

Clinical andrology: The missing jigsaw pieces

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The introduction of intracytoplasmic sperm injection (ICSI) in 1992 has revolutionized the management of infertile couples.^[1] The workup of female partner remains important in the era of ICSI since she has to go through the procedure and pregnancy. Attention has been drawn to assisted reproduction technologies (ARTs) in improving embryo quality and pregnancy outcome. In contrast, the evolution of ART has had an adverse impact on the enthusiasm of researchers and clinicians in clinical andrology. Research into the clinical management of infertile men slowed to a grind in the last three decades because ICSI technology promises the couple a baby without exploring the cause of the underlying male infertility. However, the live birth rate utilizing ICSI as the treatment of male factor infertility has stagnated at 30% despite the advancement in ART over the years.^[2] The limitation is linked to abnormalities in male gamete, including high sperm DNA fragmentation. The male gamete contributes half of the DNA content, and the importance of paternal DNA on pregnancy outcome is being increasingly recognized.^[3] In view of the high prevalence of male factor-associated infertility among infertile couples, it is essential to improve the outcome by a comprehensive evaluation and correction of male infertility.^[4] In this issue of the Indian Journal of Urology, four important topics in the field of male infertility are discussed in the reviews. These articles cover several areas of advances in the evaluation and management of infertile men.

The central role of oxidative stress (OS) in the pathogenesis of testicular damage and male

subfertility has been recognized. Increase in OS probably acts as the common pathway and has been demonstrated in clinical conditions related to male infertility including varicocele, cryptorchidism, testicular torsion, genitourinary tract infection, and inflammation.^[5] Numerous laboratory methods for measuring OS have been developed and are broadly classified as direct and indirect assays.^[6] The measurement of redox potential has been recently reported and has the advantage of assessing all known and unknown oxidants and antioxidants in real time with a single test.^[7] The development of laboratory tests for OS is of paramount importance in identifying patients who may benefit from treatment in alleviating OS. The test result is also essential in monitoring treatment progress. Further refinement of reference values of these tests with optimum sensitivity and specificity has been reported and forms a foundation for wider clinical application of the tests.^[8,9]

The understanding of OS as the central pathway in various etiologies of male infertility makes medical therapy in the form of oral antioxidant an attractive option. However, the encouraging result with the use of antioxidants as seen in animal models^[10] has not been reported consistently in human studies, and the use of oral antioxidant therapy in clinical practice is still controversial. Many of the currently available studies are limited by methodological flaws.^[11] In addition to a more stringent study design, the incorporation of OS tests in patient selection may be valuable. A consensus on the efficacy of oral antioxidant therapy in improving fertility can only be reached by inclusion of patients with high OS in the studies.

The expansion of knowledge in male factor subfertility further revealed the complex interplay among different, often coexisting, factors in infertile men. Advances in microbiological techniques allow identification of previously unknown uropathogens that may be related to male infertility. The use of appropriate antibiotic may provide relatively simple and effective treatment in this group of patients. Reproductive endocrinology represents another

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hot topic. The potential benefit of hormonal therapy in idiopathic male infertility and before sperm retrieval procedures^[12] has been reported. Better understanding and identification of pathophysiology of male infertility has significantly broadened the scope of reproductive medicine.

Tremendous development has been witnessed in the diagnostics of infertile men over the last two decades. The advancement in the evaluation of male partner drives the development of new treatment strategies. However, many of these new laboratory tests and treatments are not yet widely applied clinically. The rapidly expanding literature in the field of male infertility will probably transmit the advancements from bench to clinic and benefit infertile couples in the near future. Dramatic revolution in clinical andrology can be anticipated in the years to come. Indeed, it is an exciting time for fertility specialists to move forward in improving both natural pregnancy and ART outcomes by putting together the pieces of jigsaw which have been left aside.

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