THE EFFECT OF HYOSCINE BUTYLBROMIDE ON THE SWALLOWING OF CAPSULES

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Hyoscine butylbromide (20 mg) given intravenously to 48 patients with normal oesophageal motility significantly reduced oesophageal transit of hard gelatin capsules when swallowed in the erect and supine positions with 15 ml and 60 ml water when compared to an age/sex matched group. Delayed capsule transit and possible failed or slowed drug absorption occurring as a consequence of anticholinergic drugs on the oesophagus, constitutes a new drug interaction.

Introduction

The control of oesophageal peristalsis is complex with an interplay between central nervous system connections, intrinsic smooth muscle activity, the myenteric nervous network and local hormones (Weisbrodt, 1976). The smooth muscle of the lower oesophagus behaves differently from the muscle of the lower oesophageal sphincter (LOS) both physiologically, for example to stretch (Weisbrodt, 1976), and pharmacologically (Christensen, 1976; Misiewicz, 1974). Methods of studying oesophageal motility are limited and consist of manometry which is unpleasant and invasive and barium swallow which is insensitive (Ott *et al.*, 1981). By timing the passage of a small bolus (a hard gelatin capsule), oesophageal function can be readily assessed.

By manometric methods, anticholinergic drugs have been shown to reduce but not abolish contractions in the lower oesophagus (Kantrowitz *et al.*, 1970; Christensen, 1976), having a greater effect on the longitudinal muscle layer, and reduce LOS closure. The aim of this study was to examine the effect of the powerful anticholinergic hyoscine butylbromide on the clearance of capsules from the oesophagus, and in this way assess the functional effect of the drug.

Methods

Two groups of forty-eight patients age and sex matched (22 males, 26 females of ages 20–72 years) participated in the study after barium meal examination in which normal oesophageal peristalsis was demonstrated. One of the groups was given 20 mg hyoscine butylbromide 10 min prior to the study at

the time of barium meal examination. Informed signed consent was obtained from all patients and the project was approved by the district ethical committee.

Each patient swallowed hard gelatin capsules ('Farillon Lok-Cap' size 2) containing 97% barium sulphate powder in the erect position with 15 ml then 60 ml water and later in the supine position with 15 ml and 60 ml water. Using a stop watch the time taken by each capsule to pass from the oropharynx to stomach was measured during screening. If at 5 min the capsule remained in the oesophagus it was washed out with a large volume of water before proceeding on the next swallow.

The significance of the differences between control and drug treated transit times was assessed by the Wilcoxon matched pairs signed ranks test.

Results

Figure 1 shows the clearance of capsules from the oesophagus under four different conditions. Capsule clearance was rapid and complete in the erect position with 60 ml water, but delayed and incomplete under the other conditions. In all conditions the hyoscine butylbromide treated group showed a significant delay in transit compared with the control group.

Table 1 shows the patterns of capsule transit seen in the patients. In 13 (27%) of control patients all four capsules entered the stomach in less than 15 s, whereas this was seen in only 3 (6.25%) of the treated group. Arrested transit, when one or more of the four capsules remained in the oesophagus and disintegrat-

Figure 1 Graphs showing % of capsules remaining in oesophagus with time in erect/supine positions with 60 ml/15 ml water. — control group, --- hyoscine hydrobromide. Statistical analysis was by Wilcoxon's test.

ed, occurred in 25 (52%) controls and 39 (81.25%) treated patients. Analysed separately posture and drink volume had a highly significant effect on transit in both groups (both $P < 0.001$ Wilcoxon). Table 2 shows that supine posture was most often associated with arrested transit. The site of capsule arrest was similar in the two groups (Table 3). Once a capsule disintegrated (always between 2 and 3 min) it was never seen to enter, nor once entered, to reflux out of the stomach.

Table 4 shows the radiological diagnosis of the two patient groups. The transit times of the largest diagnostic subgroups (gastro-oesophageal reflux $\pm$ hiatus hernia) were compared with the transit times of

the other subgroups and no significant difference was found (Mann Whitney U test) in either control or treated group. In the control group there was no significant difference in age, sex, upper gastrointestinal symptoms and surgical history between those patients in whom capsules arrested and those with normal oesophageal capsule transit.

Discussion

Previous work has shown that tablets (Evans & Roberts, 1976) and capsules (Evans & Roberts, 1981; Channer & Virjee, 1982) may arrest and disintegrate in the oesophagus, particularly if taken in the supine position with small volumes of water (Channer & Virjee, 1982). This study has illustrated the effect of concurrent medication with hyoscine butylbromide.

Given intravenously hyoscine butylbromide is an effective anticholinergic drug with a short half-life (a 20 mg dose is inactivated within an hour in a 70 kg subject) (Herxheimer & Haefeli, 1966). It is used extensively in modern contrast radiology to paralyse the gastrointestinal tract. Oesophageal peristalsis as assessed by barium swallow, and manometric methods although reduced is not abolished by anticholinergic drugs (Kantrowitz *et al.*, 1970; Christensen, 1976). This study shows that clearance of a small

Table 1 Transit characteristics in the two groups

	Control	Hyoscine butylbromide
Normal transit (all capsules enter stomach in < 15 s)	13 (27%)	3 (6.25%)
Delayed transit (> 20 s without capsule disintegration)	10 (21%)	6 (12.5%)
Arrested transit (with capsule disintegration)	25 (52%)	39 (81.25%)

Table 2 Factors associated with capsule arrest

<i>Condition in which capsules arrested in the oesophagus</i>	<i>Control Number of patients (%)</i>	<i>Hyoscine butylbromide Number of patients (%)</i>
Arrest with small volume only	8 (32%)	15 (38%)
Arrest with large volume only	6 (24%)	7 (18%)
Arrest with both volumes	11 (44%)	17 (44%)
Arrest in erect position only	0	1 (3%)
Arrest in supine position only	23 (92%)	33 (85%)
Arrest in both positions	2 (8%)	5 (12%)

Table 3 Site of capsule arrest

<i>Site of arrest</i>	<i>Control</i>		<i>Hyoscine butylbromide</i>	
	<i>Number of occasions (%)</i>	<i>Number of patients (%)</i>	<i>Number of occasions (%)</i>	<i>Number of patients (%)</i>
(a) Throat	—	—	1 (2%)	1 (3%)
(b) Level of LMB	7 (14%)	4 (16%)	8 (13%)	4 (10%)
(c) Level of LOS	34 (70%)	18 (72%)	46 (77%)	29 (74%)
(d) Both (a) + (b)	—	—	—	1 (3%)
(e) Both (b) + (c)	8 (16%)	3 (12%)	5 (8%)	5 (13%)

Table 4 Radiological barium meal diagnosis

<i>Radiological diagnosis</i>	<i>Number</i>	<i>Control</i>	<i>Hyoscine butylbromide</i>
		<i>Number with capsule arrest (%)</i>	<i>Number with capsule arrest (%)</i>
Normal examination	10	8 (80%)	15 14 (93%)
Gastro-oesophageal reflux with hiatus hernia	18	7 (39%)	14 13 (93%)
Gastro-oesophageal reflux	12	5 (42%)	6 4 (66%)
Duodenal ulcer disease (duodenal ulcer, scarred cap, duodenitis)	7	5 (71%)	9 8 (89%)
Gastric ulcer	0		2 1 (50%)
Gastric carcinoma	0		2 2 (100%)
Gastric diverticulum	0		1 1 (100%)
Erosive gastritis	0		1 1 (100%)
Oesophageal varices	1	1 (100%)	
Previous pyloroplasty	2	1 (50%)	
Duodenal diverticulum			1 0%

bolus (a capsule) is delayed by hyoscine butylbromide and therefore functionally the drug has a significant effect on the oesophagus.

Many drugs have anticholinergic effects including tricyclic antidepressants, anti-Parkinsonian drugs, disopyramide and emepronium bromide. This last drug is recognised to cause oesophageal ulceration. (Collins *et al.*, 1979) and its anticholinergic properties will exacerbate the tendency for its arrest within the oesophagus. Anticholinergic oesophageal effects by inhibiting capsule transit may delay drug absorption since capsule disintegration will occur in the oesophagus with its non-absorptive stratified

squamous epithelium. This represents a potential new drug interaction of which clinicians should be aware. It reinforces the necessity of advising patients to take capsules standing with a large volume of water to ensure complete oesophageal transit.

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