Systemic antifungal therapy for tinea capitis in children: An abridged Cochrane Review

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Background: The comparative efficacy and safety profiles of systemic antifungal drugs for tinea capitis in children remain unclear.

Objective: We sought to assess the effects of systemic antifungal drugs for tinea capitis in children.

Methods: We used standard Cochrane methodological procedures.

Results: We included 25 randomized controlled trials with 4449 participants. Terbinafine and griseofulvin had similar effects for children with mixed *Trichophyton* and *Microsporum* infections (risk ratio 1.08, 95% confidence interval 0.94-1.24). Terbinafine was better than griseofulvin for complete cure of *T tonsurans* infections (risk ratio 1.47, 95% confidence interval 1.22-1.77); griseofulvin was better than terbinafine for complete cure of infections caused solely by *Microsporum* species (risk ratio 0.68, 95% confidence interval 0.53-0.86). Compared with griseofulvin or terbinafine, itraconazole and fluconazole had similar effects against *Trichophyton* infections.

Limitations: All included studies were at unclear or high risk of bias. Lower quality evidence resulted in a lower confidence in the estimate of effect. Significant clinical heterogeneity existed across studies.

Conclusions: Griseofulvin or terbinafine are both effective; terbinafine is more effective for *T tonsurans* and griseofulvin for *M canis* infections. Itraconazole and fluconazole are alternative but not optimal choices for *Trichophyton* infections. Optimal regimens of antifungal agents need further studies. (J Am Acad Dermatol 2017;76:368-74.)

Key words: children; Cochrane; systemic antifungal therapy; systematic review; tinea capitis; treatment.

Tinea capitis is caused by dermatophyte fungi (usually *Trichophyton* or *Microsporum* species; eg, *T tonsurans*, *T mentagrophytes*, *T violaceum*, *M canis*, and *M audouinii*).[1] It affects healthy preadolescent children and rarely occurs in adults.[1] It is common in countries of all income levels around the world; however, the prevalence varies across study populations within different geographic

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areas.[2] A fungal kerion describes an abscess-like mass that, if left untreated, can lead to scarring and permanent hair loss.

Antifungal agents are the primary interventions for treating tinea capitis (eg, griseofulvin, terbinafine, ketoconazole, fluconazole, and itraconazole). They are widely used in clinical practice.[1,3] The comparative efficacy and safety profiles for these agents with different dosages or durations of treatment remain unclear. We conducted this literature review to address the efficacy and safety of systemic antifungal drugs for tinea capitis in children.

CAPSULE SUMMARY

- Systemic antifungal therapy is the key intervention for tinea capitis.
- Griseofulvin and terbinafine should be considered first-line agents. Terbinafine and griseofulvin are most effective for *Trichophyton tonsurans* and *Microsporum canis*; itraconazole and fluconazole are alternative treatments.
- Optimal regimens of antifungal agents remain to be elucidated.

METHODS

Our analysis is based on a Cochrane Review most recently updated in the Cochrane Library 2016, issue 5 (www.thecochranelibrary.com).[4] Full details of the methods and all the included studies are available from the Cochrane Review.

Inclusion criteria

We included randomized controlled trials (RCTs) conducted in children with normal immunity and with tinea capitis confirmed by microscopy, growth of dermatophytes in culture, or both. All regimens of systemic antifungal therapies for tinea capitis were included.

Searches

We searched the following databases up to November 2015: MEDLINE via Ovid (from 1946), EMBASE via Ovid (from 1974), LILACS (from 1982), CINAHL via EBSCO (from 1981), CENTRAL (2015, issue 10), and the Cochrane Skin Group Specialized Register. We also searched 5 trials registers. We handsearched the bibliographies of included and excluded studies for further references to relevant trials and we contacted principal investigators for missing data.

Data extraction

Two review authors independently extracted the information from the included RCTs, and another author checked the data extraction forms for accuracy. Discrepancies were resolved by discussion.

Outcomes

Based on the protocol of the review, 2 primary outcomes were identified: (1) the proportion of participants with complete cure (ie, clinical and mycologic cure); and (2) the frequency and type of adverse events. We also assessed 4 secondary outcomes: (1) the proportion of participants with clinical cure only; (2) measurement of recurrence of the condition after the end of the intervention period; (3) percentage of drop-outs; and (4) the time taken to cure. We present the results of primary outcomes in this abridged version.

Two review authors independently assessed the risk of bias for each included RCT according to the methods recommended in sections 8.9 to 8.15 of the *Cochrane Handbook for Systematic Reviews of Interventions*.[5] The Cochrane risk of bias domains for each RCT were rated as low, high, and unclear risk of bias accordingly.

We presented dichotomous outcomes as risk ratios (RR) with 95% confidence intervals (CI). We presented the only continuous outcome, the time taken to cure, as the mean with standard differences. When we identified clinically similar RCTs we pooled dichotomous data into a meta-analysis using random-effects model (Mantel-Haenszel method) in RevMan 5.3 software.[6] We performed subgroup analyses according to dermatophyte species variation and duration of treatment, if possible. The duration of treatment was categorized into 3 groups: (1) short term (closest to 2 weeks, but between 1 and 4 weeks); (2) medium term (closest to 6 weeks, but between 5 and 8 weeks); and (3) long term (closest to 12 weeks, but between 9 and 14 weeks).

RESULTS

We included a total of 25 RCTs[7-31] with 4449 participants (Fig 1). All were parallel group studies, and 10 had a multiarm design. Sample size varied from 13 to 1549 participants. Each of the 25 studies reported the types of fungus cultured. *Trichophyton* species predominated over *Microsporum* species in the included studies; *T tonsurans* and *M canis* caused infection in the highest proportion of participants. The overall quality of included RCTs was moderate or low and in some cases very low according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria.[32] Fig 2 describes our judgements about each risk of bias item presented as percentages across all included studies.