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Pharmacological agents and acute experimental hyperlactataemia in the dog

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Experimental hyperlactataemia was produced in dogs anaesthetized with pentobarbital 30 mg/kg i.v.: (a) by administration of high doses of biguanides (phenformin 30 mg/kg intraduodenally, metformin 150 mg/kg intraduodenally) (Loubatières, Ribes & Blayac, 1973); (b) by bilateral repeated and prolonged electrical stimulation of the sciatic nerves (unidirectional and rectangular pulses of 10V, 5 ms and 60 Hz) producing repeated and prolonged contractions (60 min) of the gastrocnemius and soleus groups of muscles; (c) by hypoxia following closed circuit inhalation of a mixture of oxygen (9%) and nitrogen (91%) and (d) by continuous i.v. injection of adrenaline (1.5 $\mu g\ kg^{-1}\ min^{-1}$).

An autoanalyser was used to make continuous measurement of blood sugar in haemolysed blood with potassium ferricyanide and plasma lactate with an enzymatic method (Hohorst, 1963; Minaire, Studievic & Foucherand, 1965). Blood lactate and pyruvate were estimated in fractioned samples by the enzymatic method described by Czok & Lamprecht (1970) and blood pH was measured with a KCl electrode.

Insulin, when administered i.v. (0.085 u $kg^{-1}\ h^{-1}$) or produced *endogenously* by i.v. injection of the hypoglycaemic sulfonamide, glibenclamide (0.05 mg/kg) (Loubatières & Mariani, 1967) prevented, delayed or reduced the hyperlactataemia, hyperpyruvicaemia and acidosis which normally followed the administration of biguanides (Loubatières, Ribes & Blayac, 1973). Co-carboxylase (5 mg $kg^{-1}\ h^{-1}$) produced the same effect (Valette, Ribes, Rondot, Loubatières-Mariani & Loubatières, 1975).

The administration of sodium dichloroacetate (30 mg $kg^{-1}\ h^{-1}$) produced a reduction in the hyperlactataemia produced by phenformin (from 50.6 ± 10.2 mg/100 ml to 14.3 ± 2.8 mg/100 ml, $n = 13$), by intense muscular work (from 42.3 ± 10.3 mg/100 ml to 9.0 ± 1.5 mg/100 ml, $n = 3$), or by adrenaline (from 61.3 ± 13 mg/100 ml to 29 ± 2.3 mg/100 ml, $n = 3$). On the other hand, dichloroacetate did not reduce the hyperlactataemia produced by hypoxia (from 84.7 ± 12.1 mg/100 ml to 100.8 ± 8.7 ml, $n = 3$). These measurements of lactate were made in total blood.

Dichloroacetate slightly reduced the increase in lactataemia which can be observed in the dog presenting a permanent diabetes following the injection of alloxan (50 mg/kg i.v.). Glycaemia was not notably modified.

The therapeutic implications of these observations are under study.

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