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## [Intervention Review]

## Systemic antifungal therapy for tinea capitis in children

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## ABSTRACT

## Background

Tinea capitis is a common contagious fungal infection of the scalp in children. Systemic therapy is required for treatment and to prevent spread. This is an update of the original Cochrane review.

#### Objectives

To assess the effects of systemic antifungal drugs for tinea capitis in children.

#### Search methods

We updated our searches of the following databases to November 2015: the Cochrane Skin Group Specialised Register, CENTRAL (2015, Issue 10), MEDLINE (from 1946), EMBASE (from 1974), LILACS (from 1982), and CINAHL (from 1981). We searched five trial registers and checked the reference lists of studies for references to relevant randomised controlled trials (RCTs). We obtained unpublished, ongoing trials and grey literature via correspondence with experts in the field and from pharmaceutical companies.

#### **Selection criteria**

RCTs of systemic antifungal therapy in children with normal immunity under the age of 18 with tinea capitis confirmed by microscopy, growth of fungi (dermatophytes) in culture or both.

#### Data collection and analysis

We used standard methodological procedures expected by Cochrane.

#### **Main results**

We included 25 studies (N = 4449); 4 studies (N = 2637) were new to this update.

Terbinafine for four weeks and griseofulvin for eight weeks showed similar efficacy for the primary outcome of complete (i.e. clinical and mycological) cure in three studies involving 328 participants with *Trichophyton* species infections (84.2% versus 79.0%; risk ratio (RR) 1.06, 95% confidence interval (CI) 0.98 to 1.15; low quality evidence).

Complete cure with itraconazole (two to six weeks) and griseofulvin (six weeks) was similar in two studies (83.6% versus 91.0%; RR 0.92, 95% CI 0.81 to 1.05; N = 134; very low quality evidence). In two studies, there was no difference between itraconazole and terbinafine for two to three weeks treatment (73.8% versus 78.8%; RR 0.93, 95% CI 0.72 to 1.19; N = 160; low quality evidence). In three studies, there

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was a similar proportion achieving complete cured with two to four weeks of fluconazole or six weeks of griseofulvin (41.4% versus 52.7%; RR 0.92, 95% CI 0.81 to 1.05; N = 615; moderate quality evidence). Current evidence for ketoconazole versus griseofulvin was limited. One study favoured griseofulvin (12 weeks) because ketoconazole (12 weeks) appeared less effective for complete cure (RR 0.76, 95% CI 0.62 to 0.94; low quality evidence). However, their effects appeared to be similar when the treatment lasted 26 weeks (RR 0.95, 95% CI 0.83 to 1.07; low quality evidence). Another study indicated that complete cure was similar for ketoconazole (12 weeks) and griseofulvin (12 weeks) (RR 0.89, 95% CI 0.57 to 1.39; low quality evidence). For one trial, there was no significant difference for complete cure between fluconazole (for two to three weeks) and terbinafine (for two to three weeks) (82.0% versus 94.0%; RR 0.87, 95% CI 0.75 to 1.01; N = 100; low quality evidence). For complete cure, we did not find a significant difference between fluconazole (for two to three weeks) and itraconazole (for two to three weeks) (82.0% versus 82.0%; RR 1.00, 95% CI 0.83 to 1.20; low quality evidence).

This update provides new data: in children with *Microsporum* infections, a meta-analysis of two studies found that the complete cure was lower for terbinafine (6 weeks) than for griseofulvin (6-12 weeks) (34.7% versus 50.9%; RR 0.68, 95% CI 0.53 to 0.86; N = 334; moderate quality evidence). In the original review, there was no significant difference in complete cure between terbinafine (four weeks) and griseofulvin (eight weeks) in children with *Microsporum* infections in one small study (27.2% versus 60.0%; RR 0.45, 95% CI 0.15 to 1.35; N = 21; low quality evidence).

One study provides new evidence that terbinafine and griseofulvin for six weeks show similar efficacy (49.5% versus 37.8%; RR 1.18, 95% CI 0.74 to 1.88; N = 1006; low quality evidence). However, in children infected with *T. tonsurans*, terbinafine was better than griseofulvin (52.1% versus 35.4%; RR 1.47, 95% CI 1.22 to 1.77; moderate quality evidence). For children infected with *T. violaceum*, these two regimens have similar effects (41.3% versus 45.1%; RR 0.91, 95% CI 0.68 to 1.24; low quality evidence). Additionally, three weeks of fluconazole was similar to six weeks of fluconazole in one study in 491 participants infected with *T. tonsurans* and *M. canis* (30.2% versus 34.1%; RR 0.88, 95% CI 0.68 to 1.14; low quality evidence).

The frequency of adverse events attributed to the study drugs was similar for terbinafine and griseofulvin (9.2% versus 8.3%; RR 1.11, 95% CI 0.79 to 1.57; moderate quality evidence), and severe adverse events were rare (0.6% versus 0.6%; RR 0.97, 95% CI 0.24 to 3.88; moderate quality evidence). Adverse events for terbinafine, griseofulvin, itraconazole, ketoconazole, and fluconazole were all mild and reversible.

All of the included studies were at either high or unclear risk of bias in at least one domain. Using GRADE to rate the overall quality of the evidence, lower quality evidence resulted in lower confidence in the estimate of effect.

## Authors' conclusions

Newer treatments including terbinafine, itraconazole and fluconazole are at least similar to griseofulvin in children with tinea capitis caused by *Trichophyton* species. Limited evidence suggests that terbinafine, itraconazole and fluconazole have similar effects, whereas ketoconazole may be less effective than griseofulvin in children infected with *Trichophyton*. With some interventions the proportion achieving complete clinical cure was in excess of 90% (e.g. one study of terbinafine or griseofulvin for *Trichophyton* infections), but in many of the comparisons tested, the proportion cured was much lower.

New evidence from this update suggests that terbinafine is more effective than griseofulvin in children with T. tonsurans infection.

However, in children with *Microsporum* infections, new evidence suggests that the effect of griseofulvin is better than terbinafine. We did not find any evidence to support a difference in terms of adherence between four weeks of terbinafine versus eight weeks of griseofulvin. Not all treatments for tinea capitis are available in paediatric formulations but all have reasonable safety profiles.

## PLAIN LANGUAGE SUMMARY

## Antifungal medicines for treating children with ringworm

## Background

Tinea capitis, or ringworm, is a fungal infection of the scalp caused mainly by two species of fungi called *Trichophyton* and *Microsporum*. It is common in children. Most fungal infections can be treated with antifungal creams applied directly to the skin (topical treatments). However, because the fungal infection is found at the root of the hair follicles, where topical treatments cannot reach, tinea capitis always requires medication administered by mouth so that the treatment spreads throughout the entire body (systemic treatments). There are several different types of antifungal medicines available.

## **Review question**

Which antifungal medicine is best for treating ringworm on the scalp in children?

## **Study characteristics**

In November 2015, we searched for studies that used the gold standard design for clinical trials (randomised controlled trials) of antifungal treatments taken by mouth. We found 25 studies in which 4449 children under 18 years (4 studies with 2637 children were new to this update) had taken part.



#### **Key results**

With respect to complete cure (both cure of the infection and visible cure (i.e. fungal and clinical cure) low to moderate quality evidence suggests that newer treatments such as terbinafine, itraconazole and fluconazole are at least as good as griseofulvin, the usual treatment in children with tinea capitis caused by *Trichophyton* infections. However, new evidence in this update suggests that terbinafine may have better effects than griseofulvin for completely curing children with *T. tonsurans* infection. By contrast, in children with *Microsporum* infections, new evidence seems to indicate that griseofulvin is more effective than terbinafine.

Terbinafine, itraconazole and fluconazole appear to have similar effects in terms of the proportion of participants achieving complete cure, whereas ketoconazole appears to be less effective than griseofulvin for children with tinea capitis caused by *Trichophyton* species. However, the quality of this evidence is low. With some interventions, the proportion with complete clinical cure was in excess of 90% (e.g. one study of terbinafine versus griseofulvin for *Trichophyton* infections), but in many of the comparisons tested, the proportion cured was much lower.

The included studies reported on negative side effects, which were similarly mild and reversible for terbinafine, griseofulvin, itraconazole, ketoconazole and fluconazole. They included skin-specific effects such as itching as well as abdominal discomfort, headache and nausea.

#### **Quality of the evidence**

The quality of the evidence in this review was generally low to moderate, so further research is likely to have an important effect on our confidence in these results. Some evidence was even of very low quality. We still need more and better evidence to help us understand the effectiveness and adverse events of systemic antifungal drugs for tinea capitis in children.