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What is the best treatment for oral thrush in healthy infants?

Evidence-based answer

Nystatin oral suspension is a safe first-line therapy; fluconazole is more effective (strength of recommendation [SOR]: **B**, 1 small randomized controlled trial [RCT]) but has not been approved by the Food and Drug Administration (FDA) for use in immunocompetent infants. Miconazole

oral gel is also more effective than nystatin suspension, but is not commercially available in the United States (SOR: **B**, one small RCT). Gentian violet may be effective, but it stains skin and clothes and is associated with mucosal ulceration (SOR: **B**, 1 small retrospective cohort study).

Clinical commentary

Fluconazole isn't worth the higher cost

I reassure parents that oral thrush in infants is rarely a sign of serious illness and recommend nystatin suspension 0.5 cc qid—a smaller dose than reported in this review. Larger doses are more often spit out or swallowed, and at the smaller dose, a 60-mL bottle suppresses the yeast adequately for 2 weeks. My goal is to suppress yeast overgrowth until the infant's immune system and bacterial flora

mature. This review doesn't convince me that fluconazole, which costs more than nystatin, is worth the added expense. Gentian violet is very messy, and I rarely recommend it. For refractory thrush in breastfed infants, I recommend that the mother apply a topical antifungal to the nipple area.

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FAST TRACK

Fluconazole is more effective than nystatin oral suspension, but costs more and is an off-label use for healthy infants

Evidence summary

Few studies have compared treatment options for oropharyngeal candidiasis in immunocompetent infants. In a survey of 312 health care providers, approximately 75% of the respondents reported treating thrush with oral nystatin, citing fewer side effects and lower cost.¹ However, nystatin has proved less effective than either miconazole gel or oral fluconazole.

Nystatin is safe and available, but other options work better

Miconazole vs nystatin. An unblinded

RCT assigned 83 immunocompetent infants with culture-positive oral thrush to receive either 25 mg miconazole oral gel (not commercially available in the United States) or nystatin suspension (1 mL of 100,000 IU/mL) qid after meals. The clinical cure rate, defined as absence of plaques by day 12, was significantly higher in the miconazole group (99% for miconazole, 54% for nystatin; $P < .0001$, number needed to treat [NNT]=2). The eradication rate, confirmed by cultures collected in a blinded manner on the day of clinical cure, was also higher in

the miconazole group (55.7% for miconazole, 15.2% for nystatin; $P<.0001$, NNT=3). In successfully treated patients, infection recurred with similar frequency in both treatment groups within 4 weeks (miconazole, 12.4%; nystatin, 13.0%). Side effects—mostly vomiting and, infrequently, diarrhea—were rare in both groups (miconazole, 4.5%; nystatin 3.5%).²

An earlier, unblinded RCT of 95 infants compared miconazole gel to 2 nystatin oral gels (gel A: 250,000 IU/g with 250,000 IU administered as single dose; gel B: 100,000 IU/g with 50,000 IU administered as single dose). Each medication was given qid over the course of 8 to 14 days. The study confirmed higher clinical cure rates with miconazole gel (85.1% for miconazole vs 42.8% for nystatin gel A [$P<.0007$, NNT=2] and 48.5% for nystatin gel B [$P<.004$, NNT=3]).³

Fluconazole vs nystatin. In the only prospective RCT (unblinded) to compare oral suspensions of fluconazole and nystatin, 34 infants were randomized to receive either nystatin (1 mL of 100,000 IU/mL) qid for 10 days or fluconazole (3 mg/kg) once a day for 7 days. Mothers of breastfed infants applied nystatin cream to their nipples twice a day for the duration of the infant's treatment. The clinical cure rate—defined as absence of oral plaques at the end of therapy (day 10 for the nystatin group, day 7 for the fluconazole group)—was significantly higher in the group treated with fluconazole (100% for fluconazole, 32% for nystatin; $P<.0001$, NNT=2). The eradication rate was also higher with fluconazole (73.3% for fluconazole, 5.6% for nystatin; $P<.0001$, NNT=2). The patients treated with fluconazole experienced no side effects.⁴ Fluconazole has been shown to be effective, safe, and easy to use to treat thrush in immunocompromised children,⁵ but has not been approved by the FDA for use in healthy infants.

Gentian violet is effective, but messy and irritating

A retrospective cohort study that reviewed 69 cases of oral thrush showed that gentian violet achieved a 75% cure rate in an average of 11 days (compared to 55% in 10 days for nystatin). Both treatments shortened the duration of illness compared with the average of 34 days for untreated children.⁶ However, gentian violet can stain skin and clothes, and case studies have shown an association with ulceration of the buccal mucosa.⁷

Recommendations

A thorough literature search through the Cochrane Database Systematic Reviews, Agency for Healthcare Research and Quality, National Guideline Clearinghouse, and Medline did not yield any guidelines or consensus statements from other organizations or specialty groups on treating oropharyngeal candidiasis in infants. Neither the American Academy of Pediatrics nor the Infectious Diseases Society of America has issued applicable practice guidelines. ■

References

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FAST TRACK

Refractory thrush in breastfed infants may respond to a topical antifungal applied to the mother's nipples