ALPHA-ADRENERGIC RECEPTORS IN HUMAN PROSTATE

Seiji Furuya and Eiji Yokoyama
From the Department of Urology, Kitami Red Cross Hospital

Yoshiaki Kumamoto and Taiji Tsukamoto
From the Department of Urology, Sapporo Medical College

Strips of human prostate showed a contractile response to alpha-adrenergic agonists. There was no response to beta-adrenergic and cholinergic agents, prostaglandins, PGE 1 and PGF 2α or angiotensin II. The noradrenaline-induced contraction was inhibited by an alpha-adrenolytic agent. Electrical field stimulation elicited contraction of the prostatic specimens. This stimulation-induced contraction was antagonized by phenoxybenzamine, but not by yohimbine. These results indicate that alpha-1-adrenergic receptors are preferentially present in the human prostatic tissue.

Key words: Alpha-adrenergic receptor, in vitro muscle bath method, Electrical field stimulation, Human prostate

INTRODUCTION

The contraction of the prostatic tissue has been shown in animal experiments, but the contractile mechanism of the human prostate is not clearly understood. Histological studies have demonstrated the presence of smooth muscle cells and adrenergic nerves in human prostatic tissue. Pharmacological sympathectomy may lead to the suppression of the contraction of the prostate, resulting in ejaculatory failure. Our previous study has demonstrated that noradrenaline causes contraction of human prostatic strips. These findings seem to indicate that a sympathetic nerve mechanism controls the contraction of the human prostate.

In this paper, in order to clarify the contractile effects of the alpha-adrenergic mechanism on human prostatic tissue, a pharmacological experiment was conducted using the in vitro muscle bath method and the electrical field stimulation technique.

MATERIALS AND METHODS

Fragments from the enucleated prostatic adenoma were obtained from five patients with benign prostatic hypertrophy, aged 56 to 75 years, and who were undergoing retropubic prostatectomy. Immediately after surgical removal, these specimens were immersed in cold Tyrode's solution and stored in this solution for 30 to 60 minutes before the experiment was started. The prostatic specimens were then carefully dissected into strip preparations approximately 5 mm wide, 3 mm thick, and 15 mm long.

The prostatic strips were mounted vertically in a 50-ml organ bath (Tyrode's medium, 95% O₂ and 5% CO₂, pH 7.3) and were maintained at a resting tension of 0.5 g throughout the experiments. The changes in the tension of these strips were measured isometrically using a strain-gauge transducer and were recorded on a polygraph. The contractile responses of these strips to various drugs were examined. The drugs used were noradrenaline (3×10⁻⁶M); phenylephrine (3×10⁻⁵ M); phentolamine (2 μg/ml); acetylcho-
line (10^-3M); atropine (10^-3M); isoprot-
ernol (10^-3M); propranol (10^-3M); pros-
taglandins PGE 1 (10 µg/ml) and PGF 2α
(10 µg/ml); angiotensin II (10 mg/ml),
and tetrodotoxin (10^-5M). The drugs
were injected into the bath. The above
concentrations represent the final drug
concentrations in bath.

For electrical field stimulation, the
strips were suspended between two plati-
num wire electrodes and superfused with
Tyrode's solution. The electrical stimuli
were rectangular pulses of 1.5 msec dura-
tion at 60 Hz for 30 s at 55 volts, deliver-
ed using an electronic stimulator (Ni-
hon Koden, SEN-7103). These stimula-
tion conditions were fixed throughout the
experiments. For the evaluation of the
effect of the alpha-adrenergic antagonists,
electrical transmural stimulation of the
strips was carried out 5, 10, 15 and 30
minutes after superfusing with Tyrodes'
solution containing phenoxybenzamine (3
×10^-5M) or yohimbine (10^-4 to 10^-3M) and
the change in tension was observed.

RESULTS

After a stabilization period of up to
one hour, all specimens showed sponta-
nous rhythmic contractions (Fig. 1). These spontaneous contractions varied in
both rate and amplitude from strip to
strip. The contractile tension ranged
from 0.05 to 0.2 g above the resting ten-
sion of 0.5 g. This spontaneous activity
was not inhibited by the treatment with
phentolamine, isoproterenol, atropine and
tetrodotoxin (Fig. 2).

The prostatic strips showed a contrac-
tile response only to noradrenaline and
phenylephrine, and these brugs produced
contraction even when tetrodotoxin treat-
ment was carried out. There was no res-
ponse to isoproterenol, propanol, acetyl-
choline, prostaglandins (PGE 1 and PGF
2α), or angiotensin II. The increase in
resting tension induced by noradrenaline
was dependent on the dose added to the
bath. Noradrenaline was added to the
bath in increasing concentration (3×10^-7
to 3×10^-6M), so that a cumulative dose

Fig. 1. Spontaneous contractions of tissue strips of the human prostate

Fig. 2. Effect of tetrodotoxin on spontaneous contractions, and the contractile
effect of noradrenaline in the presence of tetrodotoxin
response curve was obtained. After treatment of the tissue strips with phentolamine (0.5 to 20 µg) for 15 min, the addition of increasing concentrations of noradrenaline was repeated, and the dose response curves in the presence of the antagonists were obtained (Fig. 3). Phentolamine caused a parallel shift to the right in the dose response curve to noradrenaline. Almost full antagonism was obtained with phentolamine at 20 µg.

Transmural electrical stimulation elicited contraction of the prostatic specimens. The contractile tension was approximately 0.2 g. This contractile response was inhibited by treatment with phenoxybenzamine. Yohimbine had no effect on the contraction of the prostatic strips at concentrations between 10^-4 and 10^-5M (Fig. 4).

**DISCUSSION**

Our results have demonstrated that two alpha-adrenergic agonists (noradrenaline and phenylephrine) caused dose-dependent contractions, and that an alpha-adrenoalytic agent (phentolamine) inhibited the noradrenaline-induced contractions in human prostatic strip. These findings support a previous study in which alpha-adrenergic receptors were found in rat and human prostatic tissues[11,12]. On the other hand, because beta-adrenergic and cholinergic agents did not have any effect on the contractile response, beta-adrenergic receptors and cholinergic receptors may not be present in human prostatic tissue. Histochemical studies have revealed the
presence of cholinergic nerves in human prostatic tissue. Our experimental results indicate that these cholinergic nerves are not involved in the contraction of the prostate. Rather, we surmise that the function of these nerves relates to the secretion of the prostate gland.

Neither angiotensin II nor the prostaglandins, PGE 1 and PGF 2α, were found to cause either contraction or relaxation of human prostatic strips. With regard to the effects of these drugs on the smooth muscle of the human urinary tract, it has been reported that angiotensin II brings about contraction of isolated muscle strips from the human urinary bladder13). PGE 2α and PGE 1 cause contraction of the bladder muscle. It has also been reported that PGF 2α causes contraction of both ureteral smooth muscle and urethral smooth muscle, and PGE 1 brings about the relaxation of these muscle tissues14-15). Accordingly, our results show a clear qualitative difference in the effects of these drugs on human prostatic smooth muscle and urinary tract smooth muscle.

We observed that the human prostatic strips contracted in response to electrical field stimulation. The stimulation conditions we employed were similar to those in another report17): Stimulation of the taenia strips isolated from the caecum of the guinea pig, caused release of noradrenaline and the tissue strips to relax. This stimulation-induced contraction of human prostatic strips was antagonized by phenoxymethylamine (alpha-1-blocker). This result suggests that alpha-1-receptors are present in the human prostatic tissue. On the other hand, our observation that yohimbine (alpha-2-blocker) did not bring about an increase in the electrical stimulation-induced contraction indicates that there are no alpha-2-receptors in human prostatic tissue. It has been reported that during transmural electrical stimulation of strips of rabbit main pulmonary artery which had been preincubated in [3H]-noradrenaline, yohimbine enhanced the overflow of tritium and smooth muscle contraction18). This is due to yohimbine's activity to block the alpha-2-receptors of the arterial tissue. Therefore, in order to prove that there are no alpha-2-receptors in human prostatic tissue, it may be necessary to measure the noradrenaline concentration in the incubation medium when applying electrical field stimulation in the presence of yohimbine.

ACKNOWLEDGMENT

The authors would like to thank Dr. T. Izumi and Prof. Dr. Y. Abiko for their valuable advice, and Miss Y. Tonooka for her assistance.

REFERENCES

1) Farrell JI and Lyman Y: A study of the secretory nerves of, and the action of certain drugs on, the prostate gland. J Physiol 118: 64, 1937
17) Kuchii M, Miyahara JT and Shibata S: (3H)-adenine nucleotide and (3H)-noradrenaline release evoked by electrical field stimulation, perivascular nerve stimulation and nicotine from the taenia of the guinea-pig cecum. Brit J Pharmacol 49: 258, 1973
(Accepted for publication, February 23, 1983)