Clinical Topics

Oesophageal transit of six commonly used tablets and capsules

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Abstract

The oesophageal transit of six commonly used tablets and capsules containing barium sulphate was evaluated radiologically using fluoroscopy in 121 healthy volunteers. To determine the influence of the subject's position and the amount of water taken each subject swallowed three preparations while recumbent and standing and with 25 ml or 100 ml of water. Failure of swallowing (defined as oesophageal transit taking more than 90 seconds) occurred in 22% of 726 swallowings, but globus was complained of in only 33% of these. Sixty per cent of the volunteers had difficulty in taking one or more of the preparations. Many preparations adhered to the oesophageal membrane and started to disintegrate in the lower part of oesophagus.

It is recommended that subjects should remain standing for at least 90 seconds after taking capsules or tablets and that all preparations should be taken with at least 100 ml of water. Small tablets are swallowed most easily. Liquid forms of medication (suspensions) should be considered for bedridden patients and those who have difficulty in swallowing.

Introduction

When drugs are taken by mouth it is assumed that they pass quickly and directly into the stomach with little or no fluid, unless some oesophageal disorder is present. Dyspepsia, including heartburn, nausea, and vomiting, does occur, however, after tablets and particularly capsules are swallowed. This may be due to the preparation adhering to the oesophageal membrane and causing local irritation as it disintegrates. There have been several reports of dyspepsia, oesophageal ulceration, and even death after the oral administration of drugs.[1-8]

Only a few studies have been conducted on the oesophageal transit of tablets and capsules.[9-12] Considerable variation in transit time has been reported, mainly because little attention was paid to the influence of the amount of fluid taken with the preparation, its size, shape, and density, and the position of the subject. An oesophageal transit time of 2-150 minutes (median 5 min) was recorded when recumbent subjects with a normal oesophagus swallowed barium sulphate tablets with unrestricted quantities of water.[12] When the medication was swallowed in the standing position without any fluids 66% of capsules and 23% of tablets stayed in the oesophagus for more than four minutes.[9] When the drugs were swallowed with 40 ml of water, however, in only 7% of the capsules and none of the tablets was passage delayed. In an investigation of barium sulphate tablets identical to those of aspirin 58% of tablets remained in the oesophagus for five minutes when swallowed supine with 15 ml of water.[10] Even large amounts of water did not wash down the tablets.

We have examined the influence of the position of the subject and the amount of water swallowed with the medication on the oesophageal transit of six commonly used tablets and capsules containing barium sulphate. We also determined the influence of the size, shape, and density of the preparations on their passage through the oesophagus.

Subjects and methods

One hundred and twenty-one volunteers with no previous history of gastric or cardiac disease were allocated randomly to two groups.

Group 1—This comprised 60 subjects aged 19-80 years (median 39 years) who received the following preparations (fig 1); A—large oval tablet (weight 1030 mg); B—large round tablet (weight 915 mg); and C—capsule (weight 510 mg, density < 1).

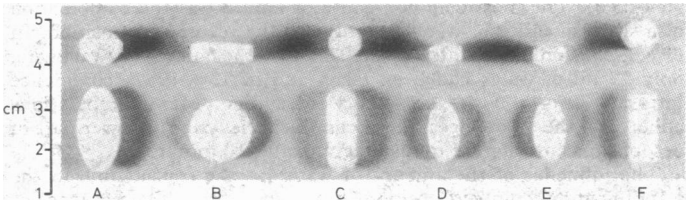

FIG 1—Size and shape of the six ingested tablets and capsules containing barium sulphate.

Group 2—This comprised 61 subjects, aged 19-64 years (median 26 years) who were given the following preparations (fig 1); D—small oval coated tablet (weight 408 mg); E—small oval uncoated tablet (weight 400 mg); and F—capsule (weight 990 mg, density > 1). The tablets and capsules contained barium sulphate granulate and were identical in size and shape to commonly used products. Further information and details of the preparations are given elsewhere.[13]

Each group swallowed the appropriate preparations while both recumbent and standing with either 25 or 100 ml of water. The amount of fluid taken was determined by a list of random numbers. The volunteers themselves selected the sequence in which the three preparations were swallowed.

The oesophageal transit time was evaluated radiologically using a Siregraph E universal-couch with monitor and fluoroscopy. The rapidity and the manner in which the preparations passed to the

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stomach were examined carefully. The position of any preparation that became lodged in the oesophagus and the time at which this occurred were recorded. A further 25 ml or 100 ml of water was taken if the drug was present in the oesophagus after 10 minutes and remained so for a further 15 minutes. Signs of globus or dysphagia were recorded. Successful oesophageal transit was based on a transit time (from swallowing to arrival in the stomach) of less than 90 seconds; times in excess of this were classified as failures of swallowing.

Statistical analysis of the influence of the subject's position and the shape of the preparation was tested by McNemar's test when data came from the same person and by the χ^2 test when data from different groups were compared; 95% confidence limits were used.

All volunteers gave informed consent and the investigation was performed in accordance with the Helsinki Declaration II.

Results

A total of 726 swallowings were studied in the 121 volunteers. The frequency with which the tablets and the capsules lodged in the oesophagus and where they were delayed for more than 90 seconds are shown in table I. Delay in oesophageal transit occurred in 22%

TABLE I—*Incidence of delay in oesophageal transit and its location*

Location of delay	Preparation						Total
	A	B	C	D	E	F	
Pyriform fossa		1	1				2
Aortic arch	3	11	2				16
Carina	4	8	5		2		19
Heart	6	11	2	2	2	6	29
Cardia	28	34	13	4	5	7	91
Total	41	65	23	6	9	13	157
Incidence of globus (%)	22	45	17	17	44	31	33

A = large oval tablet; B = large round tablet; C = capsule (density < 1); D = small oval coated tablet; E = small oval uncoated tablet; F = capsule (density > 1).

(95% confidence interval, 17·9-25·2) of all swallowings. Globus was noted in 33% (95% confidence interval, 29·3-36·7) of all swallowings. In two subjects the preparations were trapped in the pyriform fossa causing great discomfort. These symptoms disappeared quickly when extra water was taken. The probability of a successful swallowing in group 1 (standing and recumbent) for all three preparations was 13% (95% confidence interval, 11·2-14·8). The success rate in group 2 was 67% (95% confidence interval, 64·5-69·5). Overall, failure of swallowing occurred in 72 (60%) subjects (95% confidence interval, 56·4-63·6). The most common cause of failure was the combination of a small quantity of water (25 ml) and the recumbent position. In 69% (95% confidence interval, 66·0-71·4) of the failures of swallowing only 25 ml of water had been taken and in 73% (95% confidence interval, 70·7-75·3) the subjects were supine. Many preparations adhered to the oesophageal membrane, especially in the lower part of oesophagus, and started to disintegrate after 10 minutes.

The influence of the amount of water on the transit time in the standing and recumbent positions is shown in fig 2. The influence of

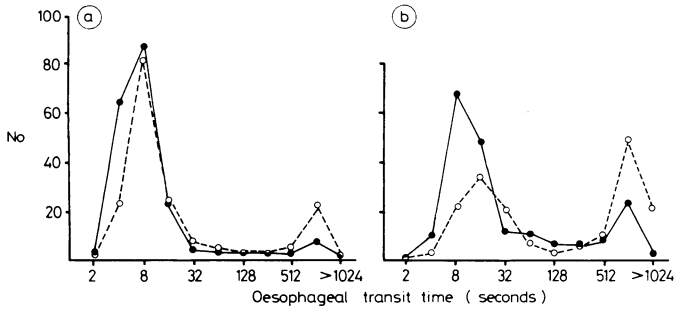

FIG 2—Oesophageal transfer times (log scale) of six different tablets/capsules taken with 25 (○) or 100 (●) ml of water while (*a*) standing and (*b*) recumbent.

the amount of water and the combination of the subjects' position and the shape and the size of the preparations are shown in table II. The amount of water taken had a highly significant effect on the transit time when any tablet was swallowed in the supine position (preparations A, B, D, and E) and when the large tablets (A and B) were swallowed standing ($p < 0.005$). This was not the case for the capsules. Large tablets (A and B) should therefore be swallowed standing ($p < 0.005$).

TABLE II—*Incidence of successful oesophageal transit in relation to fluid intake and the subject's position. (Successes and failures in both positions are excluded)*

Volume of water	Preparation					
	A	B	C	D	E	F
25 ml:						
Upright position	19	10	4	8	15	8
Supine position	1	2	4	0	0	1
Probability	0·00014	0·043	NS	0·013	0·0003	0·046
100 ml:						
Upright position	9	14	3	1	5	7
Supine position	0	3	3	1	0	0
Probability	0·0077	0·015	NS	NS	NS	0·023

A = large oval tablet; B = large round tablet; C = capsule (density < 1); D = small oval coated tablet; E = small oval uncoated tablet; F = capsule (density > 1).

The position of the subject was not important for light preparations (C, D, and E) taken with 100 ml water nor for the capsule (C) regardless of the fluid intake. Large oval tablets (A) and capsules (C) passed through the oesophagus significantly faster than the large round tablets (B) when taken with 25 ml of water ($p < 0.003$). This difference was not apparent when 100 ml of water was taken. Small tablets (D and E) had a significantly faster transit time than did large tablets, irrespective of the amount of water taken ($p < 0.006$). Small coated oval tablets (D) were swallowed significantly more easily than uncoated oval tablets (E) ($p < 0.01$). In contrast, capsule size did not seem to be as important (preparations C and F). Oesophageal transit time was not affected by smoking or age, except that subjects over 60 years had great difficulty in swallowing the large round tablet (B) ($p < 0.05$).

Discussion

Dyspepsia is common after tablets and particularly capsules are swallowed. This may be because the subjects are in a recumbent position or the preparations are taken without food or with too little fluid. This aspect has not been studied adequately in the past.[9-12] The studies which have been performed are not comparable because of differing designs. Consequently, they have reported considerable variations in transit time.

In our study 22% out of the 726 swallowings were delayed. Surprisingly, however, globus or dysphagia was recorded in only about one-third of these. This suggests that only a few of those patients who have delayed oesophageal transit will develop symptoms associated with poor swallowing. Our study showed that it was essential to take medication with 100 ml of water to ensure a rapid transfer of large tablets through the oesophagus when the subject was recumbent or standing. A similar quantity of fluid was also vital when small oval tablets were swallowed in the supine position. The quantity of water taken had no influence, however, on the passage of capsules. This finding does not support the hypothesis that capsules are more liable to stick in the oesophagus than tablets when swallowed standing both with or without 40 ml of water.[9]

Despite our results we prefer not to give capsules. A light capsule (density < 1) was trapped in the pyriform fossa, causing dysphagia and coughing. Like other workers[9 11 14] we have seen capsules adhere to the oesophageal membrane on a level with the carina, where they slowly disintegrated. Further quantities of water could not wash the capsules down into the stomach. With capsules there is therefore, a risk of ulceration, perforation, and even stricture.[1-3 5 8] The transit time of large tablets was significantly longer in elderly subjects. This might have been due

to their size and shape, but the physiological changes associated with age could also have been responsible. Some elderly patients had difficulty in swallowing 100 ml of water as they could only sip it. In recent years the number of doses taken each day has been reduced, which has led to an increase in tablet size; this is not conducive to rapid oesophageal transit. Seventy-two (60%) subjects in this study had difficulty in swallowing one or more of the preparations; of these, 52 were in group 1, indicating that small tablets were preferable. Oval tablets are more easily swallowed than round ones, particularly if they are large, as are small oval coated tablets than uncoated ones. In only one subject was oesophageal transit delayed among the subjects who took "heavy" capsules while standing. The position of the subject was not important, however, when small tablets were swallowed with 100 ml of water. Delayed transit time and retention of the preparation in the distal oesophagus are possible in patients with dyspepsia or oesophagitis confirmed by gastroscopy.[15] The preparations were taken with a minimum of 25 ml of water, since 10-20 ml of fluid is necessary to induce peristalsis.[16] A volume of 100 ml was chosen to help oesophageal transit and the bioavailability of the drug[17] and to take account of age.

Our results show that patients should remain standing for at least 90 seconds after taking medication, that tablets should be swallowed with at least 100 ml of fluid, and that small oval tablets are preferable. If large tablets have to be taken, these should be oval and not round. Capsules of a high density are easier to swallow than lighter ones. Patients who are bedridden or have difficulty in swallowing should be given liquid medication.

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Clinical curio: Liver disease and parsley

Edible umbelliferous plants such as parsnip and parsley contain appreciable amounts of psoralens, especially if diseased, and may cause phytophotodermatitis on contact with the skin. Plant psoralens may be responsible also for other conditions.[1]

A 70-year-old woman presented with a two-year history of generalised itch and pigmentation over her lower legs. She avoided sunlight to prevent sunburn. She had mild hepatomegaly, and investigations showed a serum alkaline phosphatase concentration five times the normal value, γ-glutamyl-transferase concentration 10 times the normal value, and aspartate transaminase concentration twice the normal value. The serum bilirubin concentration was normal. Her alcohol intake was small, and she had not had jaundice. She had taken digoxin and bumetanide for three years. She had also eaten large quantities—about 170 g—of fresh parsley daily for 30 years. Australia antigen, antinuclear factor, and anti-mitochondrial and anti-smooth muscle antibodies were not detected, and an intravenous cholangiogram, technetium liver scan, and cholescintography were normal. A liver biopsy specimen showed areas of recent centrizonal necrosis with associated inflammation, a moderate non-specific inflammatory infiltrate of the portal tracts, and mild fatty change. Over two years her condition remained stable, but on reducing her parsley intake by two-thirds her itch improved considerably and her pigmentation disappeared, although her liver function tests remained abnormal.

Psoralens are metabolised in the liver and excreted by the kidney[2]; parsley contains 5-methoxypsoralen.[3] We presume that in the presence of chronic liver disease a large intake of psoralen in parsley produced this patient's symptoms of pruritus, pigmentation, and a tendency to sunburn. The cause of the chronic hepatitis is unknown, but sporalens are mutagenic[1] and are furanocoumarins, which are structurally related to coumarins and aflatoxins (which are bifuranocoumarins). My thanks to Dr P Brunt for permission to describe this patient who was under his care.—PHILIP COOLES, medical registrar, Dominica, Windward Islands.

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Is thrombophlebitis after intravenous pyelography a contraindication to prescribing the oral contraceptive pill after the phlebitis has settled?

There are no reliable figures to answer this question. The risk of superficial venous thrombosis among users of oral contraceptives is increased about threefold,[1] and superficial thrombophlebitis associated with varicose veins is usually regarded as a contraindication to oral contraception.[2] It may be that superficial thrombophlebitis provoked by an intravenous injection indicates a susceptibility to thromboembolism, but I know of no evidence to suggest this. Thrombophlebitis is a relatively uncommon reaction to intravenous pyelography: but arm pain may be due to perivenous injection of contrast medium or stasis of medium in the vein,[3] and this may provoke thrombophlebitis. My personal opinion is that such a reaction is not a contraindication to prescribing one of the low-oestrogen oral contraceptives, which are probably associated with a lower risk of thromboembolism than older types of pill.[1]—JAMES OWEN DRIFE, senior lecturer in obstetrics and gynaecology, Leicester.

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Is calciferol of any value in the treatment of chilblains and does its administration carry any risk?

Chilblains are a type of cold injury that may be due simply to lack of care in keeping the skin warm but which may be secondary to poor peripheral circulation in the skin due to vascular disease or to adiposity. Calciferol has no place in the treatment of chilblains. There is little evidence that it has any effect. The proper management of chilblains is to prevent them by ensuring that the skin does not become unduly cold. It is also necessary to ensure that the diagnosis of chilblains is correct and that lupus erythematosus or cutaneous vasculitis or polyarteritis nodosa is not present. Taken in large doses calciferol can produce hypercalcaemia and renal damage, admittedly a small risk, but if it is prescribed for its placebo effect it is a risk not worth taking.—ALAN B SHRANK, consultant dermatologist, Shrewsbury.