Current Trends in the Use of Two Combination Antifungal/Corticosteroid Creams

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Superficial fungal infections are among the most commonly managed skin problems by general practitioners. Although evidence shows combination antifungal/corticosteroid topicals are more expensive and less effective than single-agent antifungals, practitioners continue to prescribe combination agents. We examined current prescription trends of 2 combination antifungal/corticosteroid medications, Lotrisone and Mycolog-II. *(J Pediatr 2017;186:192-5).*

In the late 1990s and early 2000s, several investigators reported an increase in use of prescription combination medications for the management of cutaneous fungal infections. These studies also highlighted the increased rate of harmful side effects associated with combination agents, suggesting that many nondermatologists may have an incomplete understanding of the potent corticosteroid elements. To date, there are 2 topical products commonly used: Lotrisone (Merck & Co, Inc, Whitehouse Station, New Jersey) and Mycolog-II (Bristol-Myers Squibb Co, New York, New York), of which Mycolog II recently has been discontinued. Lotrisone is a combination product composed of a high-potency topical corticosteroid, betamethasone dipropionate 0.05% cream, and a topical antifungal agent, clotrimazole 1% cream. This combination drug is approved by the US Food and Drug Administration (FDA) for topical use only, currently is not recommended for use in patients younger than 17 years of age, and is not recommended for use in cases of diaper dermatitis.[1]

Despite recommendation against its use, Lotrisone frequently is prescribed for diaper dermatitis by practitioners across multiple specialties, including pediatrics, family medicine, and dermatology. In 1999, Smith et al[2] showed that nondermatologists were more likely than dermatologists to prescribe the antifungal/corticosteroid combination agent than they were to prescribe a single-agent antifungal topical. In 2002, Railan et al[3] showed that pediatricians were not only likely to prescribe Lotrisone for extended periods longer than the 2 weeks recommended but also were not aware of the implications of the high-potency corticosteroid component. A year later, Alston et al[4] showed that physicians frequently used Lotrisone for tinea corporis or tinea faciei in children younger than the then-recommended age of 12 years and for longer than a 2-week period, resulting in recurrent and persistent infections.

Mycolog-II is a combination antifungal/corticosteroid consisting of nystatin, an antiyeast agent, and triamcinolone, a medium-potency topical steroid. Although it initially was available as a cream and ointment, both forms have since been discontinued. It was approved by the FDA for the treatment of cutaneous candidiasis and showed greater benefit than nystatin alone during the first few days of treatment. Studies showed that although Mycolog-II was well tolerated, it triggered adverse reactions caused by its corticosteroid component, similar to Lotrisone. Unlike Lotrisone, however, there were no publications advising against its use in the pediatric population; however, the FDA did recommend limiting use to the "least amount compatible with an effective therapeutic regimen."[5]

In this study, we examine the 8-year prescription trends for use of Mycolog-II and Lotrisone from 2007 through 2014. Our data suggest that pediatric and family medicine physicians continued to prescribe both combination agents for cutaneous fungal infections. Moreover, we show that even after publication of FDA regulations recommending against the use of Lotrisone cream in children and for diaper dermatitis, there was an upward trend in the rate of prescribing both creams from 2007 until 2014.

Methods

Data were collected with the Humana database, a large claims-based database encompassing 20 000 000 patient records. Of 20 000 000, we identified 9797 children aged 0-14 years who were prescribed either Mycolog-II or Lotrisone creams by pediatricians, family medicine physicians, and pediatric dermatologists from January 2007 to December 2014. These specialties were chosen with the presumption that they were most likely to evaluate and treat skin conditions in patients of this age group.

Results

A total of 9797 patients between ages 0 and 14 years were prescribed either Mycolog-II and Lotrisone creams from 2007 through 2014 by family medicine, general dermatology, pediatric dermatology, or pediatrics. The most frequently associated diagnoses are listed in **Table I** (available at www.jpeds.com) in descending order of frequency. These include diaper or napkin rash, contact dermatitis, rash and nonspecific skin eruption, and dermatophytosis of the body.

FDA Food and Drug Administration

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The authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2017.03.031

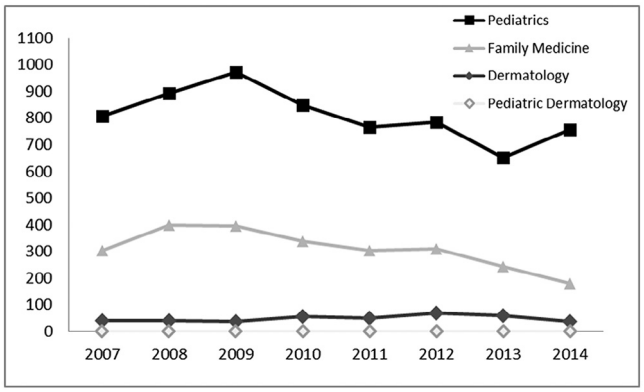

Figure. The total number of patients prescribed Mycolog-II or Lotrisone from 2007 to 2014 by pediatricians, family medicine physicians, dermatologists, and pediatric dermatologists. Analysis of Humana database provided by Galderma Laboratories, L.P.

The frequency with which these medications were prescribed was plotted as a function of time from 2007 to 2014 (**Figure**). Pediatricians, followed by family medicine physicians, were the most frequent prescribers of the cream. For pediatricians, there was a general downward trend in frequency of prescriptions written from 2009 through 2012, with a slight increase in trend in 2013 through 2014. Family medicine physicians were less likely to use the combination agents compared with pediatricians. Family medicine physicians have demonstrated a continuous downward trend in the frequency of prescribing these agents since 2008. In 2013, pediatricians demonstrated an upward trend in the frequency of prescribing these creams. There were no complete data on the frequency of prescribing these creams in 2015, and marketing of Mycolog-II was discontinued in 2015. Dermatologists were less likely to prescribe these creams compared with all specialties. We noted that pediatric dermatologists did not prescribe either combination agent.

A one-way ANOVA test was conducted to determine whether there was a statistically significant difference in the mean number of patients being prescribed Lotrisone and Mycolog-II among different specialties (**Table II**). Data were classified into 3 groups: pediatrics (n = 8), family medicine (n = 8), and dermatology (n = 8). We concluded that there was a statistically significant difference between specialties as determined by one-way ANOVA test ($F [2, 21] = 242.39$, $P < .001$). We then performed a Tukey post-hoc test to help compare the mean between paired specialties including pediatrics to dermatology, family medicine to dermatology, and pediatrics to family medicine. The test revealed that there was in fact significant differences between specialties prescribing Lotrisone and Mycolog-II. The mean was statistically significantly greater among pediatricians compared with dermatologists (760.5 ± 35.1, $P < .001$), pediatricians compared with family medicine physicians (500.5 ± 35.1, $P < .001$), and family medicine physicians compared with dermatologists (260 ± 35.1, $P < .001$).

Discussion

Superficial fungal infections and dermatitis (including atopic dermatitis, contact dermatitis, seborrheic dermatitis, and other noninfectious dermatitides) are 2 of the most common skin conditions managed by pediatric and family medicine practitioners in the US.[6] Both conditions manifest with erythematous scaly and sometimes inflammatory eruptions and must be differentiated clinically to guide proper treatment. Topical antifungal agents are useful in treating a fungal infection, whereas topical corticosteroids are indicated for an inflammatory dermatitis. There are times, however, when a fungal infection induces an inflammatory dermatitis. It is in these cases that the use of both agents with careful monitoring is of benefit to the patient.

Table II. A one-way ANOVA and Tukey post-hoc tests were conducted to determine whether there were differences between specialties in prescription of the creams

	Summary of total number of patients prescribed Lotrisone and Mycolog-II			
Specialties	**Mean**	**SD**		
Pediatrics	809.5	96.91528		
Family medicine	309	72.56130		
Dermatology	49	11.64965		
One-way ANOVA tests				
	SS	**df**	**MS**	**F, Prob. > F**
Between groups	2 390 561.33	2	1 195 280.67	242.39, $P < .001$
Within groups	103 554	21	4931.14	
Tukey post-hoc tests				
	Contrast	**SE**	**t, $P >$ |t|**	**95% CI**
Pediatrics-dermatology	760.5	35.11105	21.66, $P < .001$	672.0001-848.9999
Family medicine-dermatology	260	35.11105	7.41, $P < .001$	171 5001-348.4999
Pediatric-family medicine	500.5	35.11105	14.25, $P < .001$	412.0001-588.9999

df, degree of freedom; *MS*, mean square; *Prob.*, probability; *SS*, sum of squares; *t*, t-value from t-test.
Analysis by Galderma Laboratories, L.P. of Humana's database.