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Dynamic radionuclide imaging with 99mTc-sucralfate in the detection of oesophageal ulceration

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SUMMARY **Standard oesophageal scintigraphic techniques using 99mTc-colloids rarely identify oesophageal mucosal damage. Sucralfate can be labelled with 99mTc for the detection of oesophageal mucosal ulceration. This method uses two separate supine swallows of 10 MBq 99mTc-colloid in 10 ml, followed by a single supine swallow of 30 MBq 99mTc-sucralfate. The data are processed to give time-activity curves, mean transit times and condensed dynamic images. When oesophageal ulceration is detected, the time-activity curves using sucralfate show residual activity in the oesophagus after the transit time indicated by the colloid swallow. The condensed dynamic image shows a persistence of activity at the level of the ulceration. Erect sucralfate images taken immediately after the dynamic sequence show no oesophageal localisation. The results from a study of 62 patients have shown excellent correlation between the dynamic 99mTc-sucralfate images and endoscopy findings. Sequential sucralfate studies for healing also correlate well. The use of labelled sucralfate to detect oesophageal ulceration could modify the indications for endoscopy in gastrooesophageal reflux disease.**

The diagnosis of oesophageal malfunction is made using a combination of the barium swallow and other more invasive techniques such as endoscopy, manometry, and pH monitoring. Dynamic radionuclide scintigraphy is now becoming an established test in the assessment of functional abnormalities of the oesophagus such as stricture, spasm, and achalasia. It is simple to perform, non-invasive and well tolerated by patients, and can produce quantitative indices of function.[1,2] This technique, however, will only identify sites of mucosal damage in the oesophagus if they are sufficiently gross as to precipitate transit abnormalities, and as such is of no value in the early detection and follow up of oesophageal ulceration.

Sucralfate (Ayerst Laboratories Ltd), an aluminium salt of polysulphated sucrose, has proved of therapeutic value in the treatment of gastrointestinal tract ulceration.[3–5]

Reports have described the labelling of sucralfate with selenium-75 and technetium-99m with variable results for the detection of ulceration throughout the gastrointestinal tract.[6–10] Previous work has tended to concentrate on the applications of labelled sucralfate in the stomach, small, and large bowel, although its use has been documented in the oesophagus,[11] with mainly negative results from static imaging techniques. We describe here the use of 99mTc-labelled sucralfate in the investigation of oesophageal mucosal ulceration using a dynamic transit study. We have compared this with the barium swallow, using endoscopy as the gold standard for the detection of oesophageal ulceration.

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Methods

RADIOPHARMACEUTICAL PREPARATION

Initial swallows were made with 99mTc-labelled albumin colloid (microlite, Du Pont) as a suitable non-absorbable tracer. The kits were prepared according to the manufacturer's instructions. In preparing the labelled sucralfate, a similar method to that of Dawson[7] was utiised, although in this study we have used 500 mg sucralfate powder, labelled with 30 MBq of 99mTc-HSA (Medi-Physics) radiopharma-

ceutical per patient. The 99mTc-HSA was prepared by reconstituting a kit with 0·5 ml water for injection. 60 MBq of 99mTc pertechnetate was added in a volume of 1·3 ml, the vial shaken and allowed to stand for 20 minutes. The sucralfate was then suspended in 5 ml of HCl (pH 4) and shaken vigorously. Half the contents of the 99mTc-HSA vial was then added to the sucralfate and shaken. After centrifugation at 1400 *g* for 10 minutes, the supernatant was removed and resuspended in 5 ml water. Measurement of supernatant activity not bound to sucralfate was less than 0·5 MBq. Radiochemical purity measurements using paper chromatography were in agreement with those obtained by Dawson.[7]

99mTc-COLLOID SWALLOW

All patients made two separate swallows each, using 10 MBq 99mTc-colloid in 10 ml. The studies were performed supine with a computer acquisiton of 100 frames for each swallow at 0·5 s/frame, with a 32×32 matrix. Having swallowed the radioactive bolus the patients were instructed not to swallow again for a period of 30 s, after which time a dry swallow was permitted. The data were processed to give time-activity curves over the proximal, middle, and distal thirds of the oesophagus, whole oesophagus and stomach. Mean transit times were calculated from these curves. Condensed dynamic images were also obtained, based on the method of Svedberg.[12]

99mTc-SUCRALFATE SWALLOW

After the colloid swallows, one swallow was performed supine on each patient using 30 MBq 99mTc-sucralfate. The method of acquisition was the same as for the colloid swallow, with 100 frames at 0·5 s/frame. The data so obtained were processed in an identical manner, with time-activity curves, mean transit times and condensed dynamic images.

SUBJECTS

Sixty two consecutive patients were studied prospectively, 24 men with a mean age of 55 years (range 18–80 years). These patients presented to a specialist thoracic surgical outpatient department over a 10 month period. They represent general practitioner referrals and referrals from other consultants. Length of history was recorded at presentation an the symptoms assessed on the deMeester scale. This information is part of a larger clinical database and was not used in this particular study.

All patients had endoscopy with fibreoptic or rigid instruments, and were classified for oesophageal ulceration on a scale of 0–3: 0=no apparent oesophagitis; 1=linear ulceration; 2=discrete ulceration; and 3=confluent ulceraton with or without a fibrous stricture.

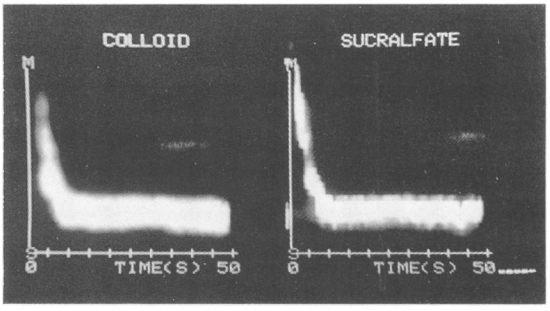

Fig. 1 *Condensed dynamic images for 99mTc colloid and sucralfate in a normal patient.*

All the sucralfate studies were done within ±20 days of the endoscopy, the majority being within ±3 days. The sucralfate studies were classified as ulceration present or absent, and if present with an indication of the level of the ulcer within the oesophagus – upper, mid, or lower.

Assessments of the endoscopy and sucralfate data were made by individual specialists at consultant level, independent of each others' results.

Results

Patients with normal oesophageal function show rapid transit of colloid and sucralfate with no significant difference in mean transit time between the two techniques. Condensed dynamic images are shown for colloid and sucralfate in Figure 1, with the vertical axes marked to indicate the relative positions of the mouth and stomach. The time-activity curves for this patient are shown in Figure 2. The typical pattern in a patient with oesophageal ulceration shows the condensed dynamic image having a persistent area of activity on the sucralfate which is not present on the colloid swallow (Fig. 3). The time-activity curves for this patient are given in Figure 4 and similarly show persistent activity in the

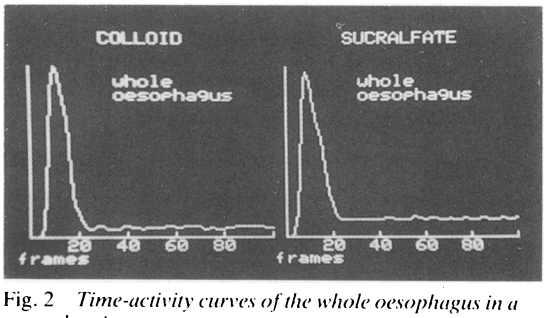

Fig. 2 *Time-activity curves of the whole oesophagus in a normal patient.*

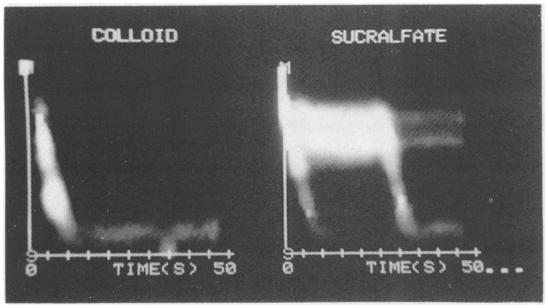

Fig. 3 *Condensed dynamic images for 99mTc colloid and sucralfate in a patient with upper oesophageal ulceration.*

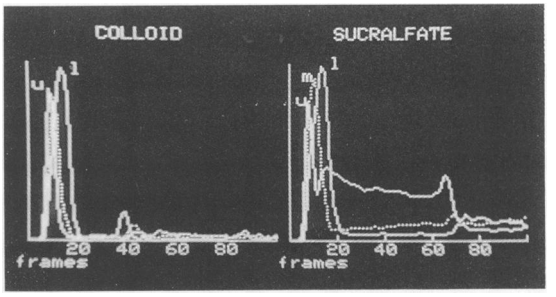

Fig. 4 *Time-activity curves over thirds of the oesophagus for the patient of Figure 3.*

region affected, though indicating the location and extent with rather less precision The mean transit time of the sucralfate bolus is naturally increased.

In all patients who were imaged in the erect position immediately after the supine dynamic sucralfate study, no oesophageal uptake could be found, even when the transit study had shown prolonged activity on the condensed dynamic image and time-activity curves.

The results are summarised in a 2×2 table, given in the Table. Using oesophagoscopy as the gold standard for determining the presence of oesophageal ulceration, the labelled dynamic sucralfate imaging has a positive predictive value of 92% for ulceration present, and 86% for ulceration absent, correlating with oesophagitis grades 1–3.

Multiple sucralfate studies have been done in a small number of patients to assess whether the technique can be used to show the response to therapy of patients with oesophageal ulceration. The images shown in Figure 5 are from one such patient and clearly show a gradual lessening of the abnormally prolonged oesophageal activity during the course of therapy.

Discussion

Work published by Goff[11] using delayed static imaging at 30 minutes post administration or later showed labelled sucralfate to be a poor indicator of oesophageal ulceration, giving positive results only in cases of deep penetrating ulcers within the gullet.

Patient positioning is important, however, as supine transit is a peristaltic phenomenon and when the study is done in this position all the mucosa comes into contact with the swallowed bolus. If ulceration is present the sucralfate will come into contact with exposed protein and binding may occur, the rest of the bolus passing through the oesophagus and into the stomach. Thus the dynamic sucralfate study will show an 'afterglow' compared with the colloid swallow.

As most ulceration in the oesophagus is superficial, our experience suggests that sucralfate tends to adhere only in the immediate period after swallowing. This makes the transit study more likely to produce a positive result than delayed static imaging.

In the erect position the swallowing of fluids is not a simple peristaltic activity and not all the mucosa comes into contact with the bolus. Erect swallowing studies with labelled sucralfate would therefore have a reduced probability of producing a positive result, and thus have little clinical value. We have shown the supine transit study to be a sensitive indicator of oesophageal mucosal damage. One particular example of this can be seen in Figure 5, where the patient had little endoscopic evidence of any remaining ulceration at the time of the third study, but nevertheless produced a slightly abnormal sucralfate study. This may be the result of incomplete healing at the mucosal level, causing the sucralfate to remain positive in an oesophagus which is visually normal at endoscopy.

Endoscopy does of course provide more precise

Table *Sucralfate – 2×2 table of results*

	Oesophageal ulceration			
	Present	*Absent*	*Total*	
Sucralfate +ve	44	4	48	ppv 0·92
Imaging −ve	2	12	14	npv 0·86
Total	46	16	62	
	true +ve 0·96	true −ve 0·75		
	Prevalence 0·74			

ppv=positive predictive value; npv=negative predictive value.

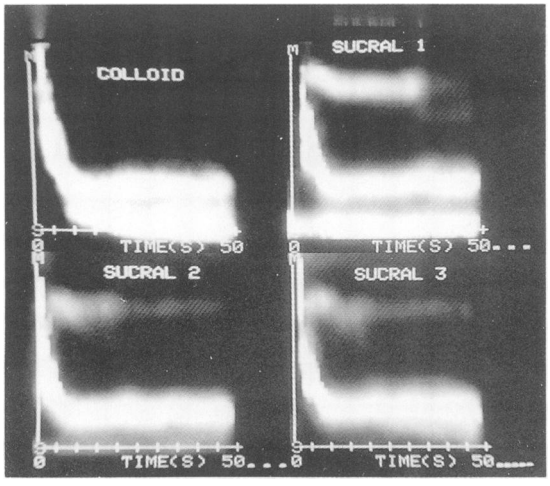

Fig. 5 *Condensed dynamic images for 99mTc colloid and three successive sucralfate studies over a four month period.*

information regarding the location and extent of any site of ulceration than is possible with a radionuclide study. We have indeed found no correlation between the endoscopic grading and the degree of sucralfate activity at the site of the lesion.

Endoscopy is, however, a much more invasive examination requiring a high skill level, and there is a small possibility of iatrogenic ulceration from the endoscope itself. We have shown this eventuality in one patient within the study, who recorded a negative sucralfate study before the endoscopy and a positive repeat sucralfate study done within 24 hours of the endoscopy, where the oesophagus had been traumatised in its upper third. While this is not a major clinical problem, it does indicate the sensitivity of sucralfate in the detection of minor oesophageal damage.

Having shown a 92% positive predictive value for dynamic sucralfate imaging of oesophageal ulceration, we now limit endoscopy to initial evaluation and to acquire histology for the exclusion of a malignant process. Subsequent follow up is by dynamic sucralfate imaging.

It is important that all oesophageal ulcers are biopsied to exclude malignant disease. In this study, however, the use of endoscopy did not add any information with regard to oesophageal disease when the labelled sucralfate study was normal. The 99mTc-sucralfate dynamic transit study is rapid, non-invasive and has a low radiation dose. These properties, combined with a high probability of a correct result, suggest that the sucralfate study has real value: (i) as a screening test in deciding who should be endoscoped and (ii) a test suitable for following the progress of a patient undergoing therapy for oesophageal ulceration without resort to further endoscopy.

Further studies are warranted to assess the full potential of the dynamic sucralfate study.

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