PLETHYSMOGRAPHIC STUDY WITH FRUSEMIDE AND PIRETANIDE IN HEALTHY VOLUNTEERS

Biamino, Wessel, Schüren, Ramdohr, Nöring & Schröder (1974) made extensive studies of the effect of frusemide on venous compliance in normal subjects. The compliance increased, which might explain the observed fall in the forward load on the left ventricle (Dikshit, Vyden, Forrester, Chatterjee, Prakash & Swan, 1973; Schenk, Biamino & Schröder 1975). Frusemide was therefore compared with piretanide, a new highly effective diuretic (Merkel, Bormann, Mania, Muschaweck & Hropot, 1976) in a plethysmographic study.

A double-blind cross over experiment was made in five healthy male volunteers. Their mean $\pm$ s.e. mean age was 24.6 ± 1.36 years and their mean weight 65.8 ± 5.9 kg. Intravenous bolus doses of frusemide (40 mg) and piretanide (12 mg) were given at intervals of 1 week. Venous pressure was measured using a thin cannula passed into a forearm vein and connected to a Statham transducer. Changes of forearm volume were recorded using a mercury in rubber strain gauge. Measurements were made at the following times:

10.5 min and immediately before each bolus, and 3, 5 and 10 min after each bolus. Each measurement was repeated three times.

Venous compliance was calculated as the ratio between the slopes of the curve for volume change and the curve for pressure change plotted against time, i. e. $\text{compliance} = \Delta v / \Delta p$.

Venous compliance was found to increase before the tenth minute. The mean increase was 16.8% for frusemide which is consistent with the data of Biamino *et al.* (1974) and Dikshit *et al.* (1973). With piretanide the mean increase was 19.9%. There was a significant difference between initial compliance, and that measured at the fifth minute ($P=0.01$) and at the tenth minute ($P=0.05$) with piretanide. These

significances were found using the Dunnett test. Both drugs evoked comparable diureses during the first hour after injection.

The data show that piretanide has an effect on venous compliance like that of frusemide. Results were similarly found in another randomly allocated experiment in patients with heart failure.

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PARACETAMOL AND ASPIRIN ABSORPTION FROM SAFAPRYN AND SAFAPRYN-CO.

Bajorek, Widdop & Volans (1978) demonstrated that oral codeine phosphate (15–30 mg) does not delay the absorption of paracetamol (1.5 g) when given 30 min previously. This may seem surprising since other narcotic analgesics can delay gastric emptying and greatly slow the rate of paracetamol absorption (Nimmo, Wilson & Prescott, 1975; Nimmo, Heading, Wilson, Tothill & Prescott, 1975). However, Crone & Ardran (1957) found that intravenous morphine in subtherapeutic doses increased the amplitude of

gastric peristalsis and 'propulsive power' of the stomach for approximately 30 min in healthy volunteers; this 'augmented activity' being followed by a longer phase of inhibition of peristalsis. This could conceivably explain the failure of inhibition of paracetamol absorption by codeine in the studies of Bajorek *et al.* (1978) and it may be that low doses of narcotics initially have a stimulating effect on gastric emptying.

Little is known of the absorption of paracetamol