

Varicocele adversely impacts germ cells metabolism by down-regulating MCT-4 and GLUT-3 proteins level; a rat model study

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Introduction:

Varicocele is considered the main treatable cause of male infertility, detected in 35% and 80% of primary and secondary infertile men, respectively. It is characterized by dilated efferent testicular veins with retrograde blood flow. Suggested pathophysiological processes include oxidative stress, inflammation, heat stress, among others. Because varicocele alters testicular metabolism, in this study Glucose transporter-3 (GLUT-3) and Monocarboxylate transporter (MCT-4) proteins level, as key transporters of glucose and lactate, in testicular tissue of experimentally induced varicocele in rats were examined.

Methods:

A total of 40 male adult *Wistar* rats were subdivided into sham (Sham-2) and varicocele two months (VCL-2), and sham (Sham-4), and varicocele four months (VCL-4) induced groups (N= 10 rats *per* group). Following 2 (Sham-2 and VCL-2) and 4 (Sham-4 and VCL-4) months after varicocele induction, left testicular tissues were dissected out and fixed with formalin (10%) fixative solution. Then, samples were stained with H&E for histopathological, Johnsen score (JS), Tubular differentiation and Spermiogenesis indices (TDI and SPI) examinations. IHC was carried out for Glut-3 and MCT-4 proteins, and positive cells *per* mm² was calculated. Moreover, the

pixel-based frequency analyses were performed by image J software to assay IHC-positive reactions intensity, mean intensity, IHC stained area percentage, and proteins expression pattern.

Results:

Our results demonstrated TDI, SPI, JS, and protein levels of Glut-3 and MCT-4 diminished in varicocele-induced groups versus the sham groups. No histological alterations were observed, while IHC analysis demonstrated a reduction in Glut-3 and MCT-4 proteins levels in VCL-4 group compared to VCL-2 group.

Conclusions:

VCL decreases testicular Glu-3 and MCT-4 protein levels. We suggest that VCL-induced reduction in glucose transporters may result in low lactate production by Sertoli cells. Reduced lactate production in corroboration with diminished monocarboxylate transporters may result in altered supply of energy to germ cells, spermatogenesis arrest, and might be another important reason for germ cells apoptosis in VCL.

Keywords: Varicocele, Rat, Testis, Glut-3, MCT-4