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ORIGINAL ARTICLE

Oxidative stress and acrosomal morphology: A cause of infertility in patients with normal semen parameters

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Abstract *Introduction:* Acrosome has a vital role in the process of penetration of zona pellucida (ZP). It is highly susceptible to elevated reactive oxygen species (ROS) and oxidative stress (OS). As generally accepted that OS stress has deteriorating effects on sperm functions, we studied the effect of OS on sperm parameters and acrosomal structure in infertile patients with normal semen parameters.

Patients and methods: 30 infertile patients with normal semen parameters and 20 normal fertile controls were included in this study. Semen analysis was performed according to WHO parameters. Oxidative stress was evaluated by measurement of Malondialdehyde (MDA). Acrosomal anomalies were detected by transmission electron microscopy (TEM).

Results: Statistically no significant difference was found between infertile patients and controls regarding semen parameters (p value >0.05). MDA values were statistically highly significant in infertile patients than normal controls (p value <0.001). Acrosomal anomalies were statistically highly significant in infertile patients than normal controls (p value <0.001). Acrosomal anomalies were positively correlated with MDA values. Pearson correlation was 0.645 for correlation between redundant or detached acrosome and MDA values and 0.707 for correlation between acrosomal inclusions and MDA values.

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Conclusion: Percentages of MDA values and acrosomal anomalies were higher in infertile patients than normal subjects. The positive correlation between acrosomal anomalies and MDA values means association between OS and acrosomal anomalies which may indicate negative effects of OS on the acrosomal structure.

1. Introduction

Acrosome is an exocytotic organelle derived from the Golgi apparatus and located at the tip of the sperm head of many mammalian species including humans. Human spermatozoa must have properly formed acrosomes to be able to penetrate the ova and to proceed in fertilization (1–3).

Biosynthesis of acrosome starts in late spermatogenesis by the formation of proacrosomal vesicles in the perinuclear region near the Golgi apparatus of pachytene spermatocytes (4). During the meiotic cell divisions, these vesicles are distributed to the four daughter spermatids. Vesicles coalesce to form one granule attached to the round spermatid nucleus and continues to enlarge by the added material from Golgi apparatus (5,6). During late spermiogenesis, remodeling of acrosome nucleus interaction occurs to give the characteristic shape of sperm head. At this stage Golgi apparatus stops to contribute in acrosomal synthesis. Further maturation occurs during the epididymal transfer to give the characteristic appearance of acrosome on the anterior two thirds of sperm head (7–9).

The acrosome of normal fully mature spermatozoon is formed of outer acrosomal membrane (OAM), acrosomal matrix and inner acrosomal membrane (IAM) (10). OAM fuses with plasma membrane to start the acrosomal reaction at the start of fertilization. IAM is tightly adherent to the nuclear membrane (11). The most important part of acrosome is the acrosomal matrix (12). It is an electron dense material between acrosomal membranes. It consists mainly of proteins, containing many different proteins including proteases, glycosidases, and various zona pellucida (ZP) binding proteins. These proteins are vital for acrosomal reaction and ZP penetration (13,14).

The main function of the acrosome is the acrosomal reaction occurring during gamete interaction. Acrosomal reaction includes fusion of the OAM and plasma membrane to expose the acrosomal matrix and underlying IAM. Once exposed, the acrosomal matrix releases its proteases and other proteins including ZP binding proteins to start the penetration of ZP (15). Acrosome may have other functions such as its involvement in sperm morphogenesis (16,17). The acrosome also anchors the spermatid nucleus to the Sertoli cell through Sertoli-spermatid junctions, including the apical ectoplasmic specializations until the time of spermiation (18,19).

The specialized structure of acrosome, consisting of membranes and proteins, renders it sensitive to high levels of reactive oxygen species (ROS) an oxidative stress (OS) (15). The effect of OS on male fertility has been extensively investigated in recent years (20). Many reports correlated abnormal sperm parameters to OS (21–23). OS negatively affect sperm membranes and proteins. Oxidative modification of proteins by reactive species, especially ROS, is implicated in the etiology or progression of disorders and diseases. Proteins are oxidized by free radicals, whereby the constituent amino acids are variously modified or degraded (24). Lipid peroxidation of sperm membranes and oxidation of proteins negatively affect the acrosomal structure and function (25,26).

Men classified as having idiopathic male infertility have an unexplained reduction in semen quality with no history associated with fertility problems and have normal findings on physical examination and endocrine laboratory testing. Their routine semen analysis shows decreased number of spermatozoa (oligozoospermia), decreased motility (asthenozoospermia), or an increased proportion of abnormal forms (teratozoospermia). These abnormalities usually occur together and are described as the oligoasthenoteratozoospermia syndrome (27). In many cases of male infertility, high level of ROS may be produced and negatively affect sperm functions in the absence of detectable causes and abnormal findings in semen analysis (28–30).

In this study we examined the acrosomal structure and morphology in patients with idiopathic infertility and compared them with those in the normal controls. Furthermore, we correlated acrosomal anomalies with levels of OS.

2. Patients and methods

2.1. Patients

Of 255 consecutive patients, examined between August 2011 to October 2013 in the department of Dermatology, Venereology and Andrology, Qina university hospital, south valley university, 30 patients (Group 1) with primary infertility without any apparent cause and normal semen parameters with the following criteria: sperm concentration was >15 million per milliliter, forward progressive motility $>32\%$ and normal sperm morphology $>4\%$ were included in this study (31). A thorough general and genital examination and complete investigations were performed to exclude any known cause of infertility (as Varicocele, smoking, genetic causes, infectious causes and any other known causes that can be detected by routine investigations). 20 subjects (Group 2) with normal semen parameters and proven fertility admitted to the department for andrological evaluation were included as a control group.

2.2. Semen analysis

Semen samples were collected after 3–5 days of sexual abstinence. Samples were collected by masturbation and examined directly after liquefaction. Semen analysis was performed according to WHO guidelines. Ejaculatory volume, pH, viscosity, sperm concentration, sperm motility and sperm morphology were detected under standardized conditions (31). 200 sperms have been counted per sample to detect the percentage of normal spermatozoa, head abnormalities, midpiece abnormalities and tail abnormalities. Leukoscreen test was