Sexual Function/Dysfunction: Basic Research & Pathophysiology

Moderated Poster 38

Sunday, May 15, 2022 **7:00 AM-8:15 AM**

MP38-01

BIOACTIVE FIBROUS MEMBRANE CONTAINING ENDOGENOUS NERVE GROWTH FACTOR PROMOTES CELLULAR AND FUNCTIONAL RECUPERATION OF IMPAIRED CAVERNOUS NERVE: AN *IN VIVO* ANIMAL STUDY

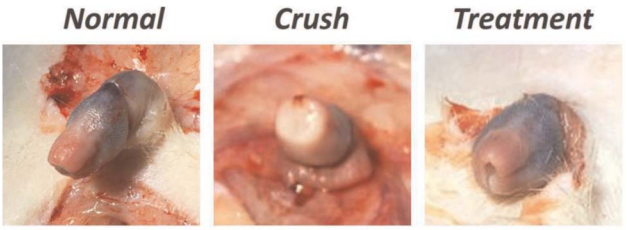
Paulo Mota, Cabeceiras de basto, Portugal; Marta Casanova, Braga, Portugal; Helena Vala, Carmen Nóbrega, Vila Real, Portugal; Alain Morais, Braga, Portugal; Catarina Silva, Guimarães, Portugal; Sara Anacleto, Braga, Portugal; Alexandre Barros, Guimarães, Portugal; Rui Reis, Braga, Portugal; Estêvão Lima, Cabeceiras de basto, Portugal; Albino Martins, Nuno Neves, Braga, Portugal*

INTRODUCTION AND OBJECTIVE: Prostate cancer is a frequent disease and the radical prostatectomy one of the most used treatment when the cancer is localized. This procedure commonly causes erectile dysfunction (ED) by injure the cavernous nerve (CN) during the surgery.With this research we investigate the ability of a bioactive fibrous membrane (FM) to regenerate the damaged CN in a rat model of CN injury.

METHODS: Male Sprague–Dawley (SD) rats were distributed by 4 experimental groups: *sham* (only a lower midline abdominal incision), negative control (lower midline abdominal incision with pelvic dissection and CN crush but no FM implantation), electrospun fibrous membrane [*eFM*] (with CN crush and FM implantation) and electrospun fibrous membrane biofunctionalized with NGF from rat urine [*eFM-uNGF*] (with CN crush). Function was evaluated five weeks later after an injection of apomorphine by glans observation (visual scoring) and intracavernous pressure (ICP) measurements. Neurogenic genes expression and Histological and Immunohistochemical analysis of CN and cavernous tissue was performed.

RESULTS: in this model of bilateral CN crush the treatment with implanted bioactive fibrous membrane induces CN regeneration and restoration of erectile function ($p < 0.001$) (figure), showing a significant increased number of smooth muscle cells and nNOS and eNOS contents. Additionally, the bioactive fibrous membrane promotes a CN protective effect and increase the nerve regeneration capacity by increasing the number of myelinated axons and nNOS-positive cells, recovering from the CN fibrosis observed in rats not treated.

CONCLUSIONS: This personalized regenerative strategy could help better recovery of erectile function after CN injuries, and it may constitute an effective novel option to prostate cancer patients suffering from ED after being subject to radical prostatectomy.



	Normal Rat	Bilateral Cavernous Nerve Crush Injury Rat Model	
		Crush	Crush + Treatment
Erection (%)	97 ± 24	9 ± 36	64 ± 24

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MP38-02

IMPAIRED NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD+) MEDIATING ENDOTHELIUM-INDEPENDENT RELAXATION WITH AGING ON HUMAN CORPUS CAVERNOSUM

Serap Gur, Ankara, Turkey; Suresh C. Sikka, Sudha Talwar, New Orleans, LA; Didem Yilmaz-Oral, Adana, Turkey; Asim Abdel-Mageed, Wayne J. G. Hellstrom, New Orleans, LA*

INTRODUCTION AND OBJECTIVE: Nicotinamide adenine dinucleotide (NAD^+), a small-molecule cofactor for NAD^+-dependent enzymes, such as the sirtuins (SIRT) is a coenzyme for redox reactions, making it central to energy metabolism. SIRT-stimulation by hydrogen sulfide (H_2S) reverses redox changes. Remarkably, ageing is accompanied by a gradual decline in tissue and cellular NAD^+ levels leading to a slow rate of glycolysis, mitochondrial electron transport, and ATP formation. This study aimed to evaluate the effect of aging on NAD+-induced relaxation of human CC.

METHODS: Human CC from ED patients (n = 12) undergoing penile prosthesis surgery were processed for organ bath. After pre-contraction with phenylephrine (Phe, 10μM), concentration-response curves were performed for NAD+ (10nM-100μM) on CC from middle-aged and aged individuals. Underlying mechanisms of relaxation were evaluated by inhibitory agents, namely L-NAME [an inhibitor of NOS], ODQ (a soluble guanylyl cyclase inhibitor), and tetraethylammonium (TEA, non-selective K^+ channel blocker). The relaxation responses to electrical field stimulation (EFS), acetylcholine (ACh), sodium hydrogen sulfur (NaHS, a donor of H_2S), adenosine (Ado), and contractile response to EFS were examined in the presence or absence of NAD+(10μM). Cellular localization of eNOS, nNOS, and VEGF expressions was performed by Western blotting and immunofluorescence. For the primary cell culture of human penile tissue samples, the cells in growth media for 2 weeks were characterized for smooth muscle cell protein marker, treated with 500μM of NAD+ either 6 hours or 24 hours, and cell lysate was quantitated for eNOS, nNOS, VEGF, and GAPDH expressions.

RESULTS: NAD+ reduced the maximal contractile response induced by Phe (46.2±9.9%). The NAD+-induced relaxations were not affected by inhibitors. NAD+ induced relaxations were significantly lower (11.1±5.3%, p = 0.0270) in the aged (75.6±1.2 years) group when compared (40.7±6.9%) middle-aged (63.0±4.0 years) group. NAD+-evoked relaxations of HCC were augmented with NaHS and Ado incubations. Using Western blot analysis, confocal imaging, and