Effect of Clenbuterol on Contractile Response in Periurethral Striated Muscle of Rabbits

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KISHIMOTO, T., MORITA, T., OKAMIYA, Y., HOSHINA, K. and TAKESHITA, T. Effect of Clenbuterol on Contractile Response in Periurethral Striated Muscle of Rabbits. Tohoku J. Exp. Med., 1991, 165 (3), 243-245 — The effect of clenbuterol, a selective β2-adrenoceptor agonist, on isolated periurethral striated muscle preparations from rabbits has been investigated. The periurethral striated muscle produced a contraction in response to field stimulation. An application of clenbuterol resulted in a dose-dependent potentiation of the field stimulation-induced contraction. This potentiation was antagonized by propranolol and was greater than that of isoproterenol, suggesting a β2-agonistic action. ——— clenbuterol; periurethral striated muscle

Urinary continence has been maintained by both relaxation of bladder and contraction of urethra. Clenbuterol caused a dose-dependent decrease in tension of the urinary bladder smooth muscle isolated from rabbits, but caused only a slight relaxation of the urethral smooth muscle (Kishimoto et al. 1989). On the other hand, an increase in maximal urethral closure pressure was recognized in clinical study with clenbuterol (Morita 1989). In this paper, we investigate the effect of clenbuterol on the external urethral sphincter (periurethral striated muscle) isolated from rabbits.

Male Japanese white rabbits weighing about 3 kg were used. Periurethral striated muscle was sectioned from the urethra and cut transversely. The strip was suspended in an isolated organ bath containing a modified Krebs Henseleit solution (37°C, pH 7.4), to record the contractile response isometrically. The strips were allowed to equilibrate for at least 1 hr after application of an initial tension of 1 g. Muscle strips were stimulated between two parallel platinum electrodes at 40 Hz using 0.5 sec trains of 0.5-msec pulses at 15-sec intervals. The drugs used were clenbuterol hydrochloride (Dr. Karl Thomeae GmbH, Germany), isoproterenol hydrochloride (Sigma, St. Louis, MO, USA) and propranolol hydrochloride (Sigma, St. Louis).

The contraction of 1-2 g was evoked by transmural field stimulation. After the response of the muscle to stimulation was repeated at 15-sec intervals and the amplitude of contraction became stable, clenbuterol (10^-8 M) was applied, as shown in Fig. 1. Clenbuterol produced a gradual potentiation of the field stimulation-induced contraction. The force of the contraction increased about 40% within 10-20 min after the application. Propranolol at 3 × 10^-6 M had little effect on the field stimulation-induced contraction (data not shown). The excitatory effect of clenbuterol was antagonized by the application of propranolol (3 × 10^-6 M), suggesting an attribution to β-agonistic action. In Fig. 2, the

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Fig. 1. Effect of clenbuterol on field stimulation-induced contraction in rabbit periurethral striated muscle. At the first triangular mark, clenbuterol (10^{-8} M) was applied to the muscle strip, and propranolol (3 \times 10^{-6} M) at the second one.

Fig. 2. Dose-response curves for the effects of clenbuterol (●) and isoproterenol (○) on the periurethral striated muscle. The ordinate represents the percentage increase in the contractions induced by field stimulation from controls. Each drug was cumulatively applied to the muscle strip at approximately 10-min intervals. Each value is the mean ± s.e. for 7 muscle strips.

*\( p < 0.05 \); **\( p < 0.01 \) (vs. control).
action of clenbuterol was compared with that of isoproterenol. Cumulative addition of each drug (10^{-9}-10^{-6} M) caused a graded potentiation. A significant effect by clenbuterol was recognized from the dose of 10^{-9} M. Also, the potency of clenbuterol was significantly greater than that of isoproterenol. After drug treatment with final dose (10^{-6} M), both the excitatory effects of clenbuterol and isoproterenol were reversed by application of propranolol (3 \times 10^{-6} M).

Holmberg and Waldeck (1977) observed an increase in fast-contracting skeletal muscle contraction by isoproterenol. They considered that the response of skeletal muscle was mediated by \beta_2-adrenoceptor stimulation, since the effect was blocked by \beta_2-blocker but not by \beta_1-blocker. The present study shows that the potentiation by clenbuterol is greater than that by isoproterenol. This finding also suggests that the response to clenbuterol or isoproterenol is mediated mainly by \beta_2-adrenoceptors. These data explain that the increase in urethral pressure on clinical study with clenbuterol may be attributed to the enhanced tension of periurethral striated muscle by clenbuterol. And these data also suggest that clenbuterol may be a promising drug for the treatment of urinary incontinent patients.

References

