319

Jeong J Y[1], Kang J [1], Kim S J [2], Hong E K [3], Oh S[4], Kim K M [4]
1. Dept. of Urology, Eulji Hospital, Eulji Medical University, 2. Department of Physiology, School of Medicine, Sungkyunkwan University, 3. Medvill Co. Ltd., 4. Department of Urology, Seoul National University College of Medicine

IN VIVO PHARMACOLOGICAL EFFECTS OF PALMATINE AS AN (1-ADRENOCEPTOR ANTAGONIST IN THE RABBIT

Aims of Study

We previously reported that berberine and palmatine (isoquinoline alkaloids) induced dose-dependent relaxation of phenylephrine-induced contraction of both prostate and urethral smooth muscle strips in the rabbits (32nd Annual Meeting of ICS 2002). Of the two alkaloids, palmatine showed stronger antagonistic effect on the urethral tissue than berberine ($p<0.05$), while the effects of the two alkaloids on the prostatic tissue revealed insignificant differences ($p>0.05$).[1] In the present study, we describe in vivo α1-adrenoceptor antagonistic actions of palmatine in rabbit in comparison with in vitro effects of this drug on the isolated prostate, urethral and vascular smooth muscle tissues of the rabbit.

Methods

For in vivo pressure measurement study, we used male New Zealand White rabbits (3.0-3.5 kg). After anesthetized with urethane (800 mg/kg i.v.), a midline incision was made in the lower abdomen, and the urinary bladder was completely drained out with needles by bladder wall puncture. To prevent filling of the bladder, polyethylene tubes (PE-50; Becton Dickinson & Co., Sparks, MD) were inserted into bilateral ureters, and urine from kidneys was led outside.[2] Using a 3-F MIKRO-TIP catheter transducer (SPR-524; Millar, Houston, TX) positioned in the prostatic urethra, urethral pressure was recorded continuously. To record the blood pressure, the right femoral artery was cannulated with a polyethylene catheter which was connected to an amplifier (PowerLab Quad bridge Amp 8sp; AD Instruments, U.S.A) through a pressure transducer (PX260; Edwards Lifesciences, Irvine, CA). After a stabilizing period, phenylephrine (1 μg/kg) was given intravenously several times. When the increases of the urethral pressure became stable, palmatine was administered intravenously (0.5-3.0 mg/kg) followed by the administration of phenylephrine in no time interval.

Results

In anesthetized rabbits, the increases in urethral pressure were reproducibly elicited by an i.v. injection of phenylephrine (1 μg/kg). The mean values of the initial increments in urethral pressure and mean blood pressure before i.v. bolus injections of palmatine were 19.0 ± 3.1 mmHg and 87.6 ± 5.4 mmHg (n=5), respectively. Palmatine (0.5-3.0 mg/kg), administered intravenously, dose-dependently inhibited phenylephrine-induced increases in prostatic urethral pressure. The maximal inhibition was obtained when palmatine dose 3.0 mg/kg was given, and at that point, the decrease of urethral pressure increment was 73.1% (Fig. 1). The ED_{50} for the urethral pressure was calculated at 1.75 mg/kg. Palmatine showed no effect on mean blood pressure until 1.5 mg/kg of palmatine was administered, and the maximal inhibition was obtained when palmatine dose 2.0 mg/kg was given, and at that point, the decrease of mean blood pressure was 37.3 % (Fig. 2). Also, palmatine showed no apparent effect on heart rate in the tested dose range.

Conclusions

These results indicate that palmatine exhibited α1-adrenoceptor antagonistic action in anesthetized rabbits in vivo, and the effect was selective for the lower urinary tract over the cardiovascular system. It is expected that palmatine may improve the bladder outlet obstruction associated with benign prostatic hyperplasia by lowering the urethral pressure through its α1-adrenoceptor antagonistic action.

References

1. J Korean Continene Society 2002; 6(2): 62-71.
2. Neurourol Urodyn 1994; 13: 471-3.

Fig. 1. Effect of palmatine on the changes in urethral pressure induced by phenylephrine (1 μg/kg i.v.) in anesthetized rabbits. Palmatine was given intravenously. Each point represents the mean±S.E of five experiments.

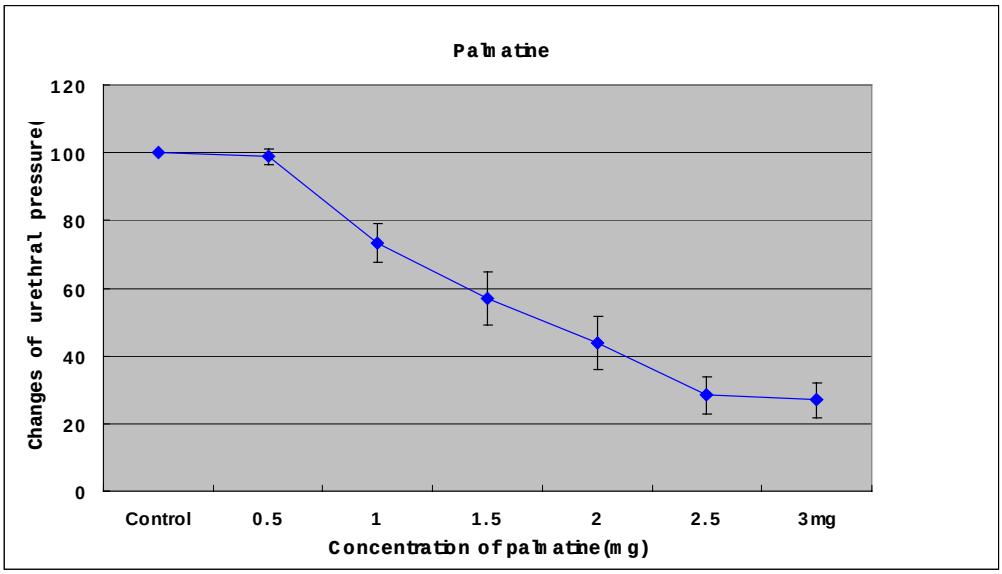

Fig. 2. Effect of palmatine administered intravenously on the mean blood pressure in anesthetized rabbits. Each point represents the mean±S.E of five experiments.