the management of infertility in this country as compared to existing guidelines published by the American and European Urological Associations.

We attempted to determine these differences in the surgical management of azoospermia by reviewing the existing literature from India. A search was performed on Medline/Pubmed using the keywords azoospermia, surgery, India, vasoepididymostomy, vasectomy reversal, ejaculatory duct obstruction, TURED and male infertility in varying combinations. The same search was repeated on Google and on the website of the Indian Journal of Urology since a number of articles from India are published in this journal which was not indexed with Pubmed prior to 2008. In addition, personal emails were sent to prominent urologists performing surgery for azoospermia in India to obtain their opinions and reprints of their published articles.

We located less than 50 manuscripts that suited our search terms. Our subjective assessment leads us to believe that the practice of surgery for obstructive azoospermia in India differs from that in the West in five broad areas. These are (a) social importance, (b) etiology, (c) diagnostic facilities, (d) outcomes reporting and (e) economy and training.

For correspondence: Dr. Rajeev Kumar, Department of Urology, All India Institute of Medical Sciences, New Delhi, India.
E-mail: rajeev02@gmail.com

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While we do not attempt to provide a comparative study of these differences, we will discuss these issues in this manuscript.

SOCIAL ISSUES

Parenthood is considered one of the most important life achievements in the Indian society. The value of fertility, and the ignorance about infertility, is such that it is not uncommon to find a male with multiple wives, simply because he has been unable to obtain a child from the previous wife.^[1] The importance of infertility as a public health problem affecting the individual and the family's mental and social wellbeing has resulted in its inclusion in the national program for reproductive and child health.^[2] The importance of surgery to the psychological wellbeing of the couple can be also be gauged from the fact that the overwhelming majority of patients seeking vasectomy reversal in India do so not because they have remarried or want additional children but because they have lost an only child.^[3] This compares with 2.6% patients in the US who seek a vasectomy reversal for this reason.^[4]

It is a well-established fact that the outcomes of surgical reconstruction for azoospermia may be delayed for many months after the actual surgery.^[5] This necessitates the need for patience in defining success. Time, however, seems to be at a premium in a majority of Indian men being treated for infertility. The centrality of fertility in Indian social life has resulted in stigmatization of infertility. A couple failing to conceive within a socially accepted period after marriage is likely to seek help, often from shady unqualified individuals who offer quick, 'guaranteed' solutions and the couple usually ends up spending a number of years before reaching a trained professional for help. This further delays fertility evaluation and treatment and often limits the options then available.

The widely held misconception that infertility is usually due to the female partner is another specific problem faced in the management of infertile men. It is rare to find a man presenting with an abnormal semen report before the female partner has been fully evaluated. Extensive female partner workup has usually been completed before the male is even evaluated, again delaying cause-specific treatment and limiting options.

ETIOLOGY

The diagnosis of obstructive azoospermia in India is most often 'idiopathic'.^[6] Unlike literature published from other centers where unknown causes make up under one-fourth of all cases,^[7,8] a review of our own unpublished data suggests that we were able to determine the cause for obstructive azoospermia in under 20% of our cases. Part of this stems from a difference in the etiology of obstructive azoospermia

seen in Indian men. Although there is little published data on etiology, since vasectomy is an uncommon method of contraception, infection and inflammation are probably the two most important causes.

In a seminal paper on the possible etiology of obstructive azoospermia in Indian men, Phadke *et al.*,^[9] noted a 42% incidence of azoospermia among men with smallpox compared with 18% among men with non-smallpox causes of infertility. The majority of these cases were obstructive (79%) compared with 46% in the control series. While smallpox as a disease has been long eradicated from India, it is not uncommon to still find an occasional man in his late 30s or early 40s presenting with azoospermia and the telltale marks of smallpox on his face. Interestingly, this disease tended to affect the terminal part of the epididymis more than the body or the testis and reconstruction with a vasoepididymostomy (VEA) was usually feasible.

Another region-specific etiology is tuberculosis. Tuberculosis may result in infertility through a number of mechanisms.^[10] Direct involvement of the epididymis or the testis may result in an occlusion of the tubules.^[11] Alternatively, obstruction may occur from the scarring and distortion of normal anatomy. These two causes within the scrotum usually manifest as normal volume azoospermia. Another possible site of involvement is within the prostate/ejaculatory duct region. Inflammation here may cause either a discrete focus of obstruction with dilated ejaculatory ducts or a more diffuse fibrosis, both presenting with low-volume azoospermia. Tuberculosis does not always present as an acute condition and patients may have no recollection of it or specific physical findings. It may thus be one of the causes of a negative surgical exploration for 'idiopathic' obstructive azoospermia. However, even in such cases, empirical anti-tubercular therapy is not indicated. Unfortunately, the outcomes of surgery in such patients are usually poor and they are rarely correctable. Interestingly, Shah presented a series of 34 cases where a significant number with epididymal tuberculosis had resolution of azoospermia after anti-tubercular therapy without any surgery.^[12]

Hydrocele, scrotal calcifications and dense adhesions are also sometimes seen in men undergoing scrotal exploration for obstructive azoospermia, particularly among residents of north-central India. We believe that these could be related to past episodes of scrotal filariasis that is endemic in these parts of the country and is at times referred to as *epididymitis sicca* (Dr. VNP Tripathi-personal communication). The tunica is extremely thick with thin flimsy ductules that are difficult to anastomose (Dr. Rupin Shah-personal communication). The adhesions and scarring in these cases is often so dense that it is impossible to identify the epididymis for a reconstruction. This also makes epididymal injury likely during hydrocele surgery in these men. The association of filariasis and

male infertility including azoospermia has been previously reported.^[13,14]

The large number of 'idiopathic' cases has a significant impact on the outcomes of surgery in our cases. We reviewed the three-year data of all surgical explorations performed for obstructive azoospermia at our centre (unpublished data). While we were able to perform the requisite surgery in all patients with a known cause for azoospermia (previous vasectomy, ejaculatory duct obstruction diagnosed on a trans-rectal ultrasound TRUS or surgically injured vas deferens), among patients with idiopathic vaso-epididymal obstruction, we had a negative surgical exploration in 40% men. Informal discussions with other colleagues who regularly perform this surgery confirm our belief that our experience is not unique. The high rate of failed explorations significantly negatively impacts the perceived benefits of this surgery.

DIAGNOSTIC FACILITIES

While we have discussed the potential role of variable etiology as a cause for the high numbers of 'idiopathic' obstructions and negative explorations in our cases, there is also a potential contribution from varying standards of evaluation and diagnostic facilities. The diagnosis of obstructive azoospermia is based on the presence of normal spermatogenesis within the testis. In the absence of normal spermatogenesis, even if all clinical parameters suggest obstruction, the patient most likely has non-obstructive azoospermia and is not amenable to surgical correction.^[15] Some studies have even suggested that testicular histology may be enough, without a hormonal assay, in diagnosing obstructive azoospermia.^[16] Fine needle aspiration cytology (FNAC) is a minimally invasive technique used to obtain testicular tissue to determine the status of spermatogenesis. The minimal invasiveness of this technique, in comparison with the standard testis biopsy, is achieved at the cost of total tissue available for evaluation. This increases the difficulty in appropriately reporting the sample. While they found a good correlation between FNAC and biopsy, Mehrotra and Chaurasia reported finding inadequate samples in over 10% FNAC specimens obtained for azoospermia.^[17] Additional techniques may help improve the reporting on FNAC specimens.^[18]

The lack of a trained cytopathologist may result in sub-normal spermatogenesis seen in cases of hypospermatogenesis being reported as normal and a negative surgical exploration. Similarly, the failure of an inappropriately trained laboratory technician to identify a few immotile sperms in the ejaculate of men with severe oligospermia and reporting this as azoospermia may result in a negative exploration.

Genetic abnormalities are an increasingly recognized cause

of azoospermia and male infertility. Aberrations vary from those on the long arm of Y chromosome (Yq microdeletions) to aneuploidy. A number of reports have suggested that the genetic abnormalities found in Indian men may be different from those reported in the Western literature.^[19,20] Singh *et al.*,^[21] recently reported the absence of any androgen receptor mutations among a group of 399 infertile men including 277 with azoospermia. Since there is poor correlation between the genotype and phenotype,^[22] genetic abnormalities may be missed during a routine workup and may be a cause for failure of reconstructive surgery.

OUTCOMES REPORTING

Appropriate evidence-based evaluation of any technique requires the presence of adequate literature on the subject. This is also necessary to regenerate faith in the procedure and allow systematic comparison with competing technologies such as IVF. Since we believe that etiologies and outcomes in India are not exactly similar to those currently reported from other centers, it becomes even more important to publish such data from India.

Unfortunately, there are extremely few reports on the outcomes of reconstructive surgery for azoospermia from India. In one of the earliest reports, Pai *et al.*, found VEA to be successful in under 20% of all cases.^[23] Kapur *et al.*^[24] in 1989 reported their results of vasoepididymostomy and found a patency rate of 59% in the absence of adverse factors such as abnormal histology, absence of fluid in the epididymis or hypoplastic epididymis. We have recently reported our modifications and outcomes with both the standard two-suture and longitudinal two-suture techniques of VEA in men with idiopathic vaso-epididymal obstruction. Our success rates have varied from under 40% to 80% in different sub-populations.^[25,26,27] These data suggest that outcomes in our patients may not be as unfavorable as generally perceived.

While data from India on trans-urethral resection of the ejaculatory ducts (TURED) and VEA continues to be scarce, a number of published studies have looked at vasectomy reversal techniques and reported their outcomes. Among the earlier series, Pai *et al.* reported their success rates and follow-up of 10 years following vasectomy reversal.^[23] They performed a splinted anastomosis and reported a 70% patency rate. Singh and Sharma used 8-0 silk sutures with a flap technique for anastomosis and reported a 79% patency rate.^[28] Mehrotra *et al.*,^[29] in 1981, reported greater than 80% patency rates among 114 patients but only a 20% pregnancy rate. Recently, Singh and Kaza reviewed their data of 60 patients, 30 of whom had a macroscopic reversal while another 30 had a microsurgical procedure.^[30] All surgeries were performed unilaterally. Eighty-eight per cent of their patients had a patent anastomosis with a 75% conception rate among those attempting a pregnancy.

ECONOMY AND TRAINING

Over 80% of all medical treatment is paid for 'out of pocket' in India. Infertility treatments, even for the medically insured, are not covered under insurance plans. Cost of treatment is thus an important consideration in managing infertility. Surgical reconstruction, if successful, is a one-time procedure usually with costs less than 20% of a single cycle of IVF with intracytoplasmic sperm injection ICSI that is generally required for azoospermic men. This basic fact makes it amply clear that this would be the preferred choice of men given both options, something that we have routinely experienced while advising our patients about both these options.

A major problem in delivering optimal treatment lies in the lack of availability of appropriately trained urologists. There are no Andrology fellowships in India (one has recently been approved from 2010) and few centers perform these surgeries regularly. An attitude of 'I can also do this-it causes no harm' is often employed with the presumption that the results are no better at any other center. Not only does this contravene the principle of *Primum non nocere*, it also belittles the gains made in this field by other practitioners.

CONCLUSIONS

Surgery for obstructive azoospermia in the Indian patient is associated with a number of features that may not be appropriately explored in the existing literature. There continues to be a lack of research in etiology, evaluation of outcomes and reporting of results. The little available literature suggests that such surgery may have good outcomes. Appropriate training opportunities are essential to provide a fillip to this fledgling field.

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