Evaluation of indium scintigraphy in patients with active inflammatory bowel disease

M S BUXTON-THOMAS, R J DICKINSON, P MALTBY,
J O HUNTER, AND E P WRAIGHT

From the Departments of Nuclear Medicine and Medical Gastroenterology, Addenbrooke's Hospital, Cambridge

SUMMARY Recent reports have indicated a possible role for $^{111}\text{Indium}$ leucocyte scintigraphy in the management of patients with acute inflammatory bowel disease. Our experience with this technique in 15 patients (nine with ulcerative colitis, six with Crohn's disease) is described. Perfect agreement was not obtained between scintigraphic appearances and other conventional means in the assessment of extent of disease. Good correlation, however, was found between disease activity and recovery of labelled leucocytes in the faeces. While this latter finding could be used as an objective means of assessing response to therapy, it is concluded that conventional indium scintigraphy, using indium oxine-labelling of mixed leucocytes, is insufficiently reliable to replace usual methods for determining extent of disease in patients with inflammatory bowel disease.

Recent reports from the UK^{1,2} and USA³ have indicated a possible role for $^{111}\text{Indium}$ leucocyte scintigraphy in the management of patients in exacerbation of chronic inflammatory bowel disease. The migration of labelled leucocytes to the areas of active inflammation enables scintigraphic estimation of the extent of the disease while its severity is related to the proportion of the leucocyte label which is shed in the faeces. This report describes the findings in our evaluation of the technique.

Methods

PATIENTS

Fifteen consecutive inpatients who were admitted in exacerbation of chronic inflammatory bowel disease were included in the study. Each gave informed consent to the intended investigation. Six patients had Crohn's disease and nine had ulcerative colitis diagnosed according to conventional criteria.

SEVERITY OF DISEASE

Disease severity was estimated on admission of the patient to hospital according to the criteria of

Truelove and Witts⁴ or the Crohn's disease activity index (CDAI).⁵

EXTENT OF DISEASE

The results of the four hour $^{111}\text{Indium}$ scintigrams were compared with those obtained by conventional radiological or endoscopic techniques or, in some instances, by inspection of resected specimens. No attempt was made to correlate scintigraphic findings with histological appearances and the comparisons were based on the gross macroscopic or radiological appearances only (Table). In two patients (no 4 and 11, Table) limited colonoscopy was performed because of the severity of their disease. In each instance the colonoscope was passed to the splenic flexure and it was only possible therefore to confirm left sided disease in these patients. Although the disease might have extended further for the purposes of comparison it was assumed that the disease did not extend proximal to the splenic flexure. One patient (patient 1, Table) did not have conventional assessment during her admission. In this instance it was assumed that the disease was restricted to the left hemicolon as had been shown in four previous barium enemas and was reconfirmed in a subsequent outpatient examination.

TREATMENT RECEIVED

All the patients were given active treatment on admission to hospital which included replacement of

Address for correspondence: Dr M Buxton-Thomas, Department of Nuclear Medicine, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

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Table Clinical details of patients

No	Diagnosis	Extent of disease			Activity in stools (%)	Severity of disease	Treatment at time of scintigram (days)	Treatment (Pred)
		Conventional means	Test used and days post scint	Indium scintigram				
1	CD	Patchy, L sided	Barium enemas*	Negative	1.7	CDAI=421	5	10 mg ED
2	CD	Total	Colectomy 11	Total	26.5	Severe	6	40 mg
3	UC	Total	Barium enema 14	Total	18.4	Severe	4	40 mg
4	UC	≥L sided	Colonoscopy 13	L sided	61	Severe	>14	30 mg
5	CD	R sided with perianal fistulae	Colectomy 14	Rectal	2.8	Severe	0	Bowel/rest TPN
6	UC	L sided	Colonoscopy 1	L sided	10	Severe	>14	30 mg
7	UC	Total	Barium enema -5	Total	24	Severe	7	40 mg
8	UC	L sided	Colonoscopy 6	L sided	37	Severe	6	40 mg
9	UC	Total	Barium enema 4	Caecum	7	Severe	10	40 mg
10	CD	R sided	Barium enema 8	R sided	19	CDAI=303	0	ED
11	UC	≥L sided	Colonoscopy 2	R sided	—	Severe	<14	40 mg
12	CD	Total	Barium enema 12	Total	31	CDAI=268	5	40 mg
13	UC	L sided	Colonoscopy 1	Focal	25	Severe	>14	10 mg
14	CD	Terminal ileum	Surgery 10	Terminal ileum	10.6	CDAI=194	>14	30 mg
15	UC	Total	Barium enema -9†	Rectal	21	Severe	>14	40 mg

* Barium enemas performed before and after this exacerbation showed left sided disease.

† Subsequent colectomy showed no evidence of disease proximal to the sigmoid colon.

Pred = Prednisolone. ED = Element Diet. TPN = Total Parenteral Nutrition.

blood and fluids where necessary. In addition 13 patients received corticosteroids. Of these one patient (no 1, Table) was continued on a small dose of prednisolone which she had been taking long term and given an elemental diet while six patients (nos 4, 6, 12, 13, 14, 15) were maintained on high dose prednisolone which had been initiated in the outpatient department. Two patients (nos 5 and 10) received total parenteral nutrition and an elemental diet respectively as primary therapy and did not receive corticosteroids. All the patients (except nos 5 and 10) had been receiving active therapy for a minimum of four days at the time the scintigrams were performed.

SCANNING TECHNIQUE

Sixty millilitres of blood were withdrawn from each patient and after separation the white cells obtained were labelled using indium oxine kits supplied by Amersham International according to their protocol.⁶ The labelled cells were then injected intravenously and imaging carried out using an Elscint double headed whole body scanner. Anterior and posterior images were obtained at four and 24 hours. Disease extent was assessed on the four hour scintigrams.

Stools were collected and counted from each patient for three days after injection of the labelled cells and the percentage activity of the total dose injected was calculated.

Results

Fifteen patients were studied and details are given in the Table. Stool activity was counted in 14 of the 15 patients and was greater than 2% in all but one instance thus confirming disease activity.¹ Scintigraphic agreement was obtained in nine patients (see Fig. 1). The scintigrams, however, underestimated the gross extent of disease in six instances (Fig. 2).

In one patient (no 15) in whom there was a marked discrepancy between the scintigraphic and radiological findings subsequent colectomy showed no evidence of disease proximal to the sigmoid colon in spite of prior radiological evidence to the contrary.

Discussion

These results show that while the recovery of labelled leucocytes in the faeces reliably correlates with conventionally derived indices of disease activity in patients with active ulcerative colitis or Crohn's disease, indium scintigraphy is not an entirely reliable method of estimating disease extent. The failure to obtain correlation between conventional and scintigraphic means might be explicable either by the effect of steroid therapy on the kinetics of the ¹¹¹Indium labelled white cells or by therapeutic reduction of the disease activity.² In

Fig. 1 Four hour indium scintigram showing total colitis (Patient no 3).

this regard it is notable that of the discrepant scintigrams two were in patients with low stool counts and it might be that these results related to low disease activity in spite of clinical evidence of active disease. This explanation alone, however, would not account for the other discrepant results nor can the effects of steroids be necessarily implicated in view of the positive scans obtained in the other patients on high dose steroids. Notwithstanding any theoretical explanation for our results if indium scintigraphy is to assume a place in the management of the patient with ulcerative colitis or Crohn's disease, it will have to prove itself reliable in those acutely ill patients receiving active therapy.

Although the previous studies of indium scintigraphy have reported good results they have also failed to obtain correlation between the scintigraphic and conventional means of assessment of extent of disease in all the patients.¹⁻² These results taken with those reported here show that indium

scintigraphy cannot be entirely relied upon to give an accurate assessment of the disease extent. Our data, however, confirm that the recovery of leucocytes from the faeces may provide a reliable quantitative estimate of disease activity although it is notable that indium labelling is no more accurate in this regard³ than the conventional clinical criteria on which therapeutic decisions will depend.

New labelling techniques, however, have since been developed using indium acetyl acetonate and indium tropolonate. Comparisons have shown that labelling either crude or pure granulocytes in plasma with ¹¹¹Indium tropolonate gives high labelling efficiency with minimal alteration in cell behaviour.⁷ These techniques may therefore result in better assessment of disease extent and may indeed supersede conventional criteria for accurate assessment.

Indium scintigraphy is expensive with long labelling procedure and our findings show that it is insufficiently reliable to replace conventional methods of clinical assessment. While it has research interest and may provide objective means of assessing response to therapy, it has no advantages to warrant its routine use in patients with inflammatory bowel disease.

Fig. 2 (a) Four hour indium scintigram showing focal activity at splenic flexure (Patient no 13). Colonoscopy showed inflammatory polyposis at this site and active colitis distally. (b) Barium enema from the same patient showing a left sided colitis.

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