Short communication

The Effects of Tetracaine on the Electrical and Mechanical Activity of the Guinea-Pig Ureter Smooth Muscle

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The existence of two populations of potential-operated Ca^{2+} channels in the ureter smooth muscle have been suggested: (1) inactivating Ca^{2+} channels which are responsible for the generation of action potentials and phasic contractions, and (2) non-inactivating Ca^{2+} channels opened during sustained depolarization which are responsible for the generation of tonic tension (Kochemasova and Shuba 1979; Aickin et al. 1984). Reuter and Seitz (1968) introduced the idea that Na-Ca countertransport might be responsible for Ca movement in cardiac muscle. Heart muscle is known to produce contractile responses to low-Na solutions, an effect thought to reflect the activity of Na-Ca exchange mechanism (Chapman 1974). Aickin et al. (1984) observed in Na-loaded ureter smooth muscle a low-Na contracture mediated by the Na-Ca exchange. Unlike potential-operated Ca^{2+} channels, the Na-Ca exchange proved to be completely insensitive to organic Ca^{2+} antagonists (Aickin et al. 1984).

Our study was aimed at characterizing the effects of tetracaine on the action potentials and phasic contractions as well as contractures of the ureter muscle stimulated by high-K and Na-free solutions.

Simultaneous electrical and mechanical records were obtained from isolated pieces of whole guinea-pig ureter using the double sucrose-gap method (Bülbring and Tomita 1969) and tension alone was recorded with the continuous superfusion technique (Brading and Sneddon 1980).

Fig. 1 shows the inhibitory effects of 0.5 mmol/l tetracaine on the evoked action potentials and phasic contractions of the ureter muscle. Dose-response curve of the tetracaine-induced inhibition of phasic contractions mediated by the action potentials is illustrated in Fig. 2 (curve d). IC_{50} for phasic contractions was 0.2 mmol/l. The experiments with high-K contractures showed that tetracaine had a stronger inhibitory effect on the depolarization-induced tonic tension (Fig. 2,

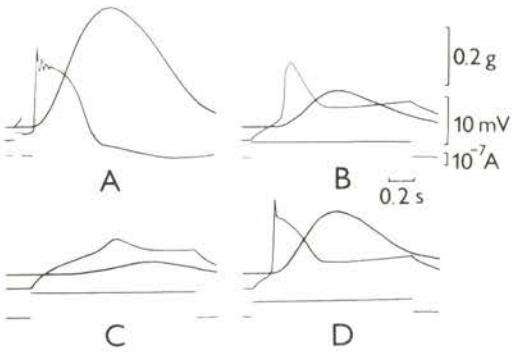

Fig. 1. Effect of tetracaine (0.5 mmol/l) on the ureter smooth muscle. The middle trace shows the electrical, the upper trace the mechanical response and the lower trace shows depolarizing current pulses (double sucrose-gap method): *A*, Krebs solution; *B*, *C*, during exposure to tetracaine for 1 and 5 min; *D*, during the washout with Krebs solution for 10 min. Note the increase in duration of the depolarizing current pulse to evoke the action potential in the presence of tetracaine.

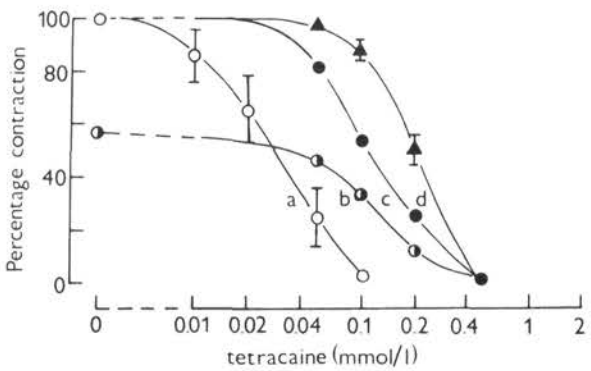

Fig. 2. Effects of teracaine on the mechanical responses of normal and Na-loaded tissue. Open circles show the responses to 1 min applications of 126 mmol/l K^+ (*a*); filled circles, the responses of Na-loaded tissue to 1 min applications of 126 mmol/l K^+ (*c*); semi-filled circles show the responses of Na-loaded tissue to Na-free (Tris) solution (*b*); the values were expressed as percentages of the control 126 mmol/l K^+ response in the absence of tetracaine; filled triangles show the effect of tetracaine on the amplitude of the evoked phasic contractions expressed as percentage of the control phasic contractions evoked in the absence of tetracaine (*d*). Each point represents the mean of measurements on four different preparations. S.E. of the mean, where larger than the symbol, is represented by the bars. Note that tetracaine suppresses the high-K^+ responses at lower concentrations than it does the phasic contractions and Na-free contractures.

curve a). IC_{50} for K-contracture was 0.03 mmol/l i.e. roughly 10 times lower than IC_{50} for phasic contractions. The finding of different IC_{50} for phasic and tonic contractions gives further support for the existence of two populations of voltage-operated Ca^{2+} channels. Na-loaded ureter smooth muscle responds with contractures to application of Na^+-free solution irrespective of the Na substitute used (Aickin et al. 1984). The experiments with Na-loaded tissue showed that tetracaine blocked Na-free contractures with either Tris or K^+ used as Na^+ substitute (Fig. 2, curves b and c, respectively). Both Na^+-free contractures are blocked by tetracaine at 0.5 mmol/l with IC_{50} 0.1 mmol/l. One interesting point which emerges from the results obtained is the difference in IC_{50} for Na-free contractures and phasic contractions associated with the action potentials. In other words, tetracaine blocks the Na-Ca exchange more effectively than voltage-operated inactivating Ca^{2+} channels responsible for generation of the action potential and phasic contractions. In frog atrial trabecule tetracaine inhibits the slow inward current and the release of Ca^{2+} from the sarcoplasmic reticulum (Chapman and Leoty 1981). Inhibition of Na-free contractures mediated by the Na-Ca exchange is not a general property of all local anesthetics, since procaine which also blocks ureter muscle contractions mediated by the action potential and sustained depolarization failed to suppress Na-free (Tris) contractures (Aickin et al. 1984). It is concluded that tetracaine in addition to its Ca^{2+}-channels blocking action has an inhibitory effect on the Na-Ca exchange in the ureter smooth muscle of the guinea-pig.

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Received May 27, 1985 / Accepted June 25, 1985