Modification of the negative inotropic effect of lanthanum by ouabain and some other positive inotropic agents

J. HALLIDAY & S.E. HARDING
(introduced by I.K.M. MORTON)

Department of Pharmacology, King's College, London

The contractility of cardiac muscle is dependent upon a pool of calcium located at the external surface of the sarcolemma, (Langer, 1976), and it has been suggested that ouabain acts through this pool to increase the force of contraction (Nayler, 1973). To investigate this possibility we studied the interaction of ouabain and lanthanum ($LaCl_3$) upon isolated atria, and compared the effects of ouabain with those of three other inotropic agents. Lanthanum was chosen for investigation of the superficial calcium pool because it has a high affinity for calcium binding sites on the external sarcolemma, displacing calcium on an equimolar basis, and yet does not penetrate the cell: it has a negative inotropic effect on beating cardiac muscle (Langer & Frank, 1972).

Other procedures used to increase the force of beating of the heart muscle were; lowering of the external sodium concentration, addition of adrenaline to the bathing solution, and addition of veratrine, (a mixture of alkaloids which increases membrane permeability to sodium, (Horackova & Vassort, 1974).

Isolated guinea pig left atria, driven at 3Hz, (pulse width 500 μs and supramaximal voltage), suspended in HEPES buffer, (Mayer, van Breeman & Casteels, 1972), were exposed to bath concentrations of $LaCl_3$ between 0.1 and 1 mM. The decrease in force produced by the lanthanum in controls was compared to that in preparations to which a positive inotropic agent had been added 30 min previously.

The results obtained for one concentration of $LaCl_3$, 300 μM, are shown in Table 1.

It may be concluded firstly, that the mechanism of action of ouabain could be at least partly due to an effect on the superficial calcium pool; secondly, that this alteration is unlikely to be simply a consequence of internal sodium accumulation, since veratrine does not have the same effect; and thirdly, that although adrenaline and ouabain may both act by increasing calcium flux across the sarcolemma, their actions on the membrane calcium pool differ markedly.

S.E. Harding is an MRC student.

References

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Table 1

Treatment	*%(†) Increase in force due to treatment after 30 min*	*%(†) Decrease in force due to $LaCl_3$: Controls*	*%(†) Decrease in force due to $LaCl_3$: Treated preparations*	*Overall effect of treatment on $LaCl_3$-induced negative inotropic effect*
Ouabain (0.25μM)	31.7 ± 5.7 (6)	34.2 ± 1.5	21.5 ± 3.1*	Limited protection
Veratrine (0.5–2.0 μg/ml)	33.4 ± 4.3 (7)	42.0 ± 5.0	37.4 ± 3.1	No change
Lowered sodium in buffer (67.6 mM [50% normal])	51.8 ± 12.4 (8)	46.1 ± 1.6	27.6 ± 4.0**	Limited protection
Adrenaline (1.5μM)	25.3 ± 5.4 (6)	39.8 ± 1.4	56.7 ± 2.5**	Enhancement

Values given are mean ± s.e. mean. The number of experiments are given in parentheses.
*$P<0.01$
**$P<0.01$ Students '*t*' test, unpaired, against controls
The 100% point is taken as the force of contraction immediately before treatment (†) or addition of lanthanum ($LaCl_3$, †)