Antioxidants modulation of sperm genome and epigenome damage: Fact or fad? 
Converging evidence from animal and human studies

Abstract

DNA damage is the most common effect of oxidative stress on human spermatozoa. Since an imbalance between scavenging antioxidants and pro-oxidants have been implicated in the pathophysiology of oxidative-based DNA damage, the administration of antioxidants has been practiced for years in an attempt to improve sperm quality necessary for reproductive success. A growing body of evidence has implicated several regimens of antioxidants, by oral administration or in vitro supplementation to culture media, in improving various sperm parameters namely DNA damage. While these studies exhibited heterogeneity in treatment regimens, variability in methodology, there is currently a lack of quality evidence on the association between micronutrients and sperm DNA integrity. Yet, another ancillary effect of antioxidants administration on sperm is the shaping of the epigenome. Recent evidence from animal and human studies explored the epigenome after antioxidants supplementation, which invokes the so-called “fortification” of the epigenome. However, few studies on humans analyzed the sperm epigenome specifically global methylation profile using antioxidants formulations, some showed an interventional effect others didn’t. However, the promising experimental studies on mice were congruent and supported the notion that epigenetic marks in spermatogenesis are dynamic and can be modulated by nutritional exposure. Moreover, the sperm epigenome transfers a so-called epigenomic map to the offspring which influences their development. This lack of strong clinical evidence on the beneficial effects of antioxidant and micronutrients supplementation on sperm genome and epigenome, should not deter us from more basic and clinical research on this issue. Hopefully, further epigenome-wide studies focusing on the prenatal environment, to evaluate developmental influences and the role of antioxidant therapy, will be a promising route for embodying the possibility of “normalization” and restoration of some offspring health cues.