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Frequency of dramatic price increases for topical medications, 2014-2018

To the Editor: Topical medications are a ubiquitous treatment in dermatology. Although the average prices of generic topical medications have been declining, dramatic price increases have been identified as an issue affecting patient access to care.[1,2] The US Government Accountability Office has estimated that almost half of these increases have affected dermatologic drugs.[3] Decreased competition and supply shortages have been suggested as reasons for fluctuation, but little is known about whether the frequency of price increases is changing over time.[4]

To evaluate trends in dramatic price increases of more than 100% for topical medications, we performed cross-sectional and longitudinal analysis of National Average Drug Acquisition Cost data from the Medicaid Pharmacy Pricing database from January 1, 2014, through December 19, 2018. This data set is maintained by the Centers for Medicare and Medicaid Services (CMS) and accounts for manufacturer-to-pharmacy discounts, which provides a more accurate estimate of true drug costs. However, the National Average Drug Acquisition Cost data are not able to account for negotiations between drug manufacturers and pharmaceutical benefit managers.

The present study was deemed exempt from obtaining institutional review board approval by the University of Pennsylvania institutional review board because all data are publicly available and deidentified. Statistical analyses were performed with Stata/IC, version 14.2 (StataCorp, College Station, TX). The frequency of price increases of more than 100% was recorded and stratified by drug class, whether the medication was branded or generic, and reporting year. To account for differences in the number of medications in each drug class, we compared the mean number of price increases of more than 100% per medication in each category (Fig 1) and the magnitude of these price increases (Fig 2).

Drug classes (percentage of price reports) included topical corticosteroids (TCS) (28.6%), antifungals (19.8%), treatments for acne/rosacea (11.4%), antibiotics (7.0%), retinoids (7.0%), antineoplastics (4.1%), emollients (2.3%), calcineurin inhibitors (1.6%), antivirals (1.1%), antiparasitics (1.0%), and other miscellaneous medications (16.2%). Overall, 60.6% of price reports were for generic medications.

Overall among branded medications, TCS, antineoplastics, and retinoids accounted for the most frequent price increases per medication in each class (0.37, 0.13, and 0.08 during the study period, respectively). Among generics, antineoplastics, retinoids, and TCS had the most price increases (0.08, 0.08, and 0.06 increases per medication during the study period, respectively). Frequency of price increases was associated with drug class for branded and all medications (chi-square test, $P < .001$ for both) but not generic medications ($P = .54$). Moreover, for branded, generic, and all medications, frequency of price increases trended down from 2014 through 2018 (chi-square test for trend, $P = .002$, .021, and .002, respectively).

Among branded medications, antineoplastics showed the highest median price changes for a 30-g supply ($878.96), followed by antifungals ($128.66) and antibiotics ($114.95). For generics, the largest mean (interquartile range) price increases were among antineoplastics ($156.36 [$64.78-$195.30]), retinoids ($54.36 [$47.74-$56.14]), and TCS ($33.46 [$6.83-$71.18]).

These data suggest that dramatic price increases for topical medications are decreasing, although true prices are difficult to measure because of factors such as pharmacy benefit manager rebates to payers. This reduced frequency of price increases may be related to antitrust litigation by the US Department of Justice against collusion and scrutiny

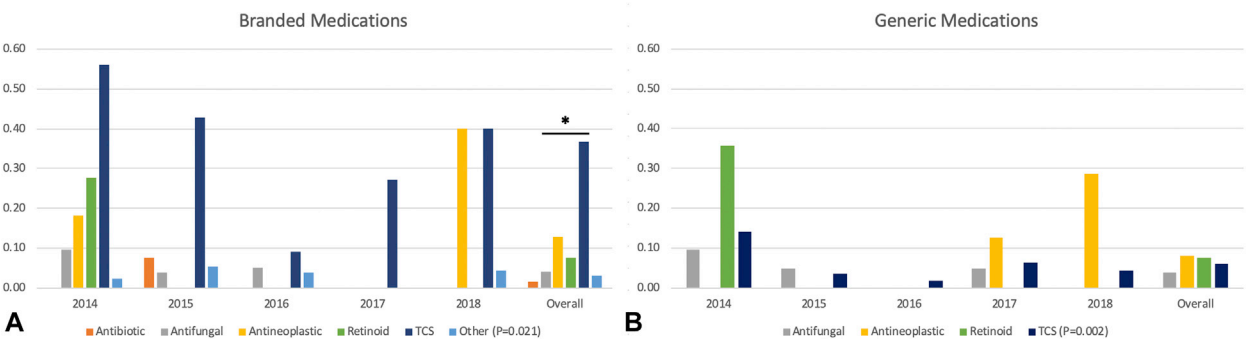

Fig 1. Frequency of annual price increases of more than 100%, 2014-2018. Shown are the frequencies of price increases of more than 100% per medication in each class plotted versus reporting year. Results are stratified by drug class and (**A**) branded versus (**B**) generic. *P* values corresponding to chi-squared test of independence between reporting year and price increase of more than 100% are shown in the figure key. *Statistical significance of chi-squared test of independence between drug class and frequency of price increase of more than 100%. *TCS*, Topical corticosteroids.

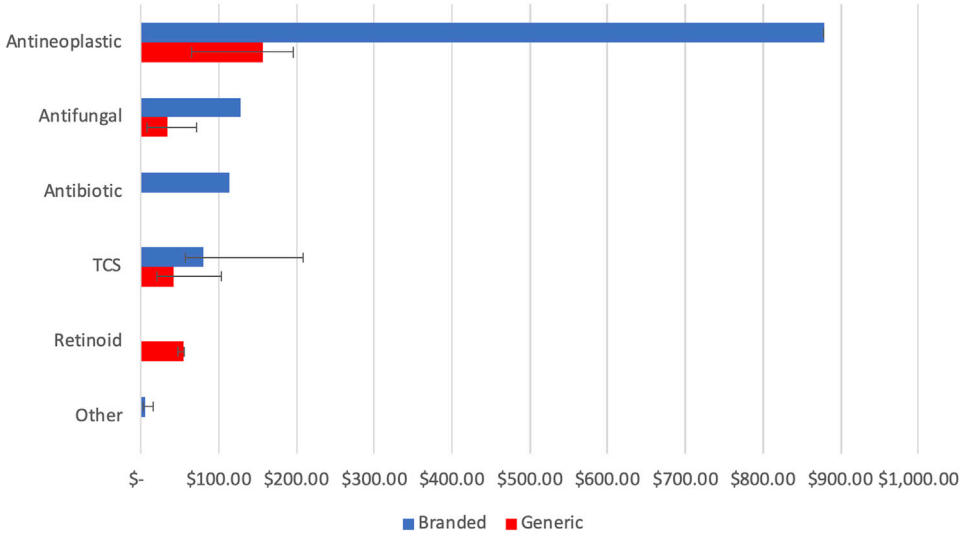

Fig 2. Median price increase per 30-g supply. Shown are median price increases of more than 100% per medication in 2019 US dollars, with error bars denoting interquartile range. Values represent price per gram scaled to a 30-g supply of topical medication. Results are further stratified by medication class and branded versus generic. Branded antineoplastic, antifungal, and antibiotic medications had only 1 price increase of more than 100%, so no interquartile range is reported for those categories. *TCS*, Topical corticosteroids.

of the pharmaceutical industry on Capitol Hill. Growing public awareness of this issue may also be influencing pharmaceutical manufacturer behavior.[5] However, prices for many generic topical medications remain high, and dramatic price increases continue to occur. In addition, many of these price increases resulted in substantial increases in the medication price. Physicians and policymakers must remain vigilant to ensure patient access to topical medications.

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Increased risk of alopecia areata for people with hidradenitis suppurativa in a cross-sectional study

To the Editor: Hidradenitis suppurativa (HS) is a chronic inflammatory disease with hair follicle abnormalities and associations with autoimmune and inflammatory diseases[1]; alopecia areata (AA) is an autoimmune disorder of the hair follicle.[2] Because both disorders involve hair follicles, understanding the relationship between these 2 diseases may help elucidate the pathogenesis of each. In a Korean study, AA was more common in patients with HS than in patients without HS (adjusted odds ratio, 1.35).[3] Because HS is distinctly different in the Asian population, we investigated the relationship between HS and AA in a US sample.

A cross-sectional study was performed by using the MarketScan Commercial Claims database (Truven Health Analytics, Ann Arbor, MI). No institutional review board approval was needed. Inclusion criteria were age 12 years and older with continuous enrollment for the period of January 1, 2005, through December 31, 2014. The HS group included individuals with 2 separate HS-related claims in an 18-month period. A control group was created by randomly selecting individuals (10:1) who were never diagnosed with HS, pilonidal cyst, acne conglobata, or dissecting scalp cellulitis over the same interval after matching for age and sex. Risk ratios (RRs) were investigated for any alopecia and then specifically for AA and lichen planopilaris. Potential confounding factors, including hypothyroidism and Down syndrome, were identified and included in the chi-squared tests. RRs and confidence intervals were calculated by using Altman's methods and significance was set at P of .05 or less.

Table I. Characteristics of the study groups

Patient characteristics	HS group (n = 3 645)	Control group (n = 36 450)
Age, mean ± SD	34.4 ± 14.2	36.8 ± 13.4
Female sex, n (%)	2789 (76.52)	27 294 (74.88)
Urban/suburban, n (%)	3064 (84.07)	29 783 (81.71)
Region, n (%)		
Northeast	382 (10.48)	4312 (11.83)
North Central	862 (23.65)	9386 (25.75)
South	2148 (58.93)	19 041 (52.24)
West	232 (6.36)	3273 (8.98)
Unknown	21 (0.58)	437 (1.20)

SD, Standard deviation.

A total of 40 095 patients were identified: 3645 patients with HS and 36 450 matched control individuals (Table I). When compared with the control group, the HS group had significantly higher risk of any AA (RR = 2.22) including alopecia totalis or universalis (RR = 2.17) (Table II). We also identified an increased risk of lichen planopilaris (RR = 1.54). HS was also associated with hypothyroidism (RR = 1.17) and Down syndrome (RR = 11.46); however, after controlling for these potential confounding factors, the relative risk for AA was still elevated (RR = 2.09; 95% confidence interval, 1.69-3.20; $P < .001$). The findings of this study are limited by a lack of clinical outcome data, temporal association, and detection bias for skin conditions.

Our findings are consistent with those of Lee et al[3] and showed an increased risk of AA in a US-based HS sample. As currently understood, AA is caused by the loss of immune privilege at the hair follicle either because of local hair follicle epithelium disruption or a dysregulated immune response.[2] HS pathogenesis involves hair follicle disruption and a sustained dysregulated immune response.[4] Both AA and HS likely involve an inciting event at the hair follicle that leads to subsequent inflammation. In support of this hypothesis, the lesions of patients with HS and AA have considerable overlap in the expression of key inflammatory cytokines, including tumor necrosis