

SUMMARY

Seminal oxidative stress (OS), an imbalance between the generation of reactive oxygen species (ROS) by spermatozoa and leukocytes and the antioxidant properties of the seminal plasma, has been widely incriminated as a cause of male infertility (Aitken and Clarkson, 1987; Aitken and Clarkson, 1989; Sharma and Agarwal, 1996; Pasqualotto et al, 2000).

There is substantial evidence from a number of observational (Kodama et al, 1997; Han Ming Shen et al, 1999; Barroso et al, 2000; Ollero et al, 2001) and interventional (Hughes et al, 1996; Lopes et al, 1998a; Aitken et al, 1998; Twigg et al, 1998a; Twigg et al, 1998b; Duru et al, 2000) studies that OS is a major causative factor in the increased level of DNA damage seen in spermatozoa of infertile patients. Spermatozoa and leukocytes are the two important sources of reactive oxygen species (ROS) in semen, the former as the predominant form in the oligozoospermic patients (Aitken et al, 1992; Aitken, 1999; Gil Guzman et al, 2001). Excessive production of glucose 6 phosphate dehydrogenase (G6PD) mediated nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) generation is the most important factor behind the high level of ROS generation observed in the spermatozoa of infertile patients (Aitken, 1999; Gil-Guzman et al, 2001).

Apoptosis plays an important role in regulating germ cell proliferation (Sakkas et al, 1999a). Several studies have suggested that dysregulated apoptosis is also a major factor responsible for male infertility and sperm DNA damage (Sun et al, 1997; Lopes et al, 1998b; Oosterhuis et al, 2000; Gandini et al, 2000). Though several markers of apoptosis have been studied in ejaculated human spermatozoa of infertile patients, caspase activity, which is perhaps the most characteristic biochemical feature of apoptosis, is yet to be studied and localized in mature and immature spermatozoa of the infertile patients. The possible correlation between the caspase activity and the DNA damage, in the mature and immature spermatozoa of fertile men and infertile patients, also is yet to be examined.

There are several studies, which suggest that OS and apoptosis are interlinked in the causation of sperm DNA damage (Gandini et al, 2000; Gil Guzman et al, 2001). It is possible that increased seminal OS in infertile patients may be responsible for triggering apoptosis in the maturing germ cells. This apoptotic activity may be responsible for the increased DNA fragmentation in the ejaculated spermatozoa of infertile patients, which have escaped programmed cell death.

The objective of this study is to investigate the pathogenesis of DNA damage seen in the spermatozoa of infertile patients. The results of this study may have important implications as they may allow for development of possible strategies to prevent or treat this sperm DNA damage

Key words:

1)Seminal Oxidative stress, 2)Sperm DNA damage, 3)Apoptosis, 4)Caspases, 5)NADPH