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ORAL HYOSCINE BUTYLBROMIDE DOES NOT ALTER THE PATTERN OF SMALL INTESTINAL MOTOR ACTIVITY

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1 Continuous recording of proximal jejunal motility in conscious healthy subjects was made following ingestion of 200 mg hyoscine butylbromide (ten times the recommended therapeutic dosage).

2 There was no detectable modification of fasting or postprandial motor activity, although the therapeutic potency of the standard intravenous dose was confirmed.

Introduction

Hyoscine butylbromide (Buscopan, Boehringer-Ingelheim) an atropine-like drug has a prompt inhibitory action upon the motility of the human gut after parenteral administration, but is suspected to be inactive when taken orally (Guignard, Herxheimer & Greenwood, 1968). Nevertheless, oral preparations are still marketed as antispasmodics, allegedly acting 'predominantly on the intramural parasympathetic ganglia' (Buscopan data sheet, Boehringer-Ingelheim) in view of absent systemic anticholinergic effects. We have studied the action of this drug on the small intestine of normal subjects to test this hypothesis.

Human small intestinal fasting motor activity is cyclical, consisting of alternating periods of activity and quiescence (Thompson, Wingate, Archer, Benson, Green & Hardy, 1980). The periodic activity, which migrates slowly down the small bowel, shows two components, a period of irregular activity followed by a period of regular contractions (the activity front). Since an action by a drug upon the intramural ganglia would be expected to affect the cyclical pattern, we have attempted to determine what effect, if any, the drug exerted upon such activity.

Methods

An ingested pressure-sensitive radiotelemetry capsule (Rigel Research Ltd, Gander Green Lane, Sutton, Surrey) tethered at the duodeno-jejunal flexure, was used for measurement of intraluminal pressure changes in healthy fasted subjects (Thompson, Laidlow & Wingate, 1979). Changes in the frequency of radiotransmission induced by changes in gut pressure were detected by an array of aerials placed on the skin of the abdomen and fed into a radioreceiver. The voltage output of the receiver, varying in size with gut pressure changes, was recorded on magnetic tape, which was then replayed to give a permanent graphic record.

Six normal volunteers underwent study on 2 successive days. On the first day, used as a control period, no drug was given. On the second day, subjects received 20 tablets each containing 10 mg hyoscine butylbromide orally with sips of water, during an established phase of irregular contractile activity (Phase II); they were given a standard hospital lunch 2 to 3 h later. Studies continued for at least 3.5 h.

One further subject received 20 mg hyoscine butylbromide intravenously during recording of gut activity to act as a positive control. All subjects were asked to report the presence or absence of blurred vision, dryness of mouth or sweating. Pulse rate was also recorded throughout the study periods.

Motor activity following oral drug administration was assessed by comparison of the number of contractions for 30 min following the administration of the drug with a similar period in the control day, and also by comparison of the incidence of activity fronts in the period between drug administration and the administration of the meal with a similar period in the control study. In addition, the presence or absence of the normal change of pattern of motor activity following a meal was noted. Statistical comparisons were made by the Wilcoxon signed rank test.

Results

No subject reported any untoward effects following the oral drug although blurred vision was reported after the intravenous dose. Pulse rate measurements

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remained unchanged after the oral, but increased after the intravenous drug.

Motor activity was totally abolished for 15 min following intravenous administration of the drug, confirming that the method is able to detect a well-documented effect of the drug.

No significant difference was found in the number of contractions following drug administration ($P > 0.1$) (Figure 1) or in the incidence of activity fronts (Phase III) of the migrating complex in the preprandial period ($P > 0.1$).

Feeding activity (disruption of the fasting pattern by irregular contractile activity) was documented in all studies after administration of the meal.

Discussion

While indirect studies (Guignard *et al.*, 1968) have provided similar evidence, this study seems to be the first to demonstrate directly, the absence of any effect of oral hyoscine butylbromide upon small gut motor activity. There is certainly no evidence that the drug, when administered orally (even in doses 10 times those recommended by the manufacturer), has any effect upon normal patterns of motility. While the principle reason for this inactivity seems to be poor absorption (Bromster, Carlberger, Lundh, Moller & Rosen (1968), it could be claimed that a direct transmucosal action upon the gastric musculature

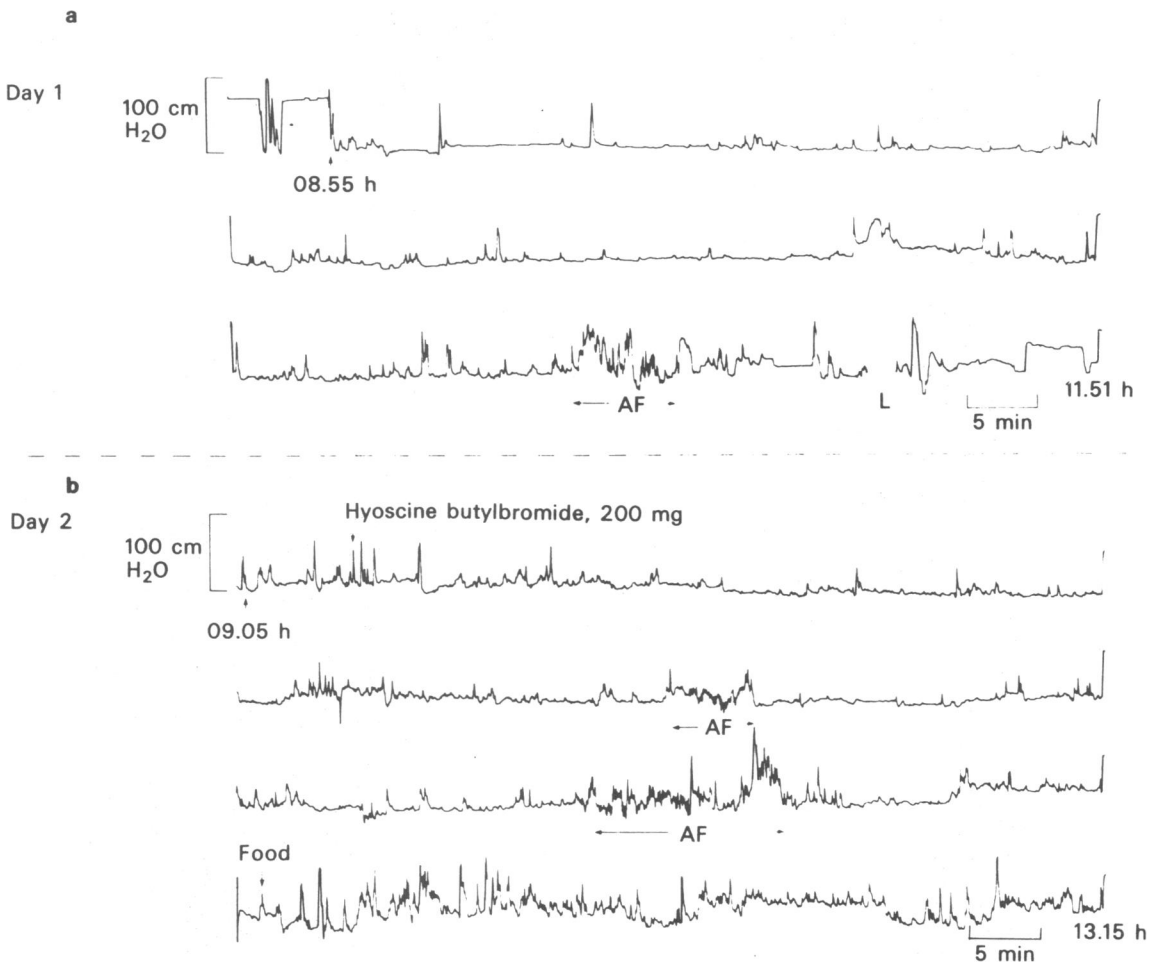

Figure 1 Continuous recording of intraluminal pressure change in the proximal jejunum of a subject on two successive mornings: Day 1 (a) without medication, and Day 2 (b) following the administration of 20 mg hyoscine butylbromide. On both occasions, the incidence of 'activity fronts' is within the normal range, and on Day 2, the normal change of pattern following food is seen. L = signal loss; AF = activity front (phase II) of the migrating motor complex.

could sufficiently reduce the passage of the drug into the small intestine to prevent the development of drug levels necessary for a recordable effect. The prompt appearance of a feeding response after the standard meal however seems to be inconsistent with this view, as are the results of previous studies of the action of the drug upon gastric emptying (Helstrom, Rosen & Soderlund, 1970).

With this radiotelemetry technique, instability of the baseline (Figure 1) precludes the use of the conventional assessment by 'motility index' as the amplitude of contractions cannot be measured with precision. The present technique of counting the number of contractions in unit time has been shown to be capable of defining, for example, diurnal variations in irregular contractions (Ritchie, Thompson & Wingate, 1980) and the incidence of activity fronts in a 2 h period has also been shown to be a useful index in, for example, the assessment of the effects of stress (McRae, Thompson, Wingate & Younger, 1980). It seems unlikely that the ingestion of tablets with a little water would *per se* affect the motility pattern; while a mixed nutrient meal will do so (Thompson *et al.*, 1980), the pattern of motility was found to be unaffected by the ingestion of 50 mg of glucose in 200 ml water in a study of motility in relation to glucose tolerance (Thompson & Wingate, 1980).

An action of the drug upon the colon has not been excluded but it seems unlikely that the drug could have a specific action on one site in the gut but not another. Furthermore, the drug has no greater effect on the bowel habits of patients with the irritable bowel syndrome than placebo (Ritchie & Truelove, 1979). Thus, any action that oral hyoscine butylbromide might exert upon the myenteric plexus of normal subjects or in the irritable bowel syndrome seems to be of no functional significance, making its clinical value dubious.

It is suggested that this method of recording physiological enteric motor activity may be appropriate in the clinical evaluation of other drugs for which therapeutic modification of motor activity is claimed.

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