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ORAL SUCRALFATE IN ACUTE RADIATION OESOPHAGITIS

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Eighty patients with carcinoma in the middle third of oesophagus and with acute radiation oesophagitis following external beam and intracavitary radiotherapy were managed by two different schedules. Group 1 (n = 40) received an antacid containing sodium alginate whereas Group 2 (n = 40) were given a 10% sucralfate suspension during 4 weeks. In Group 2, 32 patients had significant relief of symptoms within 7 days of treatment and most ulcers had healed by 12 days of treatment as seen on endoscopy. Patients in Group 1, on the other hand, showed little improvement of symptoms and had persistent ulcers even after 4 weeks of therapy. We conclude that sucralfate is useful in the management of acute radiation oesophagitis.

Acute radiation oesophagitis is a troublesome problem in patients with carcinoma oesophagus who receive radiation therapy. Oesophagitis is more pronounced when a high radiation dose is locally obtained in the oesophagus; e.g. at intracavitary radiotherapy. With the increasing use of intracavitary radiation treatment with the aim of obtaining a high dose in the involved area, severe radiation oesophagitis will be seen more frequently. The oesophageal epithelium is moderately radiosensitive, similar to that of the oral mucosa (1). Epithelitis is produced with a dose of 30 Gy delivered in 2 1/2–3 weeks and usually leads to moderate substernal burning and difficulty in swallowing with reduced food intake (2). There are no clearcut guidelines in the management of this condition. Antacids including those containing alginic acid have been tried for symptomatic relief but the results are discouraging (3). Sucralfate is a locally acting anti-ulcer agent (4) that shields the base of peptic ulcers by formation of a viscous coagulum; it also has a cytoprotective effect (5). Following our experience of good results with topical sucralfate in radiation proctitis (6, 7), we undertook a prospective study to evaluate the usefulness of oral sucralfate in radiation oesophagitis.

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Material and Methods

Eighty consecutive patients with oesophageal carcinoma who all developed increasing dysphagia 2–6 weeks following start of radiation treatment were included in the study. Each patient received external beam irradiation (EBI) with 35 Gy delivered in 15 fractions over 3 weeks (c. 23 Gy per fraction) followed a week later by intracavitary irradiation (ICI) in 2 sessions with 6 Gy at each session calculated at 1.0 cm from the source axis. All patients had locally advanced lesions with more than 5 cm of the oesophagus being involved and had dysphagia to solids since 1 to 5 months. Haematological and biochemical parameters, including liver function tests, were normal in all the patients. During treatment with EBI all patients had worsening of dysphagia to a state when swallowing semisolids became painful. Following treatment with ICI, 1–2 weeks later, all these patients could swallow only liquids.

These patients were then randomly assigned to one of the two treatment groups by the radiation therapist. Forty patients received an antacid containing sodium alginate (Visco gel, Aristo, India: sodium alginate 200 mg, magnesium hydroxide 500 mg, aluminium hydroxide 250 mg and simethicone 100 mg per 5 ml of suspension) 20 ml, 4 times a day orally (Group 1). Group 2 received 10 ml sucralfate suspension made by dissolving 1 g tablet in 10 ml water

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which was swallowed 4 times a day. (Since the suspension and granular forms of sucralfate are not available in India, the patients made the suspension by crushing 1 g tablet into a fine powder which was then dissolved in 10 ml of water.) The patients were assessed weekly for 4 weeks clinically and endoscopically. Dysphagia status was graded from I to IV (dysphagia to solids: I; to semisolids: II; to liquids: III; total dysphagia: IV). Decreased dysphagia by at least one grade was regarded as an improvement. Endoscopically, the changes assessed were friability, hyperaemia and ulceration.

Statistical analysis of the data was made using χ^2-test with Yates' correction.

Results

The table shows symptomatic and endoscopic response to treatment in the two groups. Endoscopic assessment was based on persistence or absence of mucosal ulcerations and/or oedema and the severity of these signs. It was observed that persistence of dysphagia correlated very closely with the presence and severity of ulceration and oedema as seen endoscopically. It was, however, not possible to grade the severity of ulceration and oedema separately since in most cases, these signs occurred together. At each week of follow-up, the conditions were better in Group 2. After one week of therapy, 36 (90%) patients were still symptomatic in Group 1 whereas only 8 (20%) patients in Group 2 had not improved. All patients in Group 2 showed endoscopic and symptomatic improvement after 2 weeks, whereas 14 patients in Group 1 had still not improved by 4 weeks ($p < 0.01$). Even if in most patients in Group 1 the severity of oedema and ulceration had diminished after 4 weeks, these patients had more pronounced signs than the patients in Group 2. The 14 patients in Group 1 who had not improved by 4 weeks then received sucralfate suspension for 2 weeks. Eight of them improved symptomatically and endoscopically while the other 6 had to be intubated.

Table

Symptomatology and endoscopic findings in patients with radiation oesophagitis treated with antacid or sucralfate

Group	Weeks of treatment							
	1		2		3		4	
	S	E	S	E	S	E	S	E
1 (n = 40) (Antacid treatment)	36	36	28	26	22	20	14	14
2 (n = 40) (Sucralfate treatment)	8	8	2	2	0	0	0	0

$p < 0.01$ χ^2-test
S—Persistence of dysphagia of same grade
E—Ulceration and oedema of mucosa on endoscopy

Discussion

High dose-rate intracavitary irradiation following EBI produces severe oesophagitis characterized by ulceration, oedema and flocculation of the oesophageal mucosa (3). Over 90% of the patients have been reported to have radiation-induced superficial ulcers after treatment (8). Hishikawa et al. (9) reported that the capillary vessels of submucosa are destroyed by ICI and fibrosis and fibrinous exudates are found in the muscle layers. This causes oedema and ulceration. There are no clearcut guidelines for the management of this condition. Antacids containing sodium alginate have been reported to give significant relief of the symptoms (3), but no prospective, controlled studies have been reported.

Sucralfate has been used extensively in the treatment of gastroduodenal ulceration, reflux oesophagitis, erosive gastritis and radiation proctitis (6, 7, 10, 11). Sucralfate coats the mucosa and is assumed to exert its protective action by adsorption of pepsin and bile salts, stimulation of bicarbonate and mucous secretion and stimulation of endogeneous synthesis of prostaglandin E2. It has also been reported to increase epidermal growth factor binding to ulcerated areas and to stimulate macrophage activity. In addition, sucralfate seems to stimulate endogenous sulfhydryl compounds, protect vascular integrity of the mucosa and stimulate cell restitution and cell prolifertion at the microscopic level (6, 10–12). According to clinical observations sucralfate promotes healing of radiation-induced ulcers and oedema as observed in our earlier studies on radiation proctitis (6, 7) and also reported by other authors (13, 14).

To be effective the drug must come into contact with the affected mucosa which is achieved by the use of a suspension. We have empirically used a 10% solution without any side-effects. We have recently started to use sucralfate also in oral, oropharyngeal and oesophageal neoplasms before and during radiation treatment and have observed good results (15) in agreement with recently published reports (16, 17). However, further studies are needed to determine the optimal dose, type of application and duration of sucralfate treatment in acute and chronic radiation-induced tissue changes.

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