THE MECHANISM OF LIDOCAINE CONTRACTION AND RELAXATION IN RESTING TRACHEAL SMOOTH MUSCLE. E. B. Weiss. Saint Vincent Hospital, Worcester, Mass.

Lidocaine (L) causes smooth muscle (SM) relaxation in-vitro after agonist contracture. Less understood in resting SM is a biphasic response: myocontraction at low L concentrations followed by high dose L myorelaxation. This report examines some mechanisms of this phenomena. Under resting isometric conditions, guinea pig trachealis SM (TSM) exposed to L produces a biphasic response over 0.43 to 8.54 mM L: maximal tension of +0.82 $Kg/cm^2$ at 2.13 mM is followed by relaxation, maximal at 4.27 mM at -0.38 $Kg/cm^2$. At 2.13 mM L a greater tension occurred at pH 7.00 vs. pH 7.40 ($p < 0.01$); myorelaxation was also right-shifted ($p < 0.01$). pH 7.90 reduced contraction ($p < 0.01$) but not relaxation ($p > 0.8$). Several antagonists were tested: atropine 2 and 10 ug/ml had no effect; 2.0 ug/ml diphenhydramine reduced competitively, and 8 ug/ml non-competitively L induced tension (relaxation was unaffected); propranolol (1.0 ug/ml) was non-inhibitory; phentolamine 2 ug/ml caused competitive and 10 ug/ml non-competitive inhibition. 2,4 dinitrophenol ($10^{-4}$g/ml) produced complete but reversible metabolic inhibition. EGTA (1.0 mM) or $Ca^{++}$ free media totally abolished L effect. Pretreatment of TSM with D-600 (1.0 ug/ml) or Lanthanum (0.5 mM) reduced or abolished L action. In 80 mM $K^+$ most contractile doses of L yielded myorelaxation: viz. L at 2.13 mM exhibited -0.25 $Kg/cm^2$ relaxation. In $Ca^{++}$ free $K^+$ 80 mM all contractile concentration of L were relaxant; with 2.13 mM L, replacement of $Ca^{++}$ to $Ca^{++}$ free media failed to restore tension. Pretreatment of TSM with Indomethacin (0.5 ug/ml) was fully inhibitory and influenced by extracellular $Ca^{++}$, being attenuated at lower $Ca^{++}$ levels. Prostaglandin (PG) $F_{2\alpha}$ and PGE were measured by radioimmune assay. Adding L to TSM, the ratio $PGF_{2\alpha}$/PGE rose from control of 0.13 to 0.77 at 2.13 mM ($p < 0.01$), falling at L 8.54 mM to 0.52 ($p < 0.05$). L biphasic action upon TSM in-vitro involves both extracellular $Ca^{++}$ influx and intracellular $Ca^{++}$ binding as well as PG activity. (Supported by the Foundation for Research in Bronchial Asthma and Related Diseases and Biomedical Research Grant #5-S07RR05660-03).