Tissue-specific expression of connexin 43 in the cavernous artery may explain why ED occurs prior to cardiac-cerebral vascular disease.

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**MP86-06**

**COMBINATION THERAPY USING HUMAN ADIPOSE-DERIVED STEM CELLS ON THE CAVERNOUS NERVE AND LOW-ENERGY SHOCKWAVES ON THE CORPUS CAVERNOSUM IN A RAT MODEL OF POSTPROSTATECTOMY ERECTILE DYSFUNCTION**

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**INTRODUCTION AND OBJECTIVES:** We investigated combined therapeutic efficacy of human adipose-derived stem cells (h-ADSCs) application on injured cavernous nerve and low-energy shockwave therapy (SWT) on the corpus cavernosum in a rat model of post-prostatectomy erectile dysfunction.

**METHODS:** Rats were randomly divided into five groups: Control, BCNI (bilateral cavernous nerve injury), ADSC (BCNI group with h-ADSCs on the cavernous nerve), SWT (BCNI group with low-energy SWT on the corpus cavernosum), and ADSC/SWT (BCNI group with a combination of h-ADSCs and low-energy SWT). After four weeks, erectile function was assessed using intracavernoosal pressure (ICP). The cavernous nerves and penile tissue were evaluated through immunostaining, western blotting and a cyclic guanosine monophosphate (cGMP) assay.

**RESULTS:** ADSC/SWT significantly improved ICP compared to the other experimental group. ADSC had significantly increased ß-III tubulin expression of cavernous nerve, and SWT had markedly enhanced vascular endothelial growth factor (VEGF) expression in corpus cavernosum. The ADSC/SWT group had a significantly increased alpha smooth muscle content (P < .05), neural nitric oxide synthase (nNOS) of the dorsal penile nerve (P < .05), endothelial nitric oxide synthase (eNOS) protein expression (P < .05), and cGMP level (P < .05) compared to ADSC or SWT alone group. In addition, ADSC/SWT reduces the apoptotic index in corpus cavernosum.

**CONCLUSIONS:** In this study, h-ADSCs showed effect on recovery of injured cavernous nerve and low-energy SWT improved angiogenesis in the corpus cavernosum. The h-ADSCs combined with low energy SWT showed beneficial effect on the recovery of erectile function in a rat model of post-prostatectomy erectile dysfunction.

**Source of Funding:** none

**MP86-07**

**IMPACT OF TISSUE SEALING SHEET ON ERECTILE DYSFUNCTION IN A RAT MODEL OF NERVE-SPARING RADICAL PROSTATECTOMY**

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**INTRODUCTION AND OBJECTIVES:** Recovery rates for erectile dysfunction (ED) following radical prostatectomy (RP) remain unsatisfactory, even with cavernous nerve (CN)-sparing surgery. We found that ED following CN dissection occurred due to not only technical nerve injury, but also other factors such as inflammatory changes or surgical stress. Intraoperative bleeding, a parameter of the surgical stress, influenced the recovery of erectile function after nerve-sparring RP. A tissue sealing sheet, TachoSil®, has recently been used to prevent intraoperative bleeding in RP. However, the efficacy of tissue sealing sheet for erectile function following nerve-sparring RP remains unclear. We evaluated the effect of tissue sealing sheet on nerve injury-related ED.

**METHODS:** Male Sprague-Dawley rats were randomly divided into 3 groups and subjected to sham operation or bilateral CN dissection with or without TachoSil®. In the group with TachoSil®, immediately after CNs were dissected bilaterally from the major pelvic ganglion to the apex of the prostate without crushing or cutting, CNs were sealed with TachoSil®. One urologist performed all operations. Another researcher assessed erectile function by measuring intracavernosal pressure (ICP) and mean arterial pressure (MAP) during electrical pelvic nerve stimulation. Erectile function was evaluated 4 weeks postoperatively. Next, expressions of interleukin-6 (IL-6) and tumor growth factor-β (TGF-β) mRNA in the major pelvic ganglion (MPG) and CN were examined by real-time polymerase chain reaction at 6 and 24 h after surgery.

**RESULTS:** Four weeks after CN dissection, the TachoSil® group showed significantly greater ICP/MAP than the group without TachoSil®. ICP/MAP in the TachoSil® group was similar to that in the sham group. Also, expressions of IL-6 and TGF-β in both groups with and without TachoSil® were increased at 6 and 24 h after surgery compared with the sham group. Importantly, expressions of IL-6 and TGF-β in the TachoSil® group were markedly suppressed in the MPG and CN compared with the group without TachoSil®.

**CONCLUSIONS:** The TachoSil® tissue sealing sheet attenuated postoperative inflammatory changes and improved erectile function following CN dissection in a rat model of nerve-sparring RP. These results suggested that the tissue sealing sheet may reduce not only intraoperative bleeding, but also inflammatory changes. The tissue sealing sheet may thus represent a useful therapeutic approach to improve ED occurring after nerve-sparring RP, and is available for robotic-assisted laparoscopic prostatectomy.

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**MP86-08**

**EFFECT OF COMBINATION THERAPY WITH NERVE GROWTH FACTOR AND BASIC FIBROBLAST GROWTH FACTOR IN A RAT MODEL OF CAVERNOUS NERVE INJURY**

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**INTRODUCTION AND OBJECTIVES:** Prostate cancer patients who undergo radical prostatectomy often experience postoperative erectile dysfunction (ED) because of cavernous nerve injury. This study evaluated combined therapeutic effect of nerve growth factor (NGF) and basic fibroblast growth factor (bFGF) in a rat model of cavernous nerve injury.

**METHODS:** A total of 30 Sprague-Dawley rats (10-week old) were divided into six groups (n = 5 in each): normal controls, bilateral cavernous nerve injury (BCNI group), penile subcutaneous injection of hydrogel only after BCNI (Hydrogel group), bFGF-hydrogel after BCNI (bFGF group), NGF-hydrogel after BCNI (NGF group), and bFGF/NGF-hydrogel after BCNI (Dual group). After four weeks, erectile function was assessed using intracavernosal pressure (ICP). The cavernous nerves and penile tissue were evaluated through immunostaining, western blotting and a cyclic guanosine monophosphate (cGMP) assay.

**RESULTS:** BCNI group showed significantly decreased ICP value compared with normal group. All treatment group (bFGF, NGF, and Dual) showed better response than BCNI group, and dual growth factor significantly improved ICP compared to other treatment groups. Dual group had a significantly increased expression in alpha smooth muscle content, and endothelial nitric oxide synthase (eNOS) of the dorsal penile nerve compared to bFGF or NGF alone group. In addition, Dual group showed most significant recovery in apoptotic index in
corpus cavernosum. Western blot analysis showed molecular changes in cavernosal tissues. Treatment groups showed tendency close to normal group, and Dual group showed most similar results with normal group (PECAM-1, eNOS, and cGMP).

CONCLUSIONS: In this study, dual growth factor (bFGF and NGF) showed beneficial effects on erectile function recovery in a rat model of cavernous nerve injury compared with single growth factor injection (bFGF or NGF).

Source of Funding: none

MP86-09
WATER JET DISSECTION OF THE Cavernous NERVES: A COMPARATIVE STUDY TO BLUNT Cavernous NERVE INJURY IN A RAT MODEL AND ITS IMPLICATION ON ERECTILE FUNCTION

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INTRODUCTION AND OBJECTIVES: Postoperative erectile dysfunction (ED) remains a commonly prevalent outcome after radical prostatectomy (RP) despite three decades of evolving surgical techniques and innovative prevention and treatment strategies. Water-jet technology is widely utilized for dissection in neurosurgical procedures due to its minimal effects on the function of nerves. Our objective is to study the impact of water-jet dissection (WJD) of the cavernous nerves (CNs) on postoperative erectile function (EF) and compare it to standard dissection in an established model of blunt surgical trauma of CNs in rats.

METHODS: Fifteen Sprague-Dawley male rats were randomly divided into two groups; group 1 (WJD) rats were subjected to WJD and barotrauma of bilateral CNs using a fluid pressure of 15 atm (n=8), while group 2 (BT) rats were subjected to standard dissection of the nerves and blunt trauma of bilateral CNs (n=7), in a survival surgery. After 4 weeks, postoperative erectile function was assessed by measuring the intracorporeal pressure (ICP) during 3 electrical stimulations of the CNs under anesthesia. Euthanasia was performed after harvesting the penile tissue for histopathological examination. The peak ICP was noted and the area under the curve (AUC) was calculated for each stimulation. Cross-sections from the penile tissue were prepared and stained with Masson trichrome dye. Digital copies of the slides at x100 and x200 magnifications were obtained and analyzed using image analysis software (Image J) to quantify the fibrosis ratio within each corpora cavernosa.

RESULTS: Both animal groups had a comparable preoperative weight with a mean of 609.6 ± 99.9 gm and 570.2 ± 72.8 gm in groups WJD and BT, respectively (p=0.406). WJD rats demonstrated a significantly higher mean peak ICP of 65.7 ± 32.2 cm H2O in comparison to a mean peak ICP of 33.4 ± 23.5 cm H2O in BT (p<0.0001). WJD was also associated with more sustainable rise in the ICP in comparison to BT as the mean AUC was 3425.7 ± 1671 and 2163.2 ± 1551, respectively (p=0.012). The ratio of fibrosis was comparable between the groups with a mean of 63.7% ± 11.5 vs. 64% ± 7 for x100 magnification (p=0.933), and 68% ± 11.3 vs. 64.6 % ± 8.5 for x200 magnification (p=0.372) in WJD and BT, respectively.

CONCLUSIONS: In this study, WJD of the CNs was associated with a significantly better postoperative ICP than blunt trauma. Thus WJD had less of an effect on EF in this rat model of RP. Clinical studies are needed to investigate the effect of WJD on EF in humans post RP.

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MP86-10
MELATONIN ADMINISTRATION REORGANIZES Cavernous Tissue, UPREGULATES SIRT-1 GENES, AND DECREASES OXIDATIVE DAMAGE IN Diabetic Rats

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INTRODUCTION AND OBJECTIVES: Enhanced oxidative stress due to diabetes is thought to prompt endothelial dysfunction associated with erectile dysfunction. Research has shown that free radicals modulate several signaling pathways, including those related to sirtuins, and that melatonin activates SIRT1 and decreases oxidative stress in tissues. In response, in this study we aimed to determine whether melatonin benefits the preservation of SIRT1 activation in diabetic rats.

METHODS: We administered melatonin (10 mg/kg, i.p.), insulin (6 U/kg, s.c.), or saline daily for 10 weeks to 50 streptozotocin-induced diabetic Sprague–Dawley male rats. To determine melatonin’s antioxidative effect, we evaluated MDA, c-GMP, total NOS activity, caspase-3 activity, and 8-OHdG level in cavernosal tissue and SOD, catalase, and 8-OHdG level in plasma. We assessed erectile response by determining MAP and ICP during the electrical stimulation of the cavernous nerve. We used Western blotting to determine the protein expression of SIRT1, pro-caspase-3, caspase-3, and nNOS, and the ratio of smooth muscle collagen content in the cavernosum. With results expressed as M ± SD, we evaluated the statistical significance of differences among experimental groups via analysis of variance with Bonferroni correction and significance set at p<0.05.

RESULTS: After 10 weeks, the body weights of diabetic rats were significantly less than those of controls. The ratio of max ICP to MAP had significantly decreased in diabetic ED rats compared to other groups. Both melatonin and insulin treatments reduced the oxidative stress caused by the diabetic state’s increased generation of free radicals, though combined treatment most efficiently prevented diabetes-induced damage (Table 1). The sirtuin architecture significantly deteriorated in the corpus cavernosum of diabetic rats compared with that of controls, and melatonin improved this cavernous structural disorder. The expression of the SIRT1 protein decreased in the diabetic group compared to that in the controls, though the expression of caspase-3 increased. By contrast, the expression of SIRT1 increased in the melatonin-treated diabetic group compared to that in other groups.

CONCLUSIONS: Melatonin’s ability to improve diabetes-induced ED likely relates to its activation of SIRT1 expression, which prompts the suppression of apoptosis and resistance to oxidative stress.

Source of Funding: None

MP86-11
IS THERE A RELATIONSHIP BETWEEN PHOSPHODIESTERASE TYPE 5 INHIBITORS (PDE5I) AND PROSTATE CANcer BIOCHEMICAL RECURRENCE?


INTRODUCTION AND OBJECTIVES: There have been conflicting studies looking at an association between prostate cancer biochemical recurrence (BCR) after radical prostatectomy (RP) and PDE5i use.

METHODS: Patients completed a 1 - 5 assessment of PDE5i use pre-RP and serially after RP in a prospective, quality of life study evaluating men post-RP. Men who had data on PDE5i use at 3m, 6m, 9m, and 12m in the first year following RP were included in the analysis. The tested predictors of BCR were: age, PSA, Gleason score (G), surgical margin status (SMS), seminal vesicle involvement (SVI), extra capsular extension (ECE), and lymph node involvement (LNI).