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Cardiovascular effects of inhaled adenosine (Abstract)

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Adenosine is established as effective therapy for supra-ventricular tachycardia (SVT) and is being evaluated as therapy for ventricular tachycardia, as a coronary vasodilator during cardiac surgery and for systemic and pulmonary hypertension. The half life of adenosine (15 s) is short, necessitating repeated i.v. boluses for SVT termination. We have studied an alternative route of administration – via nebuliser – which has more direct access to the heart. The respiratory effects of inhaled adenosine, bronchoconstriction in asthmatics but not normals, are well known, but the cardiovascular effects have not been studied.

We studied 8 normal subjects who inhaled saline and varying concentrations of adenosine (0.25, 0.5, 2.5 and 5 mg/ml). The nebuliser was calibrated to deliver 0.5 ml/min and readings of blood pressure (BP), heart rate (HR) and skin temperature (ST) made at 60 second intervals. Two studies were performed: (a) in which the various concentrations were inhaled for 2 minutes, and (b) in which saline was compared with adenosine 5 mg/ml, inhaled for 7 minutes.

No change was seen in BP or ST in either study. In study (a), HR rose by 6 ± 1.3 beats/min at 3 minutes ($P < 0.05$) returning to the baseline by 5 minutes. In study (b), HR rose by 7 ± 1.1 beats/min ($P < 0.02$) at 3 minutes and remained elevated throughout the study. One subject developed bronchospasm; she has no history of asthma or atopy but a methacholine challenge test suggests she is hyperreactive. The HR response is smaller (approximately 50% less) than that seen with an infusion but occurs at a comparable time.

Conclusions: (1) Adenosine is absorbed when given by nebuliser. (2) It is unlikely that enough is absorbed to terminate a tachycardia. (Higher doses limited by poor solubility.) (3) Asymptomatic hyperreactive subjects may develop bronchospasm.

Further studies will entail assessment of adenosine absorption with dipyridamole (uptake inhibitor) and using adenosine triphosphate (ATP) (more soluble).

Natriuretic mechanisms of atrial peptide in man (Abstract)

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The renal mechanisms of action of atrial natriuretic factor (ANF) have been intensively studied in experimental animals over the past few years. Relatively little, however, is known about how ANF affects nephron function in man. We have therefore examined the actions of ANF 99–126 in man using the lithium clearance technique to assess proximal and distal renal tubular function.

Six salt replete subjects were studied in the seated position on two separate occasions. Each volunteer took 500 mg of LiCO_3 at 22.00 h the night before the study. Subjects then attended the clinical laboratory at 08.30 h the following day. After an initial water load of 15 ml/kg, urine was voided every 20 minutes and the same volume of water drunk until a steady state diuresis was established. Aliquots of urine were kept for later analysis. An infusion of either (a) 5% D-glucose (placebo) or (b) ANF 0.04 $\mu\text{g/kg/min}$ was then administered during the next 20 minute urinary clearance period (CP). Urine was collected for this and 2 further CP after the infusion. Absolute Na^+ excretion (U_{Na^+V}) for each CP was: (a) 110 ± 20 ; 101 ± 16 ; 92 ± 14 ; 93 ± 17 . (b) 117 ± 33 ; $163 \pm 36^*$; $188 \pm 40^*$; $142 \pm 34^*$. Creatinine clearance (C_{cr}) (ml/min $\pm$ s.e.m.) for the equivalent CP was: (a) 105 ± 5 ; 112 ± 5 ; 110 ± 4 . (b) 107 ± 9 ; 117 ± 9 ; 116 ± 9 ; 115 ± 6 . Albumin excretion per unit C_{cr} ($\mu\text{g/ml} \pm$ s.e.m.) ($n=9$ subjects) was: (a) 0.051 ± 0.006 ; 0.052 ± 0.007 ; 0.047 ± 0.004 ; 0.047 ± 0.005 . (b) 0.038 ± 0.005 ; $0.084 \pm 0.02^*$; 0.119 ± 0.03 ; $0.088^* \pm 0.02$. Fractional Na^+ excretion (FE_{Na^+}) [% $\pm$ s.e.m.] was: (a) 0.77 ± 0.1 ; 0.66 ± 0.1 ; 0.60 ± 0.1 ; 0.64 ± 0.1 . (b) 0.83 ± 0.2 ; $1.04 \pm 0.2^*$; 1.18 ± 0.2 ; $0.98 \pm 0.2^*$. Fractional Li^+ excretion (FE_{Li}) [% $\pm$ s.e.m.] was: (a) 29.6 ± 2 ; 29.1 ± 3 ; 29.4 ± 3 ; 29.7 ± 3 . (b) 30.2 ± 3 ; 28.8 ± 4 ; $34.7 \pm 2^*$; 29.3 ± 2 . The fractional reabsorption rate of sodium in the distal nephron (FDR_{Na}) (% $\pm$ s.e.m.) was: (a) 97.49 ± 0.36 ; 97.74 ± 0.24 ; 97.97 ± 0.18 ; 97.89 ± 0.18 . (b) 96.81 ± 0.48 ; 95.68 ± 0.95 ; 95.76 ± 1.00 ; 96.33 ± 0.69 (* overall). (* $P < 0.05$; $\dagger P < 0.01$ vs control.)

The pharmacological dose of ANF used in this study produced the expected increase in urinary Na^+ excretion. This occurred in association with a rise in C_{cr} which failed to reach statistical significance. However, urinary albumin excretion, corrected for C_{cr} , did increase significantly which may mean that glomerular permeability is enhanced by ANF. FE_{Li} also rose significantly showing that fractional proximal tubular Na^+ reabsorption was