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Treatment of Tinea Capitis

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Abstract
Tinea capitis is a common fungal infection of the hair of the scalp affecting predominately prepubertal children. In the US, griseofulvin has been considered a first-line therapy agent for tinea capitis since the 1960s. However, it has been falling out of favor due to significant treatment failure, high cost, and long duration of treatment. Other antifungal agents have been researched as an alternative to griseofulvin. This paper will review the relevant pharmacologic properties, dosing, cost, efficacy, and adverse events profile for griseofulvin, terbinafine, itraconazole, fluconazole, and some adjuvant therapy options such as selenium sulfide shampoos and topical ketoconazole.

Introduction

Tinea capitis is a common fungal infection of the hair of the scalp affecting primarily preadolescents [1]. Recent surveys of elementary school children in Ohio in 2003 and Alabama in 2011 found a prevalence rate of 11% [2, 3]. Despite concerns about the rise of tinea capitis cases in the United States (US), these surveys found the rate to be stable [2, 3]. Tinea capitis is caused by dermatophytes that can utilize keratin, the primary component of the hair [1]. The causative dermatophytes belong to two genera: *Trichophyton* and *Microsporum* [1]. In the earlier half of the 20th century, *Microsporum audouinii* was the predominant cause of tinea capitis in the US [4]. Currently, *Trichophyton tonsurans* is responsible for up to 95% of cases in the US [5]. *Trichophyton violaceum* is the dominant organism in Eastern Europe and South Asia, while *Microsporum canis* causes the majority of tinea capitis cases in Africa, Western Europe, Australia, and South America [4] (Table 1).

The clinical manifestations of tinea capitis are classified as endothrix, ectothrix, or favus. In the endothrix form, hyphae grow down the follicle and penetrate the hair shaft, then grow completely within the hair shaft. This form is caused predominantly by *T. tonsurans* and *T. violaceum*. In the ectothrix form, the hyphae invade the hair shaft at mid follicle. Afterwards, hyphae grow out of the follicle covering the hair surface. This form is caused by *M. canis*, *M. audouinii*, *Microsporum ferrugineum*, and *Trichophyton verrucosum*. The hyphae grow parallel to the hair shaft in favus form then degenerate, leaving long tunnels within the hair shaft. Favus form is caused by *Trichophyton schoenleinii* and is characterized by yellow crust around the hair shafts and can result in permanent scarring alopecia [1].

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Table 1. The clinical features of tinea capitis due *T. tonsurans* and *M. canis*

Organism	*T. tonsurans*	*M. canis*
The dominant organism in	US and Central America	Africa, Australia, South America, and Western Europe
Source of infection [1]	Anthropophilic	Zoophilic Most commonly cats and dogs
Clinical presentation [82]	Less inflammation Hair loss at scalp level, characterized as black dot	Scaly, inflamed, with hair loss 2–3 mm or more above scalp Broken hair
Most common alopecia pattern [83]	Multiple and small	Few and can reach large diameter
Infectious pattern [1]	Endothrix	Ectothrix or mixed
Wood's lamp exam [82]	No fluorescence	Yellow-green fluorescence, high specificity but low sensitivity [84]
Typically resolves by puberty [1]	No	Yes

The treatment of tinea capitis requires systemic antifungal therapy because topical antifungal agents cannot penetrate the hair shaft sufficiently to eradicate infection. Griseofulvin, the former gold standard agent, has been associated with treatment failure; a retrospective review of patients' medical records revealed a failure rate of 39.3% [6]. Consequently, the recommended dose has been increased from 10–15 mg/kg to 20–25 mg/kg, creating an additional challenge and dramatically increased cost [7]. The only available liquid form of griseofulvin comes at a concentration of 125 mg/5 mL, requiring a large amount of medicine to achieve the therapeutic dose and resulting in increased cost. For instance, the required dose to treat a 20-kg child, an average 5-year-old in the US, is 16–20 mL daily for 8 weeks. In addition, the long duration of treatment decreases compliance and further increases treatment failure. This paper will discuss the available antifungal agents that have shown high efficacy and safety profiles for this common infection.

Griseofulvin

Griseofulvin is a fungistatic agent produced by various species of the mold *Penicillium*. It binds microtubules and inhibits the contraction of the mitotic spindle [8]. Griseofulvin is poorly absorbed after an oral dosage. Micronized (Grifulvin V) and ultramicronized (Gris-PEG) preparations are used to enhance absorption [9]. For micronized preparations, a peak serum concentration is achieved at approximately 4 h after an oral dose. Absorption is significantly improved with dietary fat intake, which contributes to the variability of the bioavailability [10]. The drug reaches the skin through sweat and its hydrophobic properties allow it to concentrate in the hair follicle and the stratum corneum [11]. After the cessation of therapy, griseofulvin concentration is undetected in the stratum corneum within 48 to 72 h possibly as a result of reversible protein binding and poor affinity to keratin. It has a terminal half-life of 9.5–21 h, allowing for once-a-day dosing [4, 10]. The liver metabolizes the majority of the drug through demethylation and glucuronidation reactions [9]. Griseofulvin is an inducer of coumarin-type drugs and estrogen but overall has very few drug interactions [12].

Griseofulvin has been used since the late 1960s in treating tinea capitis and is considered the gold standard therapy [1]. It is listed on the World Health Organization (WHO) essential medicines list. However, it is no longer available in Canada and some European countries [13]. It is FDA approved for tinea capitis in children of 2 years and older with a recommended dosage of 10 mg/kg/day [14]. Many experts view this dose as insufficient due to increased cases of treatment failure. Therefore, the new recommended dose is 20–25 mg/kg/day for microsized and 10–15 mg for ultramicrosized preparations for 6–12 weeks [7]. Treatment should be continued for 2 weeks after the resolution of clinical symptoms [15]. Long duration of treatment decreases compliance and contributes to treatment failure. Although the ultramicrosized preparation can be used at a lower dose, it is not available in an oral suspension formulation. The use of oral tablets is generally not less expensive than the use of oral suspension.

According to a recent systematic review, griseofulvin maintains a high complete cure rate of 72% [16]. Terbinafine was the only agent to have a higher complete cure rate of 92% [16]. However, griseofulvin was superior in treating infections caused by *Microsporum* species [16, 17]. Hence, longer courses of griseofulvin sometimes were required to cure infections caused by *M. canis* [1]. The observed advantage in treating *M. canis* has not been explained by any clinical studies but is speculated to be due to griseofulvin's ability to concentrate in sweat, unlike terbinafine, which is a lipophilic agent. Since these infections are ectothrix, the drug must reach the hair surface either through sebum or sweat [18]. Due to increased cases of treatment failure, concerns of fungal resistance to griseofulvin have been expressed. Intrinsic resistance is known to exist in dermatophytes lacking the energy-dependent transport system for this agent [19]. However, a study in 2009 observed a low frequency of in vitro resistance in *T. tonsurans* isolates from tinea capitis patients, with only 3 of 142 isolates growing at 4-fold minimum inhibitory concentration [20].

Griseofulvin has an excellent safety profile and no laboratory monitoring is required [21]. In a randomized clinical trial, the frequency of adverse events attributed to griseofulvin when used to treat tinea capitis was found to be 8.3 versus 9.2% for terbinafine [22]. Headaches and gastrointestinal upsets were the most common side effects. They were usually mild and subsided as treatment continued. Therefore, the discontinuation of the drug is infrequent and occurred in only 1.2% of patients [22]. Griseofulvin has been reported to induce photosensitivity in some rare cases, and it is therefore recommended to avoid intense and prolonged sun exposure during its use [23]. Severe adverse events are very rare and include erythema multiforme, serum sickness-like reaction, and systemic lupus erythematosus exacerbation [24–26]. It is contraindicated for patients with porphyria and hepatocellular failure [27]. Griseofulvin is pregnancy category X and should never be used in pregnant women due to its embryotoxic effects. In an in vitro study of murine spermatocyte, a dose-dependent increase in chromosomal abnormalities has been observed in spermatocytes treated with griseofulvin [28]. Therefore, men are warned against fathering a child for 6 months after receiving treatment [29].

Terbinafine

Terbinafine, also known as Lamisil®, is an allylamine derivative with fungicidal properties [30]. It is a noncompetitive inhibitor of squalene epoxidase, a key enzyme in the synthesis of ergosterol, an essential component of fungal cell membranes [8]. After an oral dose, 70–80% of the drug is rapidly absorbed and reaches a peak plasma concentration within 2 h. Its absorption is not affected by food intake [31]. Almost all of the drug travels bound to plasma proteins, and it also associates with chylomicrons, which allow for a large lymphatic distribution [32]. Its lipophilic properties account for its ability to reach a high concertation in hair follicles, sebum-rich skin, nail plate, and adipose tissue. After 12 days of therapy, terbinafine concentration in stratum corneum is 75 times higher than its plasma concentration [33]. It has a terminal half-life of 200–400 h, allowing for once-a-day dosing [32]. It is slowly eliminated from skin and has demonstrated antifungal activity for 2 months after its depletion from plasma [1]. These unique pharmacokinetic properties confer a distinct advantage to terbinafine, permitting shorter courses of therapy. It is metabolized by the liver primarily through N-demethylation enzymes. More than 15 metabolites have been identified and none of them have demonstrated antifungal activity [34]. Terbinafine is an inhibitor of the CYP2D6 and has minimal drug interactions that are clinically limited to cimetidine and rifampin [27].

In 2007, the FDA approved terbinafine oral granules for the treatment of tinea capitis in patients older than 4 years. The approved doses of terbinafine granules are based on body weight: 125.0 mg for less than 25 kg, 187.5 mg for 25–35 kg, and 250.0 mg for 35 kg or more, for continued duration of 6 weeks [35]. Laboratory monitoring for courses longer than 6 weeks may be required [36]. Most clinical trials have demonstrated a 4-week course of once-a-day dose to be effective in treating tinea capitis [17]. The duration of this course is significantly shorter than that of griseofulvin. Moreover, Friedlander et al. [37] and Haroon et al. [38] have found a 2-week course to be effective in treating tinea capitis due to *Trichophyton* species. Terbinafine oral granules are coated, which masks the taste of the medication. They can be sprinkled into the child's non-acidic food, which is especially useful for young children. However, this formulation is expensive. The tablets do not come in other doses, but a tablet can be divided as needed.

Multiple meta-analyses have demonstrated a similar efficacy for a 6-week course of griseofulvin and a 4-week course of terbinafine [17, 36, 39]. However, a difference in efficacy was found based on the infectious organism. Terbinafine demonstrated superiority in treating *T. tonsurans* and a similar efficacy in treating *T. violaceum*, while griseofulvin was superior in treating *M. canis* and

Table 2. The outcome of various clinical trials comparing terbinafine to griseofulvin for tinea capitis

First author	Year	Patients, *n*	Country	Terbinafine dose, mg/kg/day, and duration	Week of therapy	Cure rate, %	Griseofulvin dose, mg/kg/day, and duration	Cure rate, %
Deng [85]	2011	88	China	3.125–6.25 for 4 weeks	8	78.3	20 for 4 weeks	84.2
Elewski [22]	2008	1,549	International	5–8 for 4 weeks	10	45.1	10–20 for 6 weeks	39.2
Fuller [86]	2001	147	UK	3.125–6.25 for 4 weeks	12	57	10 for 8 weeks	57
Gupta [50]	2001	100	Canada and South Africa	3.125–6.25 for 2–3 weeks	12	94	20 for 6 weeks	92
Cáceres-Ríos [15]	2000	50	Peru	3.125–6.25 for 4 weeks	12	76	6.25–12.5 for 8 weeks	44
Memisoglu [87]	1999	78	Turkey	3.125–6.25 for 4 weeks	12	38.5	6.25–12.5 for 8 weeks	43.6
Haroon [88]	1995	105	Pakistan	3.125–6.25 for 4 weeks	12	92.9	6.25–12.5 for 8 weeks	79.6

Table 3. Rare adverse events reported with the use of terbinafine for tinea capitis

Subacute cutaneous lupus erythematosus [89]
Erythema multiforme [90]
Acute generalized exanthematous pustulosis [91]
Stevens-Johnson syndrome [92]
Anterior optic neuropathy [93]
Dermatomyositis [94]
Autoimmune hepatitis [95]
Acute fulminant hepatic failure [96]
Long-term taste disturbance [97]

other *Microsporum* species [36, 40]. Lipozencic et al. [41] showed that longer courses of terbinafine do not improve its efficacy against *Microsporum* species, concluding that terbinafine should not be a first line for tinea capitis infections caused by *Microsporum* species. In the US, these infections represent less than 5% of all cases of tinea capitis and should be suspected in cases with an ectothrix pattern or when contact with infected animals is found [5]. These patients generally fluoresce on Wood's light exam [1]. Table 2 lists all the major clinical trials that compared the use of griseofulvin to the use of terbinafine.

Oral terbinafine is well tolerated, with most adverse events being mild and reversible. Therefore, discontinuation related to adverse events is infrequent and occurs at a rate of 1.6% based on the largest clinical trial studying the use of terbinafine in tinea capitis [22]. Post-market surveillance of 25,884 patients reported an adverse event incidence rate of 10.5%, with gastrointestinal system (4.9%) and skin (2.3%) being the most frequently involved organs [42]. Serious adverse events are rare and are further listed in Table 3. The FDA does not recommend terbinafine use in patients with renal impairment due to decreased clearance and lack of safety studies in that population. It also should be avoided in patients with liver disease due to some rare cases of liver failure. Although it is no longer recommended to monitor liver enzymes during terbinafine treatment, physicians are advised to obtain a baseline ALT and AST [27]. Terbinafine is the agent of choice in pregnancy, and it is the only systemic antifungal used for tinea capitis listed as pregnancy category B.

Itraconazole

Itraconazole, also known as Sporanox® or Onmel®, is one of the first-generation triazoles. These agents contain three nitrogen atoms in their characteristic five-membered heterocyclic rings. It exhibits fungistatic properties by inhibiting the synthesis of ergosterol and leads to a buildup of its sterol precursors. It interferes with 14-α-demethylase, a cytochrome P450-dependent enzyme, which inhibits the conversion of lanosterol to 14-demethyl lanosterol. Itraconazole oral suspension has a bioavailability of 60% that can be improved if given after a fatty meal [43]. A peak plasma concentration is reached within 4 h, but absorption appears to be dose dependent. Therefore, higher doses allow for higher plasma concentrations [1]. More than 99% of the drug travels bound to plasma proteins. Its lipophilic properties allow it to concentrate in keratinous tissues. Skin concentrations can be several-fold higher than plasma and may persist for up to 3 weeks after discontinuation [44]. In the liver, it is converted to more than 30 inactive metabolites and 1 active metabolite known as hydroxyitraconazole [27]. This compound has a similar pharmacokinetic profile to itraconazole. The terminal half-life for itraconazole is 20–60 h, which al-

Table 4. The recommended dosage and cost of the systemic antifungal agents used in the treatment of tinea capitis

Systemic agents	Recommended dosage for tinea capitis	Available forms/dosages on the market	Estimated cost for generic, USD	Approximate cost to treat tinea capitis in a 20-kg child, USD	Cure rate [50]
Griseofulvin	Microsized: 20–25 mg/kg/day for 6 weeks or more	suspension: 125 mg per 5 mL	164.08 for 300 mL	492	92%
		tablets: 500 mg	285.12 for 30 tablets	427	
	Ultramicrosized: 10–15 mg/kg/day for 6 weeks or more	tablets: 125 mg, 250 mg	220.79 for 30 250-mg tablets	660	
Terbinafine	125.0 mg for 25 kg, 187.5 mg for 25–35 kg, 250.0 mg for 35 kg or more for 4 weeks	tablets: 250 mg	110 for 30 250-mg tablets (as low as USD 4 at select pharmacies)	110	94%
		granules packets: 125 mg, 187.5 mg			
Fluconazole	5–6 mg/kg/day for 3–6 weeks	suspension: 10 mg/mL, 40 mg/mL	82 for 35 mL of fluconazole 40 mg/mL	328	84%
		tablets: 50 mg, 100 mg, 150 mg, 200 mg	437 for 30 150-mg tablets	612	
Itraconazole	3 mg/kg/day for 2–4 weeks	solution: 10 mg/mL	383 for 150 mL	383	86%
	5 mg/kg/day 2–4 weeks	capsule: 100 mg	275 for 30 100-mg capsules	275	

The drug prices were obtained from www.GoodRx.com [98].

lows for once-a-day dosing. In contrast to griseofulvin and terbinafine, most of the drug and its metabolites are excreted in feces, not urine. Therefore, no dose adjustment is needed for patients with renal impairment [45]. It is metabolized in the liver by CYP3A4 and interacts with many clinically important agents such as warfarin, antihistamines, antipsychotics, anxiolytics, digoxin, ciclosporin, and simvastatin.

Despite being the most popular agent for tinea capitis in some European countries, itraconazole is not approved for this indication in the US [29]. However, it is approved for nail onychomycosis [46]. It comes in three formulations: oral solution, capsule, and tablets. The recommended dose for tinea capitis is 5 mg/kg/day (Table 4), and the duration varies based on causative agent: 2–4 weeks for *T. tonsurans* and 4–6 weeks for *M. canis* [1, 16]. For young children, the capsule can be opened or chewed. The recommended dose for oral solution is 3 mg/kg/day due to improved bioavailability. However, there are safety concerns associated with a compound, hydroxypropyl-β-cyclodextrins (CDs), used to enhance solubility in this formulation. In animal models, they have been associated with reports of nephrotoxicity and tumorigenicity, but there is no evidence to support these adverse events in humans [47]. Pulse therapy of one-pulse of 5 mg/kg/day for 1 week with 2 weeks off between the first and second pulses and 3 weeks off between the second and third pulses has also been shown to be effective in treating tinea capitis including infections caused by *M. canis* [48, 49].

According to a systemic review and a meta-analysis, itraconazole and terbinafine are the most effective agents in treating *Trichophyton* infections and have a similar efficacy [16, 40]. A study has found terbinafine for 2 weeks to be superior in treating *T. tonsurans* when compared to 2 weeks of itraconazole (91.1 vs 80%) [50], while in another study, 2 weeks of itraconazole was found to be superior in treating *T. violaceum* than 2 weeks of terbinafine [51]. However, these studies are small and there are no large clinical trials published until this date to compare these two agents, making it inappropriate to conclude. Regarding its use in treating tinea capitis due to *M. canis*, two studies with a total of 270 patients demonstrated a

100% cure rate by week 12 using a dose of 5 mg/kg/day of itraconazole [52, 53]. Most patients were cured within 4–8 weeks of therapy, and an equal efficacy was reported for both capsule and oral formulations [52, 53].

When used to treat tinea capitis, itraconazole is well tolerated and adverse events are uncommon with the majority of them being mild and reversible. The most common reported adverse events were stomach pain, diarrhea, and rash [50–53]. Itraconazole is reported to cause acute liver injury at an incidence rate of 10.4 per 100,000 [54]. Therefore, it is recommended to obtain baseline ALT and AST before initiating treatment [55]. Congestive heart failure and QT prolongation have also been associated with this drug [56]. Therefore, it is contraindicated in patients with preexisting liver and heart disease. Itraconazole is pregnancy category C and can be used in treating terbinafine-resistant cases that are most likely caused by *M. canis*.

Fluconazole

Fluconazole, also known as Diflucan®, is another first-generation triazole and has the same mechanism of action as itraconazole [8]. It has a low molecular weight and is highly water soluble, which helps it achieve an oral bioavailability of more than 90%. It reaches a peak plasma concentration within 1–2 h after an oral dose, and most of it travels unbound to plasma proteins [45]. Contrary to itraconazole, fluconazole bioavailability is not dependent on food intake or gastric pH [1]. It is delivered to the stratum corneum through sweat and by direct diffusion, where it accumulates in concentrations higher than its plasma concentration [57]. It can be detected in hair follicles 4–5 months after a 5-day course of 200 mg/day [58]. It has a terminal half-life of 30 h, which allows for once-a-day dosing. More than 80% of the drug is excreted unchanged in the urine. Therefore, the dose must be adjusted for patients with renal impairment [45]. Like itraconazole, it interacts with CYP3A4 enzymes.

Fluconazole was synthesized in the early 1980s and has been FDA approved for the treatment of cryptococcosis and candidiasis since 1990 in adults and children older than 6 months [55, 59]. It is available in tablets, oral suspension, and parenteral formulations [13]. The recommended daily dose is 5–6 mg/kg/day for 3–6 weeks or 8 mg/kg once weekly for 8–12 weeks [1, 55]. A meta-analysis, found no significant difference in achieving a clinical cure for tinea capitis with once-daily fluconazole when given for 3 weeks versus 6 weeks [40].

A randomized multicenter study of 880 patients with tinea capitis (isolated dermatophytes on culture: *T. tonsurans*: 86% and *M. canis*: 11%) has found no statistical difference between the use of fluconazole or griseofulvin. The mycological cure rates were found to be 44.5, 49.6, and 52.2% for 6 mg/kg fluconazole 3 weeks, 6 mg/kg fluconazole 6 weeks, and 11 mg/kg griseofulvin groups, respectively, with corresponding p values of 0.11, 0.40, and 0.64, respectively [60]. In a study conducted in Israel, fluconazole efficacy was slightly inferior to that of griseofulvin in treating tinea capitis due to *M. canis* and *T. violaceum* [61]. In another comparative study, 6 mg/kg of fluconazole for 2–3 weeks performed slightly inferior to other antifungal agents such as 3–5 mg/kg of terbinafine for 2–3 weeks and 5 mg/kg of itraconazole for 2–3 weeks [50, 62]. The mycological cure rate for *Trichophyton* species was 79.5% with the use of 8 mg/kg/week of fluconazole for 8 weeks and increased to 100% with an additional week of therapy [63].

Fluconazole is generally well tolerated. Gastrointestinal side effects and headaches are the most common adverse events [59]. Rare cases of acute generalized exanthematous pustulosis and toxic epidermal necrolysis have been reported in the literature [64, 65]. Although a clinically insignificant rise in serum aminotransferase is a common finding, the risk of liver injury is much lower and occurs at an incidence rate of 31.6 cases per 10,000 persons [66]. It is recommended to consider obtaining baseline liver and renal function tests before starting fluconazole [55].

Adjuvant Therapy

Selenium sulfide, known also as Selseb®, is a toxic heavy metal salt. It has antifungal properties and an inhibitory effect on the production of keratin in the stratum corneum. In vitro, it demonstrated sporicidal activity to *T. tonsurans*, so it can be used to decrease spore count and transmission [67]. It is available in two different concentrations. Shampoos containing 1% selenium sulfide are affordable and available over the counter, and a 2.25% selenium sulfide shampoo is more expensive and only available via prescription [68]. A study by Givens et al. [69] demonstrated that the 1 and 2.5% preparations of selenium sulfide shampoos are equally effective. Washing hair twice weekly with selenium sulfide along with oral griseofulvin have demonstrated superiority in treating tinea capitis to griseofulvin alone [67, 69]. Unlike systemic antifungals, it is used topically and does not result in a significant systemic absorption [70]. Therefore, it is a

good option for close contacts of infected individuals and asymptomatic carriers [1, 29]. Selenium sulfide is well tolerated in most patients and rarely causes adverse events. Skin irritation with pruritus is the most common side effect. Contact dermatitis confirmed by patch testing has also been reported [71]. Hair discoloration has also been reported, with all cases being reversible within weeks after cessation [68, 72]. Chen et al. [73] have found that 1% selenium sulfide shampoo is equally effective as 1% ciclopirox shampoo when used as an adjunctive treatment for tinea capitis.

Oral ketoconazole has an incidence rate of acute liver injury of 134.1 per 100,000 persons/month [54]. Therefore, it is no longer used as a systemic treatment for tinea capitis. Nevertheless, it is still used as a topical agent for adjuvant therapy. 1 and 2% ketoconazole shampoos, sold under the name Nizoral, are available over the counter for a similar price. Although there are no comparative studies between the two for tinea capitis, the 2% ketoconazole shampoo had demonstrated superiority compared to 1% ketoconazole for dandruff and seborrheic dermatitis [74]. Greer [75] has studied the use of 2% ketoconazole shampoo daily for 8 weeks as a monotherapy for tinea capitis and found a marked reduction in the number of fungal colonies in all patients, with 33% of patients achieving a complete cure. A study on the prophylactic use of 2% ketoconazole shampoo for tinea capitis prevention in a high-risk urban pediatric population did not reduce the incidences of tinea capitis infection [76]. Ketoconazole is well tolerated, with less than 1% of patients experiencing irritation and an increase in normal hair loss. Rare cases of contact dermatitis due to ketoconazole shampoo use has been reported [77].

Other Agents

Ciclopirox is a member of the hydroxypyridones class and is used as topical antimycotic agent. It has a high affinity for trivalent metal cations, which allow it to inhibit the metal-dependent enzymes that degrade peroxides within the fungal cell [78]. It is only available as 1% ciclopirox shampoo and requires a prescription. It is more expensive than 1% ketoconazole and 1% selenium sulfide. A comparative double-blinded study has shown it to be an effective adjuvant agent against tinea capitis when used twice a week, with a comparable efficacy to selenium sulfide [73]. Skin irritation is the most common side effect and occurs in less than 5% of patients. Rare cases of contact dermatitis have been reported [78].

Povidone-iodine has antifungal properties by damaging the plasma membrane [79]. Neil et al. [80] studied the use of povidone-iodine shampoo twice weekly for the control of carrier state of tinea capitis and compared it to other antifungal shampoos and a control shampoo with no antifungal properties. Up to 94% of patients had negative cultures at 4 weeks. In addition, it performed superiorly to selenium sulfide, ecoazole, and Johnson's baby shampoo, with their response rate at about 50% [80]. It is affordable and available over the counter, but it has staining properties that make it inconvenient to use. Lastly, zinc pyrithione shampoos have antifungal activity that is similar to 2.5% selenium sulfide in vitro [81]. However, there are no clinical studies on its use for tinea capitis.

Conclusion

In general, the causative organism of tinea capitis should be considered when choosing the appropriate therapy. In the US, most infections are caused by *T. tonsurans*. Therefore, unless the clinician is concerned for *M. canis* due to ectothrix pattern, yellow-green fluorescents on Wood's lamp exam, and/or exposure to infected animals, terbinafine might be used as first-line therapy. It has demonstrated superiority to griseofulvin in terms of efficacy, cost, and shorter duration of treatment, with similar adverse events rate and tolerability. Terbinafine should not be the first-line agent for tinea capitis due to *M. canis*. A large, randomized, controlled study of griseofulvin versus itraconazole versus fluconazole is needed to determine the best agent to treat tinea capitis due to *M. canis* and *T. tonsurans*. However, this might not be feasible in the US since these organisms are exceedingly rare. Therefore, the clinician must tailor the treatment based on patients' specific needs such as drug availability, duration of treatment, safety profile, and convenience, given that all three are reasonable options.

Disclosure Statement

Dr. Elewski is an investigator for Abbvie, Boehringer Ingelheim, Celgene, Incyte, Leo, Lilly, Merck, Novartis, Pfizer, Regeneron, Sun, and Valeant, and a Consultant for Boehringer Ingelheim, Celgene, Leo, Lilly, Novartis, Pfizer, Sun, and Valeant. Dr. Cantrell has no relevant conflict of interest to this publication. Ms. Alkeswani has no conflict of interest.

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