Evaluation of Penile Erectile Function Changes by Assessing The Nitrate Oxidase Expression in Rat Corpus Cavernosum with Neck Bladder Obstruction and Given Alpha Blocker

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EVALUATION OF PENILE ERECTILE FUNCTION CHANGES BY ASSESSING THE NITRATE OXIDASE EXPRESSION IN RAT CORPUS CAVERNOSUM WITH NECK BLADDER OBSTRUCTION AND GIVEN ALPHA BLOCKER

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ABSTRACT

We conducted a review of evaluation erection function by assessing the expression level of nitrate oxidase in rats with neck bladder obstruction and got alpha blocker treatment. Abnormal condition of erectile dysfunction marked by the inability to have an erection or maintain an erection during intercourse. Many factors can cause this condition. One of them is due to the low synthesis of nitric oxide. Because nitric oxide is the main mediator during erection process. Thus, nitric oxide values and erectile function are considered to have a direct relationship. While alpha blockers or alpha adrenoceptor antagonists play a role in the contraction of smooth muscle from several urinary tract organs, such as the prostate and bladder. In the case of urinary tract obstruction, alpha blockers are used as treatment. The presence of a blockade in these receptors wil cause relaxation of the bladder neck smooth muscles and smooth the urine flow. The uses of alpha blockers can improve erectile function. However, not all study results showes the significant differences in nitric oxide expression between before and after alpha blocker use. This may be influenced by many factors, including the type and dose of alpha blockers used.

Keywords: erectile function, nitric oxidase, bladder neck obstruction, alpha blockers

INTRODUCTION

Penile erection is a condition related to the hemodynamic process.[1] Hemodynamic factors that occur in the erection process include decreased of intracavernosal resistance, increased blood flow to the arterial through dilatation of blood vessels and venous flow restriction due to intracavernosal compression and subtunical venous plexus. Blood flow to the blood vessels of the penis will increase even 10 times compared to normal conditions.[2]

An abnormal condition of erectile dysfunction is characterized by the inability of a man to experience an erection or maintain an erection during intercourse.[3,4] There are many factors that cause this abnormality. Feldman in his literature wrote that the prevalence of erectile function is increases along the aging of a man, which is about 50% at the age of the fifth decade and the risk continues to increase to 70% in the 7 decade.[5,6]

One of the factors causing erectile dysfunction is due to the low synthesis of nitric oxide, for example due to inadequate expression of nitric oxide synthase (NOS) or due to loss of cavernous nirergic nerve fibers. Nitric oxide is a neurotransmitter produced by all of the endothelium lining the sinusoid and penile blood vessels and at the end of the non-adrenergic non-cholinergic nerve fibers of the nerves that innervate the cavernous.[7] This compound has a major role as the main mediator in the process of erection.[8,9 , 10,11,12]

In the process of erection, nitric oxide will be released and work to relaxing the smooth muscle and corpus cavernosa blood vessels to allow the erection process.[13] In people with vascular cell disorders (endothelial) will cause decreased nitric oxide production, so the group has a risk of experiencing erectile dysfunction. .[1] However, in relation to age, the study of Magee et al using penile rats showed that the difference in expression of mRNA nitric oxide synthase was not significantly difference between older and younger men. Thus, based on this study when associated with erectile dysfunction which increases along age as mentioned above, it may not be the result of a significant decrease in the activity of nitric oxide synthase.[14]

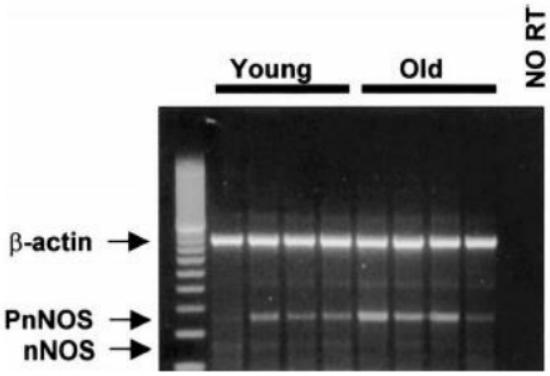

Figure 1. Expression of nitric oxide synthase in old and young age does not show a significant difference.[14]

Alpha blockers or also known as alpha adrenoceptor antagonists play a role in the smooth muscle contraction of the prostate. There are many subtypes of alpha blockers, some of those subtype are selective and do not cause any changes in vascularization of the smooth muscle of the organs affected, for example silodosin. Ejaculation dysfunction due to abnormal work of alpha blockers occurs due to failure in the emission process. This is because many beta blockers are located in organs that involves in the emission process, such as vas deferens and seminal vesicles.[16,17]

Naftopidil is another example of the alpha blocker subtype. Majima et al's research showed that naftopidil decreases the inflammation and returns perfusion of bladder tissue due to obstruction.[18] Tamsulosin works is mediated by stimulation of sympathetic nerves at alpha 1 adrenergic receptors. The presence of a blockade in these receptors causes the relaxation of bladder neck smooth muscles and expands urine flow in obstruction cases.[19]

DISCUSSION

Bastaskin et al conducted a study of 32 Sprague-Dwaley male rats to observe the performance of silodosin on erectile function in rats with partial bladder obstruction. This obstruction will cause increases of the bladder mass and will detaines the erection process. After the rats were given silodosin, the results showed that the average weight of the bladder decreased. In addition, erectile function is improved as a result of nitrergic stimulation of the nitric oxide release as a mediator in during the erection process.[20]

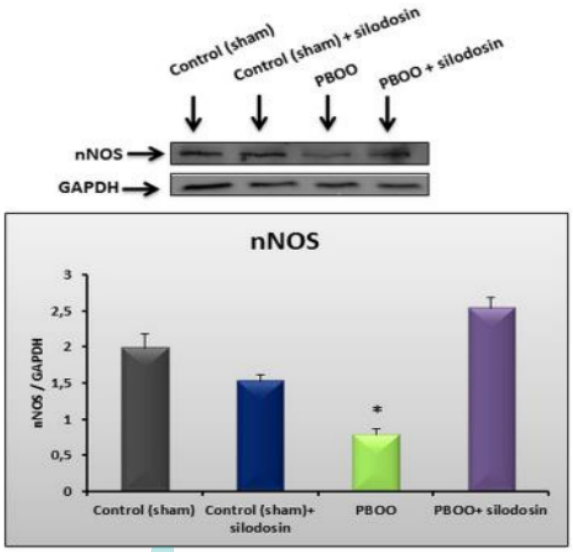

Figure 2. The highest activity of nitric oxide synthase was found in the group of mice who experienced partial bladder obstruction but received silodosin therapy compared to the control group and those who did not receive any therapy.[20]

A similar study conducted by Yono et al used a Sprague-Dawley male rat aged 10 weeks to determine the effect of silodosin on ejaculatory function. The rats was divided into four groups, group (1) received silodosin 0.1 mg/kg in a short period (three days), group (2) received 0.1 mg/kg silodosin in the long term (30 days), group (3) received silodosin 3 mg/kg in the short term (3 days) and group (4) received silodosin 3 mg / kg in the long term (30 days). The results showed that long-term administration of low-dose silodosin only increases the alpha blocker expression significantly in the seminal vesicles, but there was no similar results were found in the prostate.[21] Seminal vesicle contractions caused by alpha blocker expression, including silodosin. In human, silodisin plays an important role during emission phase of ejaculation.[22,23]

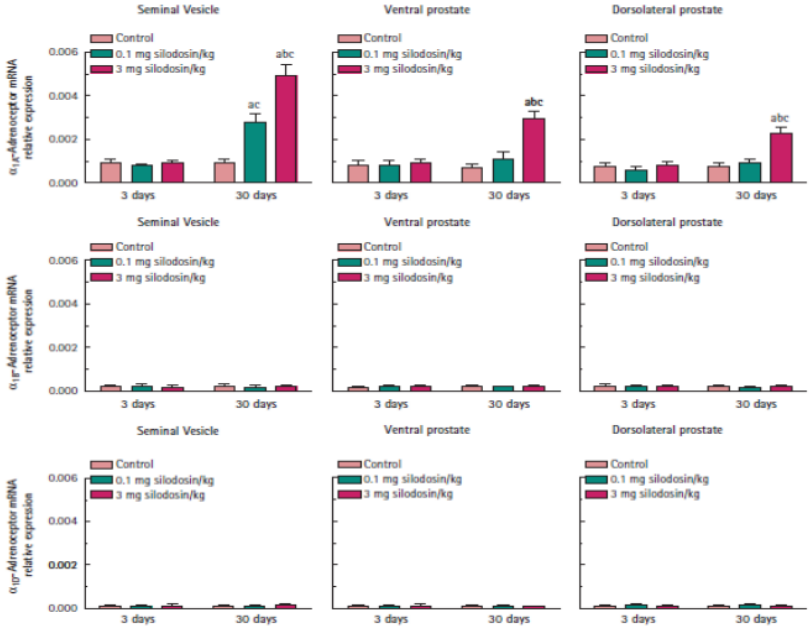

Figure 3. The effect of silodosin administration on several different anatomical structures. Increases of alpha blockers expression induced by silodosin is most effective in the seminal vesicular.[21]

Another similar study conducted by Giuliano et al, the result showed in the bladder was found 33% alpha 1A adrenoceptors, 53% alpha 1B adrenoceptors and 14% alpha 1D adrenoceptors.[24] Malloy et al found similar results, there were 34% alpha 1A adrenoceptors, 66% alpha 1D adrenoceptors and 14% alpha 1D adrenoceptors in bladder, but none at all was found in alpha 1B adrenoceptors in the bladder.[25] Alpha 1A receptors are mostly located in the lower urinary tract, 1B is mostly located in the vascular, while 1D is found in the bladder.

Research by Cihan et al examined the side effects on the sexual ability of silodosin drugs at a dose of 8 mg per day in LUTS condition due to benign prostate hyperplasia. Sexual ability in this study was assessed based on the intravaginal ejaculation latency time (IELT) and premature ejaculation patient (PEP) categories. The results showed erectile function and the ability to maintain the erection gets better after silodosin 8 mg use for 3 months. Nearly 38% of subjects experienced an increase of IELT score and 52% experienced an increase in PEP scores.[26]

Silodosin works directly in increasing the release of nitric oxide from the nitrergic nerve which then produces neurogenic relaxation. In bladder obstruction cases, an oxidative stress response will occur. Research by Goi et al showed that silodosin works by reducing oxidative stress markers. [27]

A research conducted by Kirby et al on the effect of doxazosin in reducing erectile dysfunction results showed a better reduction than placebo, respectively 5.8% and 3.3%.[28] While research by McConnel et al showed a decrease in erectile dysfunction complaints after taking doxazosin compared to placebo by 3.56% and 3.3%, respectively.[29] However, research by Gumrah et al. Observed the effect of doxasozin administration on inducible nitric oxide (iNOS) using 30 Sprague Dawley rats. The results showed iNOS expression did not change significantly between before and after the use of doxasozin.[30]

CONSLUSION

Various types of alpha blockers are used in urinary tract obstruction cases. Blockade of alpha adrenoceptors causes relaxation of the bladder neck smooth muscle and helps to smooth the urine flow. The use of various alpha blockers can improve erectile dysfunction. However, not all studies showed the differences in nitric oxide expression. This may be influenced by many factors, including the type and dose of alpha blockers used.

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