Influence of Anticancer Agent on Erectile Function; Vincristine Caused Erectile dysfunction Through Endothelial Dysfunction and Injury to the Cavernous Nerve in Rats

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Objectives:

Globally, various chemotherapeutic agents are administered to patients with cancer. Analysis of the US Food and Drug Administration (FDA) Adverse Event Reporting System (AERS) database revealed that vincristine (VCR) increased the risk of erectile dysfunction (ED). Accordingly, we investigated the mechanism underlying ED in rats administered VCR.

Methods:

Twelve-week-old male Wistar-ST rats were stratified into control and VCR groups. VCR (0.1 mg/kg) was administered intraperitoneally in a single dose to rats in the VCR group. Erectile and endothelial functions were measured using ICP and isometric tension, respectively, after 4 weeks of VCR dosage administration. Expression of biomarkers for oxidative stress (NADPH oxidase and catalase), inflammation (IL-6) and endothelial repair factors (VEGF, MCP-1, and PAI-1) was also examined.

Results:

VCR-treated rats presented significantly decreased ICP/MAP ratios (VCR: 0.48 ± 0.04, control: 0.65 ± 0.06; $p < 0.01$). Relaxation responses induced by acetylcholine and electrical stimulation were decreased in the VCR group compared to those of the control group ($p < 0.05$). The expression of NADPH oxidase-1 and IL-6 mRNA in corpora cavernosa was upregulated in the rats belonging to the VCR group compared to that of the control group rats ($p < 0.01$). Catalase, VEGF, MCP-1, and PAI-1 mRNA expression in the VCR group was downregulated compared to that in the control group ($p < 0.01$).

Conclusion:

Administering the anti-cancer agent VCR resulted in ED in rats, as the oxidative stress marker NADPH oxidase-1and inflammatory cytokine IL-6 were upregulated. VCR caused damage to rat endothelial functioning and the cavernous nerve. Therefore, cancer survivors who are administered vincristine should be carefully screened for ED.