ROLE OF MITOCHONDRIAL DYSFUNCTION IN SPERM MOTILITY: ANTIOXIDANTS DRUG TARGETED TO MITOCHONDRIA.

Silveira, P.¹; Radi R.²; Sapiro R.¹; Cassina, A.²

¹Departamento de Histología y Embriología, Facultad de Medicina UdelaR, Uruguay
²Departamento de Bioquímica, Facultad de Medicina, UdelaR-CEINBIO, Uruguay.

One of the causes of human infertility is the loss of normal function of sperm. Experimental results show increasingly the responsibility of ROS in sperm damage. Defective human sperm function is associated with high levels of reactive oxygen species (ROS) generated by the spermatozoa. These reactive species cause lipid peroxidation and DNA damage that result in loss of fertilizing potential in vivo and in vitro. In sperm cells mitochondria are the main intracellular source of ROS. These highly oxidizing and nitrating species may interact with mitochondrial proteins and lipids leading an even greater increase in ROS formation. Sperm cells are particularly vulnerable to oxidative stress because the limited volume and restricted location of their cytoplasm space constraint the availability of intracellular antioxidant enzymes capable of scavenging ROS. Our hypothesis is that one of the causes of male infertility is sperm mitochondrial dysfunction leading to an increase of nitrooxidative stress. In this work we studied mitochondrial function by High Resolution Respirometry in 130 semen samples from men that consulted an Andrology Clinic for fertility evaluation. We also used two fluorescent probes; DHR (dihidrorhodamine-1,2,3) and boronates to demonstrate the mitochondrial ROS formation. Confocal microscopy was used to show formation of ROS by living sperm cells.

The study of mitochondrial activity in the semen samples showed a positive correlation between the state of mitochondrial coupling and sperm motility. In permeabilized sperm cells, in the presence of respiratory substrates, mitochondria produced ROS. These production was inhibited by methionine (peroxinitrite sacavanger). We also evidenced that mitochondria of intact sperm cells produced peroxynitrite. Moreover, sperm motility was partially recovered when the samples were treated with mitochondrial target antioxidant drugs. These data show that mitochondrial dysfunction may contribute to impair fertility potential of sperm and cause male infertility. Support: PEDECIBA-UdelaR, CSIC, MERK-SERONO

Key words: male infertility, sperm dysfunction, mitochondria.