

Review: Antifungals absorbed or partially absorbed from the GI tract prevent oral candidiasis in cancer patients receiving treatment

Worthington HV, Clarkson JE, Eden OB. Interventions for preventing oral candidiasis for patients with cancer receiving treatment. Cochrane Database Syst Rev. 2002;(3):CD003807 (latest version 10 Apr 2002).

QUESTION

In patients with cancer who are receiving chemotherapy or radiotherapy, what treatments are effective in preventing oral candidiasis?

DATA SOURCES

Studies were identified by searching the Cochrane Oral Health Group Specialised Register, the Cochrane Controlled Trials Register (2001, issue 3), MEDLINE (1966 to May 2001), and EMBASE/Excerpta Medica (1974 to May 2001); the reference lists of related reviews and retrieved relevant studies; and by contacting authors of trial reports and specialists in the field.

STUDY SELECTION

Studies were selected if they were randomized controlled trials evaluating the effectiveness of antifungal treatments in preventing oral candidiasis in patients receiving chemotherapy or radiotherapy for cancer.

DATA EXTRACTION

Data were extracted independently and in duplicate by 2 reviewers on study quality, patient characteristics, interventions, and outcomes.

MAIN RESULTS

27 trials involving 4137 patients met the selection criteria. 7 trials involving 1153 patients compared drugs absorbed from the gastrointestinal (GI) tract (fluconazole, ketoconazole, and itraconazole) with placebo or a no-treatment control and found that fewer patients receiving the active drugs developed oral candidiasis (Table). 4 trials involving 292 patients compared drugs partially absorbed from the GI tract (miconazole and clotrimazole) with placebo and found that fewer patients receiving the active drugs developed oral candidiasis (Table). 8 studies involving 382 patients compared drugs not absorbed from the GI tract (e.g., amphotericin B, nystatin, and chlorhexidine) with placebo or a

no-treatment control and found that these active drugs did not appear to be as effective in preventing oral candidiasis (Table).

CONCLUSION

In patients with cancer who are receiving chemotherapy or radiotherapy, antifungal drugs absorbed or partially absorbed from the gastrointestinal tract prevent oral candidiasis.

Source of funding: No external funding.

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Antifungal drug interventions to prevent oral candidiasis in patients with cancer receiving chemotherapy or radiotherapy*

Comparisons	Weighted event rates	RRR (95% CI)	NNT (CI)
DA vs placebo†	6% vs 14%	55% (36 to 68)	13 (10 to 20)
PA vs placebo†	5% vs 37%	87% (73 to 94)	4 (3 to 5)
NA vs placebo‡	43% vs 61%	32% (-2 to 54)	Not significant

*DA = drugs absorbed from the gastrointestinal (GI) tract; PA = drugs partially absorbed from the GI tract; NA = drugs not absorbed from the GI tract. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

†A fixed-effects model was used.

‡A random-effects model was used.

COMMENTARY

Therapeutic advances in cancer treatment have been supported by concurrent advances in preventing and managing infections in treated patients. With more aggressive immunosuppressive chemotherapy and intensified treatment of bacterial infections, fungal infections have become increasingly complex and important (1). Initial concerns were prevention and treatment of oral candidiasis, but the focus now is prevention of systemic fungal infections with their attendant high morbidity and mortality.

The review by Worthington and colleagues on prevention of oral candidiasis includes several agents and patient groups in studies reported over 3 decades. During this period, antifungal therapy and other therapeutic management of patients with cancer have changed dramatically. The patients enrolled in these studies have varying risks, from those with hematologic malignancies where invasive fungal infection is a substantial concern, to solid organ malignancies receiving less intense chemotherapy where the problem is not as severe. Despite this variability, the observed outcomes are consistent with prophylactic therapy for oral candidiasis. Absorbed or partially absorbed antifungal agents prevented oral candidiasis, while those not absorbed were not effective.

The review does not, however, address the clinical effect because the primary outcome was mycological. Oral colonization with candida is

common in these populations (2), but the meaningful patient outcomes are clinical. These include the secondary outcomes considered in this review, such as pain, dysphagia, systemic fungal infection, duration of hospitalization, quality of life, and drug toxicity. The review was less helpful in addressing these outcomes because of the limited information in the included trials.

Prevention of oral candidiasis, in fact, has been eclipsed by concerns for prevention of systemic fungal infection for the highest-risk groups. Recent evidence suggests that prophylactic antifungal therapy is indicated to prevent invasive fungal infection for high-risk patients, usually those receiving chemotherapy for hematologic malignancies (3) or allogeneic bone marrow transplantation (4). A continuing concern with widespread use of prophylactic antifungal therapy is the emergence of resistance.

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References

- Jahagirdar BN, Morrison VA. *Semin Respir Infect.* 2002;17:113-20.
- Rex JH, Walsh TJ, Sobel JD, et al. *Clin Infect Dis.* 2000;30:662-78.
- Bow EJ, Laverdière M, Lussier N, et al. *Cancer.* 2002;94:3230-46.
- Wingard JR. *Clin Infect Dis.* 2002;34:1386-90.