Effect of left atrial size on the oesophageal transit of capsules

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SUMMARY The oesophageal transit time of barium sulphate capsules was measured using x ray fluoroscopy in 20 patients with mitral valve disease and 12 control patients in the erect and supine positions when swallowed with both 15 ml and 60 ml of water. An erect barium swallow was performed, and from a lateral radiograph the area of indentation of the oesophagus caused by the cardiac impression was measured. Left atrial diameter was derived from M mode echocardiography. In 19 patients with mitral valve disease one or more capsules remained in the oesophagus for five minutes and disintegrated there, whereas this occurred in only six control patients. Capsule transit time was significantly slower in the study patients than in the control patients in the supine position with 15 ml water. There was a significant correlation between the area of indentation and mean capsule transit time and supine 15 ml transit time. The area of indentation closely correlated with the left atrial diameter. When capsules were delayed in the oesophagus, this occurred mainly at the level of the left atrial impression in the study patients and at the lower oesophageal sphincter in the control patients.

Patients with mitral valve disease are more likely than control patients to have delayed oesophageal transit of capsules because of the anatomical deformity caused by enlargement of the left atrium.

Over 20 drugs have been implicated in causing oesophageal ulceration,¹ and most reports concerned potassium chloride, emepronium bromide, tetracycline, doxycycline, and quinidine. The ulceration is thought to be due to a local irritant effect from prolonged contact of the drug with the mucosa. Using barium sulphate capsules and x ray fluoroscopy we have shown that capsules frequently lodge and disintegrate in the oesophagus when swallowed in the supine position with a small drink volume.² Capsules lodge at sites of anatomical indentations in the oesophagus—that is, at the level of the left main bronchus and aortic arch and at the lower oesophageal sphincter. When the heart is enlarged, especially the left atrium, the oesophagus is further indented.

In this study we investigated the effect of left atrial enlargement on the oesophageal transit time of capsules.

Patients and methods

Twenty patients (16 women, four men; aged 39–66 years) with mitral valve disease undergoing routine echocardiography participated in the study. A control group without mitral valve disease comprised 12 in-patients (two women, 10 men; aged 39–61 years) awaiting cardiac catheterisation. The diagnostic categories of all the patients are shown in Table 1. Informed consent was obtained.

Hard gelatin capsules (Farillon Lok Cap size 2) were filled with 97% barium sulphate powder. Each patient was asked to swallow a capsule (a) in the erect position with 60 ml of water; (b) in the erect position with 15 ml of water; (c) in the supine position with 60 ml of water; and (d) in the supine position with 15 ml of water. The time taken by the capsule to traverse the oesophagus was measured with a stop watch during x ray fluoroscopy. If a capsule remained in the oesophagus for >30 s its position was checked every 30 s for a total of five minutes. If it remained in the oesophagus at five minutes it was washed out by a further drink in the erect or sitting position before the next swallow.

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Table 1 Diagnoses in 20 patients with mitral valve disease and 12 control patients

Diagnosis	No of patients
<i>Study patients</i>	
Pure mitral stenosis	10
Pure mitral regurgitation	1
Mixed mitral valve disease	4
Aortic and mitral valve disease	5
Total	20
<i>Control patients</i>	
Ischaemic heart disease	9
Aortic stenosis	1
Palpitations	1
Non-cardiac chest pain	1
Total	12

A supine barium swallow was performed and oesophageal peristalsis assessed by a radiologist and classified as abnormal if the primary peristaltic wave did not fully clear the barium or if there were tertiary contractions.

An erect barium swallow was performed and a single lateral radiograph taken. A radiopaque centimetre ruler was positioned on the sternum in the mid-line to establish a magnification factor. The area of indentation of the oesophagus caused by the heart was measured from this film using computer planimetry (Apple computer digitalising tablet). Two observers performed the measurements and the average of four measurements was taken (Fig. 1). Areas were corrected for magnification. Left atrial diameter was measured from M mode echocardiograms (average of five consecutive measurements).

Fig. 1 Radiograph of lateral barium swallow showing cardiac indentation. The diagram shows the area of indentation (AOI) measured from the points of maximum deflection of the oesophagus (A, B) by the heart.

A medical history was obtained after the barium swallow examination but before the capsule transit study. Patients were specifically questioned about upper gastrointestinal symptoms, dysphagia, and difficulty in swallowing tablets.

Results were analysed using non-parametric statistical methods.

Results

Table 2 shows some of the patient characteristics and responses to questioning about their tablet swallowing habits.

Fig. 2 shows the percentage of capsules remaining in the oesophagus with time under the four different conditions. When the transit times in the two groups of patients were compared (Table 3) the only significant difference was found when the capsule was swallowed supine with 15 ml of water ($p < 0.01$, Mann Whitney test). When all patients were analysed together the transit times in the erect position and with 60 ml of water were significantly faster (Table 4) than those in the supine position and with 15 ml of water.

Table 2 Characteristics of 20 (study) patients with mitral valve disease and 12 control patients. Figures are numbers of patients

Characteristic	Study patients	Control patients
<i>Drugs taken:</i>		
Slow release potassium chloride	5	
Non-steroidal anti-inflammatory	2	
Anticholinergics	2	
Diuretics	17	
Anticoagulants	11	
Digoxin	10	
Nifedipine		7
Beta adrenergic blockers		5
Isosorbide dinitrate		2
Upper gastrointestinal symptoms:	10	8
Acid regurgitation	4	3
Heartburn	4	4
Flatulence	7	7
Postprandial epigastric pain	1	0
Dysphagia	1	0
Problems with tablet taking:		
Tablet dysphagia	7	4
Tablets sticking		
In throat	6	6
Retrosternally	3	1
In epigastrium	0	1
Swallows tablets without fluid	6	3
Smokers	6	2

Capsules arrested in the oesophagus on 45 occasions in all. Thirty six of these occurred in patients with mitral valve disease and in nine in the controls. In 19 (95%) of the 20 patients with mitral valve disease capsules arrested—that is, remained and disintegrated—in the oesophagus; in contrast this occurred in six (50%) control patients ($p < 0.01$). The significant difference in frequency of capsule arrest occurred only with 15 ml of water (Table 5).

Fig. 2 Percentage of capsules remaining in the oesophagus with time in the erect and supine positions after ingestion with 15 ml and 60 ml of water. Solid line denotes patients with mitral valve disease; broken line denotes control patients.

Table 3 Median oesophageal transit time of capsule swallowed supine or erect with 15 ml or 60 ml water in 20 study patients and 12 control patients

Position and drink volume	Median (range) transit time (s)		p value*
	Study patients	Control patients	
Erect 15 ml	4 (2-300)	3 (2-5)	NS
Erect 60 ml	4 (2-300)	2 (2-300)	NS
Supine 15 ml	300 (120-300)	30 (7-300)	<0.01
Supine 60 ml	135 (2-300)	9 (4-300)	NS

*Mann Whitney test.

Table 4 Median oesophageal transit time of capsule swallowed supine or erect with 60 ml or 15 ml water in all patients

Position and drink volume	Median (range) transit time (s)	p value*
Erect	3.5 (2-300)	<0.001
Supine	300 (4-300)	
60 ml water	5 (2-300)	<0.001
15 ml water	32 (2-300)	

*Wilcoxon matched pairs signed ranks test.

Capsules arrested more frequently at the level of the left atrial indentation in the study patients ($p < 0.002$, Fisher's exact test) (Table 5). There was no significant difference between the number of patients with abnormal peristalsis in the patient groups. Six of the study patients had previously had thoracotomies. There was no significant association between a previous thoracotomy and abnormal peristalsis.

Table 5 Number of patients with capsule arrest in relation to position, drink volume, and peristalsis

	<i>Study patients (%)</i>	<i>Controls patients (%)</i>	<i>p value*</i>
Position and drink volume:			
Erect 15 ml	6/20 (30)	0/12	<0.05
Erect 60 ml	2/20 (10)	1/12 (8)	NS
Supine 15 ml	18/20 (90)	5/12 (42)	=0.005
Erect 60 ml	10/20 (50)	3/12 (25)	NS
Site of capsule arrest:			
At left main bronchus	2/45 (4)	2/45 (4)	<0.002
At left atrial indentation	21/45 (47)	0/45 (0)	
At level of lower oesophageal sphincter	13/45 (29)	7/45 (16)	
Peristalsis			
Normal	11/20 (55)	8/12 (67)	NS
Abnormal	9/20 (45)	4/12 (35)	

*Exact test.

It was possible to obtain good quality echocardiograms for all patients. Increased left atrial diameter did not correlate with total transit times (all four conditions combined; Table 6) or with transit times under the different conditions. There was a significant positive correlation between the area of oesophageal indentation and total capsule transit time ($p < 0.05$, $r_s = 0.33$ Spearman's rank correlation) and transit time in the supine position with 15 ml water ($p < 0.0005$, $r_s = 0.48$). The area of indentation closely correlated with left atrial diameter (Fig. 3) ($p < 0.0005$, $r_s = 0.74$).

The capsules which remained in the oesophagus disintegrated between two and four minutes and remained there until washed out at five minutes.

Table 6 Relation of left atrial diameter, area of oesophageal indentation, and total transit time in two groups of patients

Patients with mitral valve disease (n=20)			Control patients (n=12)		
Left atrial diameter (cm)	Area of oesophageal indentation (cm ²)	Total transit time (s)	Left atrial diameter (cm)	Area of oesophageal indentation (cm ²)	Total transit time (s)
2.2	5.1	484.5	2.1	5.3	18.5
2.8	8.3	672	2.2	3.8	313
3.0	11.5	608	2.4	5.3	310
3.7	9.6	1200	2.5	1.3	620.5
3.7	8.1	312	2.6	4.0	610
3.9	18.6	308	2.7	7.1	24
4.15	9.3	639.5	2.9	3.1	609
4.2	14.4	211	3.0	2.6	17
4.25	8.84	309	3.1	2.0	32
4.3	9.8	442	3.4	1.9	45.5
4.6	28.1	608	3.5	2.6	334
4.6	8.6	635.5	3.5	2.7	27
4.9	21.4	1200			
5.0	23.4	608			
5.2	25.1	640			
5.4	18.8	307			
5.5	9.0	905			
5.5	43.6	607			
5.7	10.9	612			
7.9	19.1	131.5			
Mean					
4.53	15.6	572	2.83	3.5	247

Fig. 3 Correlation of left atrial diameter with area of oesophageal indentation. (○) patients with mitral valve disease; (●) control patients.

Discussion

This study shows that the oesophageal transit of capsules is delayed in patients with mitral valve disease compared with that in a control group when they are swallowed in the supine position with a small drink. Under these conditions the effects of gravity and bolus volume are minimised.² In patients with mitral valve disease capsules arrested mostly at the site of the left atrial indentation. Capsule transit time correlated significantly with the area of indentation of the oesophagus resulting from left atrial enlargement. It

appears that the delay in capsule transit was caused by this anatomical deformity.

We measured oesophageal distortion in the anteroposterior direction only, but when the atrium is very large the oesophagus is also pushed laterally, usually to the right. Such distortion may produce dysphagia, but this is uncommon. Chesshyre and Braimbridge suggested that left sided oesophageal displacement is more likely to produce dysphagia because of compression against the aorta and vertebral bodies.³ Left sided oesophageal displacement also occurs when the aorta is excessively tortuous and may produce dysphagia.⁴ In our group only one patient complained of dysphagia with food, and the frequency of tablet dysphagia was no higher than in the control group. Most of our study patients had only mild to moderate left atrial enlargement, which was insufficient to produce enough oesophageal compression to cause dysphagia but sufficient to cause delayed capsule transit.

The consequences of delayed oesophageal transit of tablets and capsules may be fatal. Of the 17 reported cases of oesophageal ulceration induced by potassium chloride strictures causing dysphagia occurred in nine (53%) (six required dilatation and one was due to spasm since the apparent stricture disappeared when the drug was withdrawn).⁵⁻¹⁶ In two patients feeding jejunostomies were performed, and these patients subsequently died. Three patients presented with profound haematemesis, and all died. Postmortem examinations showed haemorrhagic necrotic ulceration and fistulae between the oesophagus and left

atrium in one and the oesophagus and the aorta in another. One further patient died from mediastinitis after oesophageal perforation. All 17 patients had cardiomegaly, and, of the 15 in whom the cause of the heart condition was stated, 12 (80%) had mitral valve disease with enlarged left atria. In 12 of the 17 (71%) ulceration first occurred soon after cardiac surgery when patients were nursed semirecumbent. This study shows that it is under these conditions that capsule arrest is most likely to occur.

Many patients with mitral valve disease are still prescribed potassium chloride tablets; indeed six of our patients were at the time of the study taking slow release potassium chloride preparations. Two other patients in our study were taking non-steroidal anti-inflammatory drugs, which have also been associated with oesophageal ulceration. Two patients were taking drugs with anticholinergic properties. We have shown that the anticholinergic, hyoscine butylbromide, given intravenously significantly delays oesophageal capsule transit in subjects with normal peristalsis.¹⁷ In patients with mitral valve disease, who are already prone to delayed oesophageal transit, these anticholinergic effects will be particularly detrimental.

We recommend that patients with mitral valve disease should be advised to swallow tablets and capsules in the erect position with a large volume of water or food and that prescribing physicians be aware of the increased likelihood of oesophageal tablet/capsule delay in these patients so that drugs known to cause oesophageal ulceration could be avoided. Slow release potassium preparations should not be prescribed for patients with mitral valve disease.

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Addendum

Since this paper was accepted for publication another fatal case of potassium chloride induced oesophageal ulceration has been reported.¹⁸

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