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ORIGINAL ARTICLE

Effects of *Panax ginseng* on the nerve growth factor expression in testosterone induced benign prostatic hyperplasia

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Abstract The prostatic hyperplasia in benign prostatic hyperplasia (BPH) leads to obstructive micturition symptoms. Previous studies showed that pontine micturition center (PMC), ventrolateral periaqueductal gray (vlPAG), and medial preopticnucleus (MPA) regions in the brain have been known to regulate the urinary bladder function. The present study shows the influences of *Panax ginseng* on nerve growth factor (NGF) expressions in PMC, vlPAG, and MPA regions in the brain. Wistar rats were used for the present study. The rats split into four groups; 4 groups ($n = 6$) in control group, BPH-induced group, BPH-induced and *P. ginseng*-treated group, and BPH-induced and finasteride-treated group. BPH in rats was induced by testosterone and the animals were evaluated for NGF expression in PMC, vlPAG, and MPA regions in the brain. The NGF expression was identified using immunohistochemistry (IHC). The NGF expression by IHC showed spots with dark brown color. In our results, NGF expressions in PMC, vlPAG, and MPA regions in the brainstem of the BPH-induced group showed increase than the control animal. These increased NGF expressions in three regions were decreased using treatment with *P. ginseng* (200 mg/kg). These results suggest that *P. ginseng* has therapeutic effects on the symptoms of BPH and is associated

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with the regulation of NGF expression in the brain. In conclusion, the administration of *P. ginseng* helps nerve growth factor activation.

1. Introduction

The most common cause of obstruction in old man was observed in benign prostatic hyperplasia (BPH). BPH shows a prostatic enlargement (Foo, 2010; Nickel, 2006). Previous study reported that neurological factors contributed to smooth muscle dysfunction as risk factor in the development of symptoms of LUTS (Skolarikos et al., 2004).

The regulation of micturition links between various regions in the brainstem and extensive tracts (Fowler et al., 2008). Many neurons in the brainstem regions are involved in the regulation of the micturition (Rickey et al., 2008). The PMC plays an important role in controlling urinary bladder function (Fowler et al., 2008; Yoshimura et al., 2014). Stimulation of neurons in the PMC region contributed to bladder contractions, relaxation of the bladder neck, and external urethral sphincter (Chancellor and Yoshimura, 2004), which results in micturition. And periaqueductal gray (PAG) and medial preopticnucleus (MPA) reported the relationship with PMC (Blok and Holstege, 1994). PAG and MPA regions of the hypothalamus in the brain associated with the control of urinary bladder function. The connection between PAG and PMC also is contributed to micturition reflex (DasGupta et al., 2007; Blok and Holstege, 1994; Rickey et al., 2008). And the ventrolateral PAG (vlPAG) plays an important role in micturition reflex (Blok and Holstege, 1994; Matsumoto et al., 2004). It was reported that electrical or chemical stimulation in the LUT showed changes in neuronal activity (Bon et al., 1996; Blok, 2002).

Several studies reported that nerve growth factor (NGF) was related to the control of micturition (Chung et al., 2008; Cho et al., 2014). And Stimulation of the bladder increased expressions of NGF in the PAG, PMC, and spinal cord (Dinis et al., 2004; Kavia et al., 2005). NGF also is an important modulator of voiding. It is released in the spinal cord or the urinary bladder (Seki et al., 2004). The NGF has been used to assess neuronal activity (Lee et al., 2003).

Previous study showed that the *Panax ginseng* CAMAYER (*P. ginseng*) protected development of prostate in the rats (Kim et al., 2014, 2015a,b; Park et al., 2015, 2016). However, PMC, vlPAG, and MPA regions in the brain have not been investigated. The present study explores the influences of *P. ginseng* on NGF expression in the brain.

2. Material and methods

2.1. Reagents and chemicals

The reagents and chemicals used in this study were procured from the Sigma chemicals (USA). All the reagents and chemical used were of analytical grade.

2.2. Preparation of the P. ginseng

P. ginseng was kindly gifted from the Department of Medicinal Crop Research (Eumsung-gun, Chungbuk, Korea) (Kim et al., 2014, 2015a,b).

2.3. Animals

7 week male Wistar rats with an average body weight of 250 ± 10 g were purchased from Central Lab Animal Inc, Korea for the present study. The in vivo and other experiments were performed according the standard methodology of the Korean National Health Institute of Health Animal Facility and it was authenticated and confirmed by the ethical committee of Kyung Hee University.

2.4. Induction of BPH and treatments

Firstly, the rats were operated for orchiectomy, except the control group. After orchiectomy, they were randomly assigned to the following groups: (A) control group; (B) BPH induced testosterone group; (C) BPH-induced and *P. ginseng*-treated group, 200 mg/kg, administered orally; (D) BPH-induced and finasteride-treated group as the positive treated control. The materials were supplemented to the animal every day up to four weeks. After 4 weeks, all rats in the four groups were sacrificed and fresh prostate was selected for the micromorphological studies.

2.5. Immunohistochemistry (IHC)

The brain of rats were cut into 35 μm thick paraffin-sections using microtome. The sections were attached on slide. Reagents such as peroxides quenching with 3% H_2O_2, primary NGF antibody, biotinylated secondary antibodies (1: 1000), phosphate buffer saline, streptavidin–HRP and diaminobenzi dinetetrahydrochloride (DAB) were used. The images were noted at 100×.

2.6. Statistical analyses

Standard error and mean were calculated for all the experiments. ANOVA and Tukey test were applied to evaluate significant differences between the groups. All statistical analyses were done using the SPSS for Windows (Micro Soft, USA).

3. Results

3.1. Effect of Panax ginseng on prostatic hyperplasia

Photomicrographs of NGF-positive cells in MPA, vlPAG, and PMC regions are shown in Figs. 1–3. The NGF expression by