EFFECTS OF DANTROLENE ON CONTRACTILE RESPONSES IN GASTRIC SMOOTH MUSCLES OF THE RAT

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1. Effects of dantrolene on contractions evoked by KCl, carbachol and caffeine were studied in circular smooth muscles of the rat stomach.
2. The use of 40mMKCl or carbachol (1 μM) induced a phasic contraction followed by a tonic contraction. Dantrolene (10–100 μM) inhibited both phases of contraction in a dose-dependent manner. The inhibitory effect was much more potent for the tonic contractions than for the phasic ones. Caffeine (3mM) caused a phasic contraction, which was not affected by dantrolene.
3. Combined application of 150mM KCl or carbachol (1 μM) with Ca (2.5mM) elicited a contraction of smooth muscles from which intracelluar Ca stores had been depleted by application of caffeine or carbachol or by treatment with ryanodine during incubation with Ca-free solution containing EGTA (2mM). Nifedipine (10mM) almost abolished the contraction induced by KCl plus Ca, but only partially reduced the contraction evoked by carbachol plus Ca. The residual response was completely inhibited by further administration of 2mM La.
4. After depletion of the intracellular Ca store, dantrolene (100 μM) inhibited contractions evoked by 150mM KCl plus Ca (0.3–10mM) and those induced by carbachol (1 μM) plus Ca (0.3–10mM) in the presence and absence of nifedipine (10 μM).
5. In Ca-free solution containing EGTA (2mM), dantrolene (100 μM) did not affect caffeine (10mM)- and carbachol (100 μM)-induced phasic contractions which were mediated by Ca released from intracellular Ca stores.
6. Dantrolene (100 μM) had no effect on Ca (pCa 6.2)-induced contraction of skinned muscle fibers.
7. These results suggest that dantrolene inhibits Ca influx through both nifedipine-sensitive and insensitive pathways without any effects on the Ca sesitivity of the contractile machinery or on Ca release from intracellular Ca stores in the gastric smooth muscle of the rat.