MECHANISM OF THE IMMEDIATE PRESSOR RESPONSE TO SARALASIN - STUDIES IN TETRAPLEGIC MAN

C.J. MAHDIRequires, R.J. UNWIN, H.L. FRANKEL, I.B. DAVIES, P.S. SHEVENT AND W.S. PEART

Medical Unit, Department of Clinical Pharmacology, St. Mary's Hospital Medical School, London W2 1PG & National Spinal Injuries Centre, Stoke Mandeville

It is unclear whether the immediate pressor response to intravenous (IV) saralasin in man is due to partial angiotensin-II-like myotropic activity (Wallace et al., 1979, Circ. Res., 44, 38-44) or increased sympathetic nervous activity (McGrath et al., 1977, Clin. Sci. 53, 341-348). To investigate this, we studied 9 tetraplegics (complete C4-8 cord transaction) with measurement of blood pressure (BP), heart rate, plasma renin activity (PRA) and plasma noradrenaline (PNA). Six normal subjects were studied as controls. Three doses of saralasin (0.5, 1.0, and 5.0 μg kg⁻² min⁻¹) were each infused IV for 20 minutes.

In the tetraplegics, saralasin consistently caused a dose-independent rise in BP, with a peak about 5 min after infusion (BP rise of 25 ± 2, 24 ± 4 and 32 ± 4 mmHg, mean ± SEM respectively). This was substantially greater than in the controls (6 ± 1, 7 ± 2 and 6 ± 2 mmHg respectively). Within each group basal PNA was unrelated to pressor responses. In the tetraplegics, PNA levels did not rise during infusion. After alpha-adrenergic receptor blockade with thymoxamine (1 mg kg⁻¹ h⁻¹) twice the dose of IV noradrenaline was required to produce a similar pressor response, but there was no alteration in the pressor response to 5 μg kg⁻¹ min⁻¹ of saralasin.

Our studies indicate that in tetraplegic patients, the competitive angiotensin-II antagonist saralasin consistently produces an immediate and transient pressor response, which is unrelated to basal PNA levels. This effect is independent of central sympathetic facilitation and is unlikely to be due to increased peripheral sympathetic activity. The pressor effect of saralasin is probably due to intrinsic angiotensin-II activity on vascular smooth muscle.

107 HYPERTENSION AND ALCOHOL WITHDRAWAL


Dudley Road Hospital, Dudley Road, Birmingham B18 7QT

Hypertension, during alcohol withdrawal, is related to the severity of the withdrawal state (Saunders JH, Beever DG, and Paton A. Clin Sci 1979; 57:295s-298s), but the mechanism is unknown. We studied 35 men and 13 women (mean age 41 years) who were admitted for "dry out". All had been drinking more than 100 g alcohol a day within 48 hours of admission. On days 1, 4 and 7 the severity of their withdrawal state was assessed numerically and blood pressure, and plasma renin, cortisol and aldosterone levels measured. Serum dopamine beta hydroxylase was measured in 18 patients.

Hypertension was present in half the patients and blood pressures were higher in those with withdrawal symptoms, but fell to normal by day 7. Mean blood pressure on day 1 correlated directly with plasma cortisol (r = 0.3, p<0.03) and inversely with urine volume (r = -0.31, p<0.03). No correlation was found with plasma renin, aldosterone, dopamine beta hydroxylase or urinary sodium excretion.

There was a correlation between falls in blood pressure and in dopamine beta hydroxylase (although mean values were within the normal range) and a significant rise in urinary volume and sodium output between day 1 and day 4.

We conclude that hypertension associated with alcohol withdrawal is not related to the renin angiotensin system but may be caused by increased sympathetic and/or adrenocortical activity.

108 PEPSIN 1 SECRETION IN NORMAL HUMAN SUBJECTS

J.B. ROBERTS, R. SHEERS, AND W.H. TAYLOR

Department of Chemical Pathology and Metabolic Medicine, Royal Liverpool Hospital, Liverpool 7

Human peptic 1 is powerfully collagenolytic and occurs in increased amount in peptic ulcer and in circumstances associated with peptic ulceration, when compared with patients with non-ulcer dyspepsia or with other miscellaneous diseases (evidence summarised in Walker and Taylor, 1980, Gut, 21, 766-771).

Because little is known about peptic 1 secretion in normal subjects, we have followed its release over 10-min periods in response to continuous intravenous pentagastrin (5 μg/kg/hr) for 70 min and to insulin hypoglycaemia (0.15 units/kg intravenously) for 90 min in 11 and 13 subjects respectively.

Basically, 21.1% of 57 10-min samples were without peptic 1. Before pentagastrin the mean basal rate of secretion of peptic 1 was 27 μg/min, rising during the first 10 min of stimulation to 50 μg/min and reaching a maximum of 122 μg/min at 50 to 60 min. The maximal mean rate of total peptic secretion was 1.82 μg/min at 30-40 min. The proportion of peptic 1 in the total peptic secretion was 2.8% basally, rising progressively to 7.8% in the terminal 60-70 min sample.

Before insulin, the mean basal peptic 1 secretion was 12 μg/min. This rate, and that of total peptic, did not change until 20 to 30 min after insulin when it rose to 32 μg/min, reaching a maximum of 127 μg/min at 50 to 60 min. The maximal mean rate of total peptic secretion was 4.17 μg/min at 60-70 min. The proportion of peptic to total peptic was 0.8% basally, rising to 3.1% at 50 to 60 min.

Thus, the maximal mean secretion rate of peptic 1 is similar for both pentagastrin and insulin hypoglycaemia, whereas the latter stimulus yields, maximally, 2.3 times as much total peptic as the former. The maximal rate of peptic 1 secretion does not coincide with the maximal rate of total peptic secretion. The maximal proportion of peptic 1 to total peptic is much less in normal subjects than in patients with peptic ulcer, in whom Walker and Taylor (1980) recorded 25.2% for pentagastrin stimulation and 8.2% for insulin hypoglycaemia.