

Quantitative assessment of the response to therapy in achalasia of the cardia

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SUMMARY Radionuclide oesophageal transit studies and manometry have been carried out in 15 patients with achalasia of the cardia, before treatment, after a course of nifedipine and after pneumatic bag dilatation. Transit studies were also done in 10 patients after cardiomyotomy and in 10 normal subjects. Images were recorded with the subjects seated in front of a gamma camera while swallowing a 10 ml bolus of ^{99m}Tc -tin colloid and then after a further drink of 50 ml water. There was marked retention of tracer in the oesophagus in patients with achalasia compared with rapid clearance in control subjects. Bag dilatation significantly reduced lower oesophageal sphincter pressure but there was no significant difference in the 50% clearance time or percentage dose retained at 100s before and after the treatments. Oesophageal clearance of tracer after the additional drink of water, was improved by bag dilatation. Oesophageal transit in the patients after cardiomyotomy was similar to that in patients who had undergone bag dilatation. There was considerable retention of the tracer in the oesophagus overnight, but this did not result in pulmonary aspiration. Radionuclide oesophageal transit studies provided a quantitative assessment of therapy in achalasia and the proportion of tracer retained after the additional drink proved to be a sensitive measure of response to treatment. Nifedipine proved ineffective as a treatment for achalasia. Bag dilatation and cardiomyotomy were of similar value.

The assessment of treatment in achalasia of the cardia is commonly based on symptoms and less frequently upon changes in the lower oesophageal sphincter pressure (LOSP)^{1,2} or the height of barium above the cardia on barium swallow.³ None of these tests, however, quantifies the functional disturbance of impaired emptying of the oesophagus or measures oesophageal food residue. Patients with a large food residue are considered to be at risk of pulmonary aspiration. Additionally, retention oesophagitis has been implicated in the aetiology of squamous carcinoma of the oesophagus complicating achalasia.⁴ Effective treatment should therefore relieve symptoms and also abolish or at least reduce any oesophageal residue.

Forceful dilatation of the cardia and Heller's cardiomyotomy remain the standard treatments for achalasia and debate continues regarding the relative merits of each. Interest in the medical treatment of achalasia has recently been revived, however, with the development of the calcium channel blocking drugs⁵ which have been shown to reduce LOSP in healthy subjects and patients with achalasia.^{1,2,6,7} Although they have been reported to relieve dysphagia in achalasia, little is known of their effect on the clearance of oesophageal food residues.^{1,8,9}

In the present study radionuclide oesophageal transit studies have been undertaken to quantify oesophageal emptying in patients with achalasia, before treatment and after nifedipine therapy and pneumatic bag dilatation. For comparative purposes, measurements were made in healthy subjects and in a separate group of patients with achalasia who were asymptomatic after cardiomyotomy.

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Methods

PATIENTS

Fifteen patients (seven men) with clinically, radiologically and manometrically established achalasia of the cardia were studied. Their median age was 45 years (20–63) and they had had dysphagia for a median of two years before treatment (three months–five years). All patients had a dilated oesophagus (≥ 40 mm diameter) but only two had a markedly dilated, 'sigmoid', oesophagus.

A separate group of 10 patients (six men), having a median age of 35 years (13–59), was studied after Heller's cardiomyotomy for achalasia. The median interval since operation was three years (one to 14). None had undergone an antireflux procedure nor developed a peptic oesophageal stricture postoperatively. Only one had dysphagia at the time of study. Normal transit values were established with a control group of 10 healthy volunteers (five men) median age 29 years (20–61).

The study was approved by the Hospital Ethical Committee and patients gave written, informed consent.

OESOPHAGEAL TRANSIT STUDY

The oesophageal transit studies were undertaken on fasted subjects seated upright in front of a gamma camera. The field of view of the camera covered the whole of the oesophagus and upper stomach. Ten millilitres of water containing 10 MBq ^{99m}Tc -tin colloid was run into the mouth by syringe, and then

swallowed as a bolus. Images of 0.5 s duration were recorded over two minutes during oesophageal transit of the tracer and the data stored by computer for subsequent analysis. At the end of the dynamic study the subjects drank a further 50 ml water and a static image of 30 s duration was immediately recorded to assess clearance of residual tracer from the oesophagus.

The gamma camera images were displayed on a television monitor and a region of interest drawn over the whole of the oesophagus taking care to avoid the mouth and the stomach. A time activity curve was generated (Fig. 1) for the whole of the oesophagus. Three indices of transit were obtained: the time for 50% of the activity to be cleared from the oesophagus; the percentage of the activity retained in the oesophagus 100 s from the start of the study. In addition, the percentage of the dose retained in the oesophagus after the additional drink of 50 ml water was recorded.

OESOPHAGEAL MANOMETRY

This was done using a triple lumen PVC catheter constantly perfused with water by a pneumo-hydraulic pump (Mui Scientific, Canada). The catheter was connected to electrically isolated pressure transducers and recordings were made using a multi-channel pen recorder. Pressure measurements were made at the upper and lower sphincter positions. Additionally the pressure and motility in the oesophageal body were assessed, using the station pull through technique.¹⁰

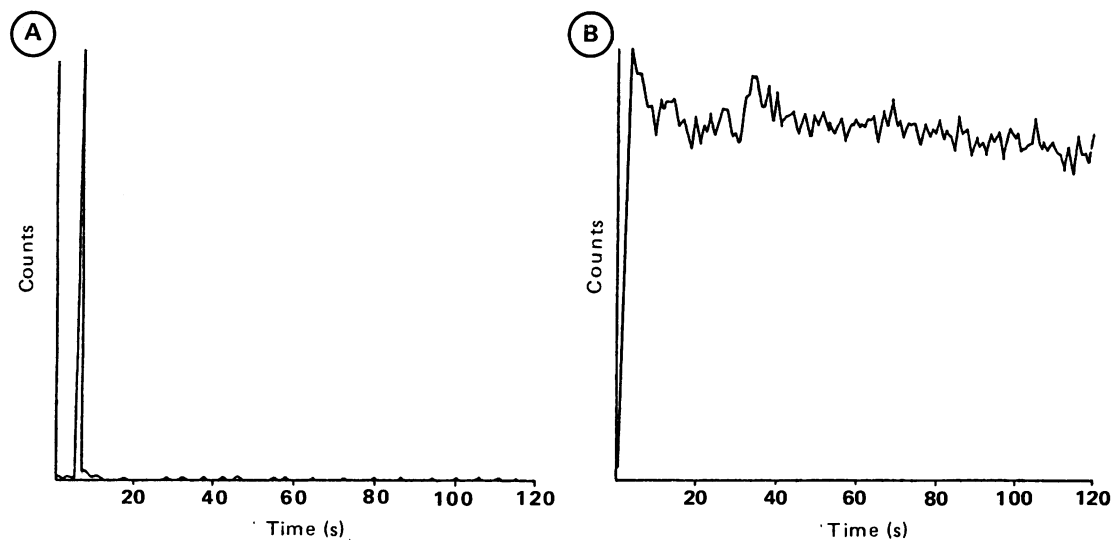


Fig. 1 Typical examples of time/activity curves for tracer in the oesophagus in: (a) healthy volunteer; (b) patient with achalasia of the cardia.

Table 1 *Dysphagia grading*

0=No dysphagia
1=Dysphagia no more than once per week
2=Dysphagia more than once per week
3=Dysphagia with every meal
4=Unable to finish meal because of dysphagia or regurgitating food or losing weight

STUDY PROTOCOL

After an initial oesophageal transit study (OTS) patients were treated with 10 mg nifedipine capsules which were opened and the contents placed under the tongue 15 minutes before meals for one month. After this course of treatment the OTS and manometry were repeated 15 minutes after a dose of the drug. The patients subsequently underwent pneumatic bag dilatation of the cardia under general anaesthesia using a 4.5 cm diameter Rider-Moeller bag. This was positioned across the cardia over an endoscopically placed guide wire and inflated to a pressure of 300 mmHg for three minutes.¹¹ The patients were reassessed by manometry and OTS one month after dilatation.

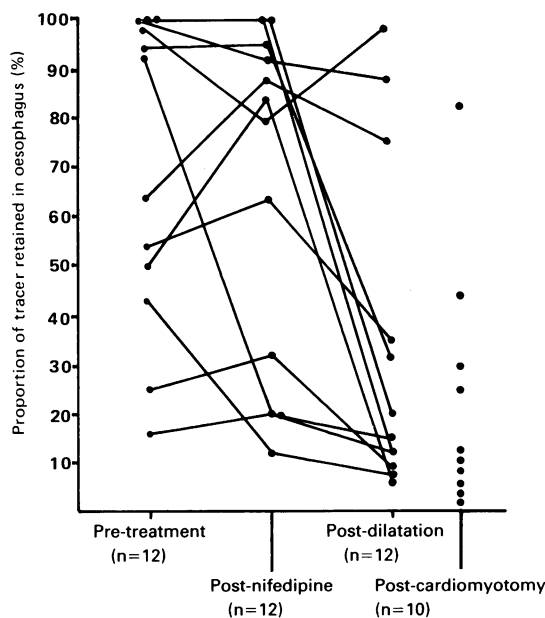
At each attendance the patients were weighed and had a symptomatic assessment of their dysphagia using the scale in Table 1. An assessment of oesophageal food residues was made at initial diagnostic oesophagoscopy and after nifedipine treatment immediately before bag dilatation. Patients were not re-endoscoped after bag dilatation. The results from these patients were compared with those from a separate group of 10 patients who had previously undergone cardiomyotomy.

Pulmonary aspiration of oesophageal contents was assessed in 10 of the 15 untreated achalasia patients. Immediately before retiring for the night the patients drank 10 ml water radiolabelled with 10 MBq ^{99m}Tc^m-tin colloid. Before breakfast the following morning a

Table 2 *Effect of various therapies on oesophageal emptying (median values)*

Subjects	Time for 50% clearance (s)	Dose retained at 100 s (%)	Proportion retained after additional drink (%)
Control subjects (n=10)	5	3	0
Achalasia (n=15)			
Pretreatment	>100	68	78
Post nifedipine	>100	72	81 [*]
Post bag diltn	>100	63	15 [*]
Achalasia (n=10)			
Previous cardiomyotomy	>100	75	11

*Mann Whitney U-test, U=34; p<0.025.

Fig. 2 *Effect of the additional 50 ml water on oesophageal retention of the tracer.*

static image of the chest was recorded and an assessment made of tracer uptake within the lungs.

STATISTIC ANALYSIS

Data were analysed by Student's *t* test and the Mann-Whitney U-test where appropriate. A value of $p < 0.05$ was taken to denote statistical significance.

Results

All 15 patients completed the study. The sublingual nifedipine was well tolerated with few side effects apart from mild headache reported by three patients. There were no complications as a result of dilatation.

OESOPHAGEAL TRANSIT STUDIES

The time activity curve for a healthy volunteer is shown in Figure 1a. This is characterised by the sharp rise and fall in count rate as the bolus of tracer passed rapidly through the oesophagus. The median 50% clearance time was five seconds with minimal retention of the dose at 100 seconds from the start of the study (Table 2). All the tracer was cleared from the oesophagus in the healthy subjects after an additional drink of 50 ml water. The patients with achalasia, however, showed a different but typical time activity curve (Fig. 1b). This was characterised by a sharp rise in activity as the tracer entered the oesophagus but the activity plateaued as little progressed into the stomach. The quantitative results in the achalasia

Table 3 Effect of various therapies on symptoms, weight gain, and lower oesophageal sphincter pressure

	Pretreatment	Post-nifedipine	Post-dilatation
Mean weight (kg)	64.2 (12.9)	64.2 (13.2)	66.8 (12.3)
Mean symptom score	3.7 (0.5)	3.0 (0.7)	1.9 (0.9)
Mean LOSP (cm H ₂ O)	21.9 (11.6)	18.8 (6.0)	12.9 (8.0)

NS: Not significant; p<0.001, p<0.01, p<0.05: Significant differences between groups.

Mean (SD); Student's *t* test.

patients before and after the treatments are shown in Table 2. Before treatment, after nifedipine and bag dilatation, the 50% clearance time remained in excess of 100 seconds and on average approximately 70% of the dose was retained in the oesophagus at 100 seconds. Overall, after the additional 50 ml water oesophageal emptying was improved only after bag dilatation (Table 2). The effect of the additional drink of water in the three phases of the study is plotted for individual patients in Figure 2. Complete data were obtained for only 12 of the 15 patients as a result of computer malfunction. Three patients had a poor emptying response to bag dilatation and in only one of these did LOSP show a significant fall indicating that a further dilatation or cardiomyotomy may be necessary. The results in the patients after cardiomyotomy were comparable with those obtained after bag dilatation (Fig. 2).

MANOMETRY

Nifedipine had no significant effect on mean LOSP (Table 3), but after bag dilatation there was a significant fall in mean LOSP compared with pre-treatment values. There was no close relationship between change in LOSP and change in oesophageal emptying after treatment. Neither nifedipine nor bag dilatation had any effect on lower oesophageal sphincter relaxation, motility in the oesophageal body or upper oesophageal sphincter function.

CLINICAL ASSESSMENT

No patients' symptoms worsened while taking nifedipine and there was a slight improvement in their mean symptom score (Table 3). Ten of 15 patients reported an improvement in symptoms on nifedipine but grade 2 dysphagia was the best result obtained and this in only three patients. After bag dilatation there was a significant improvement in mean symptom score and in none of the patients did symptoms deteriorate. Twelve of the 15 patients

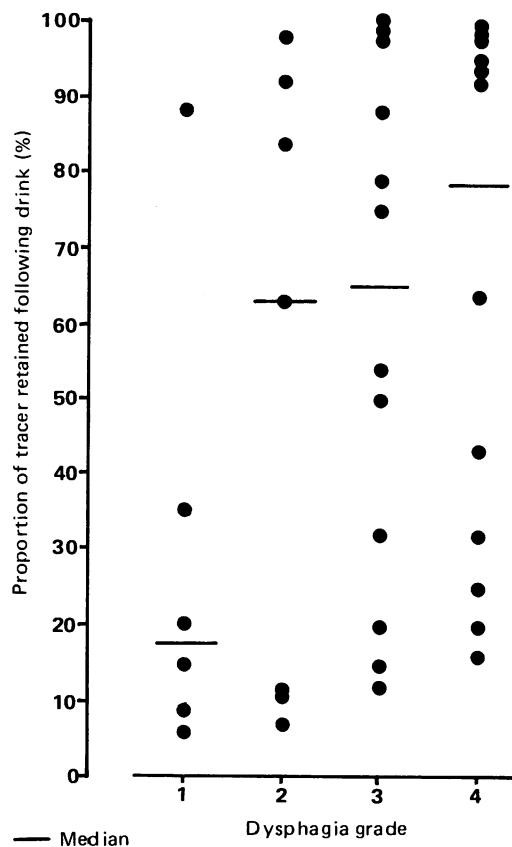


Fig. 3 Comparison of symptomatic response and retention of tracer after 50 ml water in all patients at each stage of the study.

reported an improvement in symptoms, with five achieving grade 1 dysphagia. No patient became completely dysphagia free, however, after either treatment.

A comparison of dysphagia grade and retention of radiolabelled tracer after the additional drink, irrespective of treatment stage is shown in Figure 3. The median tracer retention is lowest in the grade 1 group. For the other groups, however, there is a very wide spread of retention with little difference between the median values. The two patients who had a sigmoid oesophagus exhibited results similar to those obtained from the other patients.

Overall, there was no significant increase in the patients' weights during the study. The study period was, however, relatively short and none of the patients was particularly malnourished. All patients had an oesophageal food residue at endoscopy before nifedipine therapy and in only one patient was no residue seen after the drug treatment.

ASPIRATION STUDIES

All 10 patients exhibited marked tracer retention in the oesophagus the morning after the overnight study. In none of the patients, however, was any tracer detected in the lungs.

Discussion

Radionuclide imaging provides a simple, physiological procedure for assessing oesophageal transit. It is generally recommended¹² that studies should be carried out supine, so as to reduce the influence of gravity and thereby enhance the sensitivity for the detection of abnormal peristalsis and minor impairment of oesophageal emptying. In achalasia, peristalsis in the smooth muscled part of the oesophagus is usually unrecordable and oesophageal emptying is dependent solely upon gravity. Therefore whilst studies in the supine position are better for diagnosis, those in the upright posture are more appropriate for the assessment of the effects of treatment in achalasia. There was marked retention of the 10 ml bolus of tracer before and after all the treatments. Thus swallowing a small volume of liquid provided a sensitive test for the presence of achalasia. The additional 50 ml drink of water gave a good indication of the response to treatment.

None of the patients complained of chest symptoms and although all 10 patients in the aspiration study had a large residue of tracer in the oesophagus overnight, none showed evidence of pulmonary aspiration. In all patients upper oesophageal sphincter function was normal and presumably adequate to prevent the passage of oesophageal contents into the pharynx.

Patients were initially treated with nifedipine as this offered the potential of a non-invasive therapy. This drug has been shown in clinical trials, involving healthy subjects and patients with achalasia, to reduce LOSP.^{1,2,6,7} This finding was not confirmed, however, in the present study. An alternative drug, isosorbide dinitrate, has been reported^{7,13} to be effective in relieving symptoms, reducing LOSP and enhancing radionuclide oesophageal emptying in patients with achalasia, but it is associated with over 50% failure rate with unpleasant side effects.⁷

From the results of the present study it is apparent that little change in the LOSP followed nifedipine in a 10 mg dosage and there was little improvement in swallowing of even liquids in most patients. Three patients showed poor clearance throughout all stages of assessment (Fig. 2). For these patients, even after bag dilatation, over 70% of the tracer was retained after the additional drink of water. This objective measure can be regarded as evidence of a poor response to treatment. Interestingly, the subjective

scores for these patients after treatment showed changes from initial values of 3, 4, and 4 to 1, 2, and 3 respectively, thus confirming the difficulty of clinical evaluation based solely on symptomatic response. Although overall there was a significant reduction in LOSP after bag dilatation (Table 3) this did not correlate closely with either relief of symptoms or improvement in emptying. This poor correlation between symptomatic and objective improvement has been noted previously⁷ and presumably represents a placebo effect. The present findings indicate that symptomatic improvement after sublingual nifedipine in a dosage of 10 mg before meals, is considerably less than after pneumatic bag dilatation. This, together with the absence of objective evidence of improvement in oesophageal emptying, suggests that the drug has little place in the treatment of achalasia.

In terms of symptomatic improvement and oesophageal emptying, pneumatic bag dilatation was clearly superior to nifedipine in the treatment of achalasia. Although oesophageal emptying after the 50 ml water swallow in the upright position did not reach normality it was greatly improved by pneumatic bag dilatation and approximated to the emptying rate found after successful cardiomyotomy. Obviously, short term measurements such as these cannot form a valid basis for assessment of long term outcome. Further studies are needed to establish the duration of improvement in oesophageal emptying after pneumatic bag dilatation.

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