

## SHORT REPORT

### Efficacy of sucralfate in oral mucositis induced by systemic chemotherapy with 5-fluorouracil

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#### Summary

**Purpose:** Oral mucositis occurring in the course of radiotherapy and chemotherapy, particularly following chemotherapy with 5-fluorouracil (5-FU), significantly affects nutritional status and the quality of life of cancer patients. The purpose of this study was to investigate the effect of sucralfate in alleviating mucositis and pain associated with 5-FU-based chemotherapy.

**Patients and methods:** A total of 40 patients with cancer and receiving 5-FU-based chemotherapy were included in the study. All of them developed therapy-induced oral mucositis. The patients were assigned to receive either sucralfate suspension given orally 4 times a day for 10 days ( $n = 20$ ) or placebo ( $n = 20$ ). They were examined daily and

were evaluated with regard to the degree of mucositis, sore throat, and weight loss. Statistical analyses were carried out using the chi-square test.

**Results:** Patients in the sucralfate group exhibited significantly decreased mucositis, a slight course of throat pain, and less weight loss compared to the placebo group ( $p < 0.05$ ).

**Conclusion:** Sucralfate is an efficient topical agent in shortening the recovery period of chemotherapy-induced oral mucositis, in alleviating pain and in contributing to significantly less weight loss.

**Key words:** chemotherapy, 5-fluorouracil, oral mucositis, sucralfate

#### Introduction

Oral mucositis and ulcerations occurring in the course of chemotherapy result from rapid detachment of basal epithelial cells and damage to the mucosal barrier. This condition leads to dryness of the mouth, burning sensation of the lips, widespread pain over the mucosal membrane, and mucosal

ulcerations [1,2]. This, in turn, leads to a poor nutritional status resulting in weight loss.

Sucralfate (sucrose octa-sulphate) hastens alleviation of peptic ulcer and prevents ulcer recurrence [3]. It forms complexes with proteins such as albumin and fibrinogen and, by binding these proteins in necrotic tissues, it prevents them to be broken down by pepsin. It also strengthens physical mucosal barriers against the surrounding environment.

Sucralfate also has acid-neutralizing properties [4,5] and has been found to exert topical beneficial effects in radiotherapy-induced esophagitis and chemotherapy-induced oral mucositis and ulcerations [6].

#### Patients and methods

The study included 40 patients with cancer who developed oral mucositis during 5-FU-containing chemotherapy. Oral mucositis was treated with a

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10-day therapy of either sucralfate suspension ( $n=20$ ) given orally 4 times a day for 10 days or placebo ( $n=20$ ) which was given 4 times a day and contained a mixture of salt, bicarbonate and water.

During the first 10 days of therapy the patients were invited for a daily control and were evaluated with regard to the degree of mucositis, sore throat and weight loss. Alleviation of oral mucositis was recorded. All patients were scored in ascending order as 0, 1, 2, and 3 according to the severity of mucositis and sore throat.

Improvement of mucositis was evaluated in 3 stages including days 1-3, days 4-6, and days 7-10.

The results were analyzed using the chi-square test.

## Results

There were 5 females and 15 males in the sucralfate group with a mean age of  $58 \pm 7$  years. The placebo group included 3 females and 17 males with a mean age of  $57 \pm 7$  years. The 2 groups were similar with respect to age and sex ( $p > 0.05$ ).

Compared to the placebo group the severity of mucositis ran a significantly slighter course in the sucralfate group ( $p < 0.05$ ) (Table 1). Similarly, resolution of mucositis took a shorter duration ( $p < 0.001$ ). Complaints of sore throat were significantly less in patients receiving sucralfate ( $p < 0.05$ ) (Table 2). Also sucralfate administration was associated with significantly less weight loss ( $p < 0.05$ ).

## Discussion

Chemotherapy with 5-FU is associated with several toxicities, one of which is oral mucositis, worsening both the nutritional status and the quality of life of cancer patients [7].

Several investigators have tried different methods to prevent 5-FU-induced mucositis. It has been documented that oral cryotherapy given before chemotherapy does not give satisfactory results in preventing 5-FU-induced mucositis. Other methods include capsaicin, vitamin E, glutamine, and mouthwashes with allopurinol in 3% methylcellulose (450 mg).

Capsaicin seems to desensitize pain receptors [8-10]. Benzocaine preparations containing hydro-

Table 1. Treatment results in the sucralfate group ( $n=20$ )

| n  | Age (years) | Sex | Mucositis score | Sore throat score | Weight loss | Recovery of mucositis |
|----|-------------|-----|-----------------|-------------------|-------------|-----------------------|
| 1  | 58          | F   | 0               | 0                 | 500 g       | —                     |
| 2  | 52          | M   | 1               | 0                 | 500 g       | first 3 days          |
| 3  | 65          | M   | 2               | 2                 | 500 g       | 3-6 days              |
| 4  | 67          | F   | 0               | 0                 | 500 g       | —                     |
| 5  | 69          | M   | 1               | 1                 | 750 g       | first 3 days          |
| 6  | 48          | M   | 2               | 2                 | 1.5 kg      | 3-6 days              |
| 7  | 51          | M   | 0               | 0                 | 500 g       | —                     |
| 8  | 56          | F   | 1               | 0                 | 750 g       | first 3 days          |
| 9  | 44          | M   | 0               | 0                 | 500 g       | —                     |
| 10 | 68          | M   | 0               | 0                 | 500 g       | —                     |
| 11 | 62          | M   | 1               | 0                 | 750 g       | first 3 days          |
| 12 | 60          | F   | 1               | 1                 | 750 g       | first 3 days          |
| 13 | 58          | M   | 0               | 0                 | 500 g       | —                     |
| 14 | 53          | M   | 1               | 1                 | 500 g       | first 3 days          |
| 15 | 57          | M   | 2               | 2                 | 1.5 kg      | 3-6 days              |
| 16 | 62          | F   | 1               | 1                 | 750 g       | first 3 days          |
| 17 | 69          | M   | 0               | 0                 | 500 g       | —                     |
| 18 | 58          | M   | 0               | 0                 | 500 g       | —                     |
| 19 | 52          | M   | 1               | 1                 | 750 g       | 3-6 days              |
| 20 | 63          | M   | 0               | 0                 | 500 g       | —                     |

Severity of mucositis and sore throat score:

0: No, 1: Slight, 2: Moderate, 3: Severe

Table 2. Treatment results in the placebo group ( $n=20$ )

| n  | Age (years) | Sex | Mucositis score | Sore throat score | Weight loss | Recovery of mucositis |
|----|-------------|-----|-----------------|-------------------|-------------|-----------------------|
| 1  | 52          | M   | 1               | 0                 | 750 g       | first 3 days          |
| 2  | 50          | M   | 2               | 1                 | 2 kg        | 3-6 days              |
| 3  | 64          | F   | 2               | 1                 | 1.5 kg      | 3-6 days              |
| 4  | 61          | M   | 3               | 2                 | 2 kg        | 6-10 days             |
| 5  | 68          | M   | 1               | 0                 | 750 g       | 3-6 days              |
| 6  | 51          | M   | 2               | 2                 | 3 kg        | 3-6 days              |
| 7  | 54          | F   | 2               | 2                 | 2 kg        | 6-10 days             |
| 8  | 43          | M   | 2               | 1                 | 2 kg        | 3-6 days              |
| 9  | 67          | M   | 2               | 2                 | 2 kg        | 6-10 days             |
| 10 | 59          | M   | 2               | 1                 | 1.5 kg      | 3-6 days              |
| 11 | 56          | F   | 3               | 3                 | 2.5 kg      | 6-10 days             |
| 12 | 64          | M   | 2               | 1                 | 2.5 kg      | 3-6 days              |
| 13 | 68          | M   | 1               | 0                 | 750 g       | first 3 days          |
| 14 | 60          | M   | 2               | 2                 | 2 kg        | 6-10 days             |
| 15 | 58          | M   | 2               | 2                 | 1.5 kg      | 3-6 days              |
| 16 | 52          | M   | 2               | 2                 | 3 kg        | 3-6 days              |
| 17 | 46          | M   | 3               | 2                 | 3 kg        | 6-10 days             |
| 18 | 54          | M   | 2               | 1                 | 2 kg        | 3-6 days              |
| 19 | 62          | M   | 3               | 3                 | 3 kg        | 6-10 days             |
| 20 | 67          | M   | 2               | 1                 | 1.5 kg      | 3-6 days              |

For scoring see abbreviations in Table 1



hydroxypropyl-cellulose and sucralfate protect physical mucosal barriers [11].

Sucralfate is used in the treatment of active peptic and duodenal ulcers. Negatively charged polyanions of sucralfate form polyvalent bonds with positively charged mucoproteins of the damaged mucosa. This binding is stronger in acidic conditions; however, at neutral pH conditions such as duodenum and oral mucosa an effective binding can also occur. This dense viscous layer provides a protective coat over the ulcer. The most common adverse effect of sucralfate is constipation. Diarrhea, nausea, and dryness of the mouth can rarely be encountered [12,13].

Loprizi et al in a group of 50 patients with mucositis, administered sucralfate ( $n = 27$ ) and placebo ( $n = 23$ ). They reported a rapid recovery of oral mucositis in the sucralfate group [13].

McGinnis et al also reported beneficial effects of sucralfate in patients with radiotherapy-induced esophagitis and mucositis [6].

Our study showed that sucralfate-receiving patients exhibited rapid alleviation of oral cavity lesions, decrease in nutritional problems, and significantly less weight loss. Sucralfate proved an efficacious agent in the treatment of chemotherapy-induced oral mucositis without any serious adverse effects.

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