Review: Prophylactic interventions reduce oral mucositis in patients with cancer receiving chemotherapy or radiation therapy

Worthington HV, Clarkson JE, Eden OB. **Interventions for preventing oral mucositis for patients with cancer receiving treatment.** Cochrane Database Syst Rev. 2006;(2):CD000978.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Hospitalists ★★★★★★☆ Oncology ★★★★★★★

QUESTION

In patients with cancer receiving chemotherapy or radiation therapy, how effective is prophylaxis for oral mucositis?

METHODS

Data sources: MEDLINE (from 1966), EMBASE/Excerpta Medica (from 1974), Cochrane Oral Health Group Trials register, Cochrane Central Register of Controlled Trials, System of Information on Gray Literature in Europe, CANCERLIT, CINAHL, LILACS, and bibliographies of relevant studies.

Study selection and assessment: Randomized controlled trials (RCTs) in any language that compared prophylactic treatments with other treatments, placebo, or no treatment in patients with cancer receiving chemotherapy or radiation therapy. Studies assessing mucositis as a secondary outcome were excluded. 29 different interventions were compared in 71 RCTs (n = 5217, age range 1 to 70 y). Quality assessment of individual studies was based on allocation concealment, blinding, and withdrawals.

Outcomes: Incidence and severity of mucositis.

MAIN RESULTS

Meta-analysis showed that amifostine, ice chips, antibiotics, and hydrolytic enzymes reduced the incidence and severity of mucositis in > 1 RCT (Table). Small (n < 100) single RCTs also showed benefit for calcium phosphate (Table), benzydamine, povidone, oral care, honey, and zinc sulfate.

CONCLUSION

In patients with cancer receiving chemotherapy or radiation therapy, prophylactic interventions reduce the incidence and severity of oral mucositis.

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Intervention vs placebo or no treatment for oral mucositis in patients with cancer receiving chemotherapy or radiation therapy at 28 to 90 days*

Outcomes	Number of trials (n)	Comparisons	Relative risk (95% CI)
Mucositis	1 (301)	Amifostine vs no treatment	0.95 (0.91 to 0.99)
	2 (138)	Ice chips vs no treatment	0.63 (0.44 to 0.91)
	1 (94)	Calcium phosphate vs placebo	0.75 (0.58 to 0.99)
	2 (298)	Antibiotic vs placebo	0.87 (0.79 to 0.97)
Moderate-to-severe mucositis	4 (422)	Amifostine vs no treatment	0.84 (0.75 to 0.95)
	2 (138)	Ice chips vs no treatment	0.43 (0.23 to 0.81)
	1 (94)	Calcium phosphate vs placebo	0.63 (0.42 to 0.94)
	2 (149)	Hydrolytic enzymes vs no treatment	0.52 (0.36 to 0.74)

*CI defined in Glossary; a random-effects model was used.

COMMENTARY

It has been estimated that 5% to 15% of patients receiving standard-dose chemotherapy experience severe mucositis (1). The incidence is even higher if concurrent chemotherapy and radiotherapy or high-dose chemotherapy regimens are used. The costs of mucositis are substantial and include hospitalization, need for nutritional support and pain management, time lost from work, and other perturbations of quality of life. But how can sensible recommendations be made about treating or preventing mucositis when the quality of medical literature on mucositis is so poor?

Worthington and colleagues took on this challenge in their fourth systematic review on the prophylaxis and management of oral mucositis and candidiasis. This update adds to the number and types of treatments reviewed and includes recommendations for preventing radiation-induced oral mucositis with amifostine. Despite their efforts, many of the included studies were flawed by inadequate sample sizes, lack of control groups, and no blinding. Generalizability was also limited because half the studies were restricted to patients with head and neck cancers. Ice chips were recommended for preventing 5-fluorouracil–induced oral mucositis only.

Worthington and colleagues did not evaluate studies of mucositis in other parts of the alimentary canal. However, the Multinational Association of Supportive Care in Cancer published evidence-based guidelines for the prophylactic treatment of oral and gastrointestinal mucositis, recommending that sulfasalazine be used to prevent mucositis of the bowel induced by pelvic irradiation (2).

Well-designed trials are needed to test interventions for decreasing the incidence, morbidity, and costs of mucositis.

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2. **Rubenstein EB, Peterson DE, Schubert M, et al.** Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. Cancer. 2004;100:2026-46.