Role of oxidative stress and interleukin-6 in varicocele patients
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Objectives: Varicocele affects sperm quality thereby affecting male fertility. The exact mechanism of fertility disturbance induced by a varicocele is unknown. Both varicoceles and cytokines are involved in the production of reactive oxygen species (ROS). Cytokines released by various immunocompetent cells in the male urogenital tract are capable of influencing sperm function and fertility. It is known that IL-6 levels are elevated in the seminal plasma of infertile men. We measured the levels of ROS, non-enzymatic total antioxidant capacity (TAC), a composite ROS-TAC score, and interleukin-6 (IL-6) levels in infertile patients with varicocele comparing them to normal healthy men.

Design: Prospective study

Material and Methods: Semen specimens from 39 infertile patients with varicocele were compared for semen characteristics, levels of ROS, IL-6 and ROS-TAC score. Sixteen normal healthy men were included as controls. ROS production in the semen specimens was measured by the chemiluminescence assay and the results were expressed as Log (ROS + 1) X 10^6 counted photons/minute/20 X 10^6 sperm. Total antioxidant capacity was measured in the seminal plasma and expressed as molar Trolox equivalent. A composite ROS-TAC was calculated. A score lower than 45 was considered as abnormal. IL-6 levels were measured in the seminal plasma by an enzyme-linked immunosorbant assay (ELISA) and results were expressed as pg/mL of seminal plasma.

Results: Infertile varicocele patients had higher levels of ROS (1.96 ± 0.16) compared to controls (1.29 ± 0.27; p = 0.04). The TAC levels and ROS-TAC scores were lower in the varicocele group (1112.48 ± 69.81 Vs 1494.99, p = 0.09; 34.90 ± 2.2, and 48.08 ± 2.2; p = 0.004) respectively. High levels of IL-6 were seen in patients with varicocele compared to controls [median and 25%, 75% interquartile range; patients: 131.61 (43.87, 267.61) versus controls: 4.39 (0, 87.74; p <0.001)]. The IL-6 levels were positively correlated with ROS levels (r = 0.37, p = 0.002) and inversely related with ROS-TAC scores (r = -0.43, p <0.001). There was no relationship between IL-6 and TAC, sperm concentration, or sperm morphology. Of all the semen characteristics, only motility was negatively correlated with IL-6 (r = -0.24, p = 0.02).

Conclusions: Infertile varicocele men have high seminal oxidative stress. Elevated levels of IL-6 in the semen and its negative association with sperm motility suggest its role in the impairment of fertility in these men. Both oxidative stress and IL-6 may contribute to the pathophysiology of varicocele; and can be used as diagnostic markers of infertility in these patients. This work was supported by a research grant from the Cleveland Clinic Foundation.