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Alterations in the functional system of NO-synthase/arginase of spermatozoa in human subjects with different infertility forms

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The precise biochemical mechanisms underlying the male infertility are not clearly understood. Altered NO production has also been implicated in the pathogenesis of the male infertility. It is derived from L-arginine by NO-synthases (NOS). It is known that reciprocal regulation of arginase and NOS in L-arginine-metabolizing pathways exists. The proper balance between NOS (oxidative L-arginine methabolism) and arginase (non-oxidative L-arginine degradation) activity (expression) is essential for maintenance of NO homeostasis. The present study was, therefore, designed to evaluate the changes in the activity of L-arginine metabolic enzymes – NOS and arginase in spermatozoa of patients with infertility.

This study involved 72 infertile men with different forms of pathospermia. Subjects were classified into 4 groups as having different forms of pathospermia. The control group consisted of 20 healthy men with somatic fertility, normozoospermia and confirmed parenthood.

Spermatozoa arginase activity was measured by determining levels of urea production and expressed as nmol urea per min per mg protein. Spermatozoa NOS activity assay was performed by monitoring the rate of conversion of L-arginine into citrulline. NOS activity was expressed as pmol citrulline/min per 1 mg of protein.

The enzymatic assay revealed significant difference in NOS and arginase activity in spermatozoa between patients with pathospermia and the control group. It was found that total NOS activity in patients with oligozoospermia, asthenozoospermia and oligoasthenozoospermia were greater than that in normozoospermic fertile men. The most expressed changes in total NOS activities were observed in patients with leukocytospermia. There was

a significant decrease in arginase activity in sperm cells of patients with pathospermia compared the control group. Therefore arginase/NOS ratio was significantly decreased in patients with pathospermia. It is of interest to note that the mentioned ratio was decreased over an order of magnitude in leukocytospermic patients relative to healthy controls.

It was found a reduced eNOS activity in patients with different forms of pathospermia relative to normozoospermic men, with no group difference in eNOS activity. At the same time sperm iNOS activity was increased significantly in the all group of patients with pathospermia as compared with the control group. It indicates overproduction of NO in sperm cells of pathospermic patients. Men with leukocytospermia were distinguished to have the most expressed iNOS activity. The iNOS/cNOS ratio was increased in patients with oligozoo-, asthenozoo-, oligoasthenozoospermia and leukocytospermia compared to normozoospermic men.

Thus, the decreased arginase/NOS ratio in pathospermic patients is largely due to the reduction of arginase activity and drastic activation of NOS, supporting their prominent role in the aetiology and/or pathophysiology of pathospermia. The decreased arginase activity most likely led to increased NO production in sperm cells. Depressed arginase activity might be related to the enzyme inhibition by nitrite, the major stable metabolite of NO. The most expressed changes in NO-synthase and arginase activity were observed in patients with leukocytospermia. This leads to the distruption of L-arginine metabolism. Drastically increased iNOS/cNOS ratio in patients with decreased fertility potential indicating predominance of iNOS.