CORPORAL Cavernosal Apoptosis following Radical Prostatectomy in the Canine Model

Carlumandarlo E.B. Zaramo*, Cleveland, OH; Nina G Hall, Birmingham, AL; Rupesh Raina, Ashok Agarwal, Inderbir Gill, Craig D. Zippe, Cleveland, OH

Introduction and Objective: Erectile dysfunction (ED) following human radical prostatectomy (RP) is a well-documented event that may involve a neuropraxia-induced apoptosis leading to corporal fibrosis. We developed a canine model to assess anti-apoptotic protein, phosphorylated AKT^p473 (AKT/PKB^p473) and the pro-apoptotic protein, phosphorylated-Bad^pSer136, as markers of apoptosis in the corporal cavernosal tissue. We hypothesize that these markers may reflect the degree of neuropraxia injury following radical prostatectomy. Methods: Six adult male canines (n =6) underwent RP. At three RP time points (0.5 hr pre-RP, 0.5 hr post-RP, and 1 hr post-RP), whole blood was extracted from corporal cavernosal tissue and systemic brachial veins of each animal. To avoid rapid commencement of apoptosis, samples were stored on ice (≤30 sec.) and centrifuged at 14,000 × g for 15 minutes. Equal amounts of protein were resolved on 4-20% gradient SDS-PAGE gels and probed with rabbit antibodies against phosphorylated-AKT/PKB^pSer473, phospho-Bad^pSer136, and endothelial nitric oxide synthase (eNOS). Results were quantified by the Gel-Pro©™ program and expressed as mean integrated optical densitometry units (IOD). Results: In four of the six samples, phospho-AKT^pSer473 levels in the corpora cavernosa plasma increased from the pre-RP to 0.5-hour post-RP, returning to baseline at 1-hour post-RP. AKT levels remained unchanged in the peripheral plasma. Phospho-Bad^pSer136 levels were obtained in three of the six samples and were elevated at 1-hour post-RP. eNOS levels reflected the activity of AKT and were elevated only at the 0.5-hour post-RP. Conclusions: Our early results in a canine model demonstrate that radical prostatectomy induces corporal cavernosal apoptosis with early up-regulation of phospho-AKT and eNOS and subsequent elevation of the pro-apoptotic Bad^pSer136 protein. These protein markers reflect ongoing apoptosis in the corporal cavernosal tissue and can quantify the degree of neuropraxia following radical prostatectomy.

Data are presented as mean ± SD unless otherwise noted

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