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Intralesional Treatment With 5-Fluorouracil and Steroid Improves Allergic Contact Dermatitis Without Causing Skin Atrophy and Rebound Lesions

To the Editor:

Intralesional triamcinolone acetonide (TA) injections can rapidly and effectively treat severe localized dermatitis. However, these treatments are associated with adverse effects such as dermal atrophy, hypopigmentation, capillary dilation, and Cushing syndrome.[1,2] These adverse effects may be attributable, in part, to the large doses of TA required to obtain the desired outcome.[3] The combination of 5-fluorouracil (5-FU) and TA has been shown to be superior to TA monotherapy in patients with keloids and hypertrophic scars.[4] Furthermore, combination therapy reduces the required dosage of both drugs. However, limited data are available on the use of intralesional TA injections along with 5-FU for the treatment of allergic contact dermatitis (ACD).

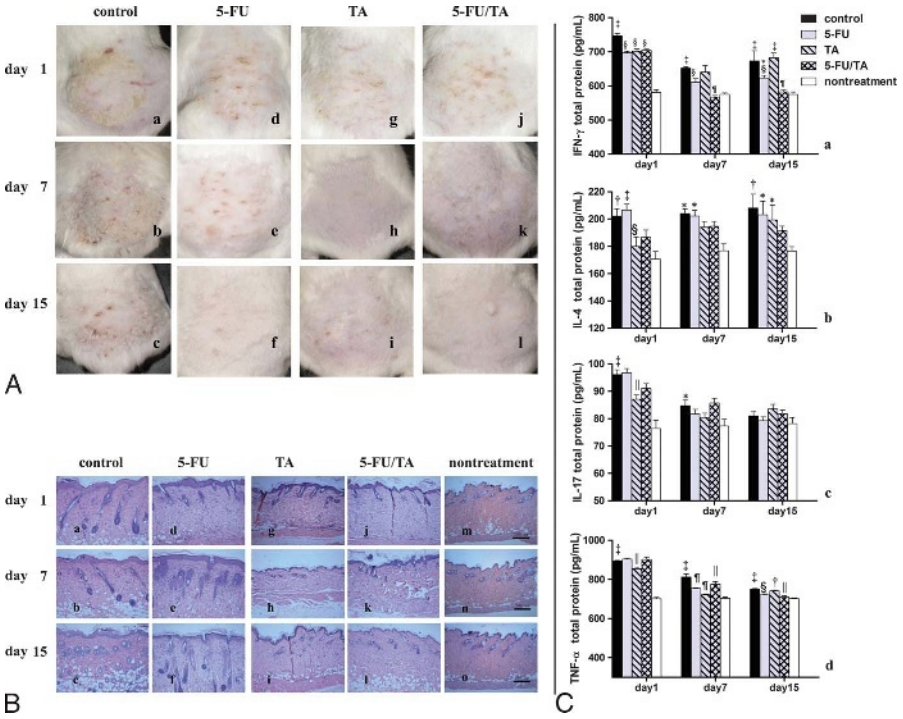

FIGURE 1. A, Changes in the skin lesions on day 1 (a, d, g, j), day 7 (b, e, h, k), and day 15 (c, f, i, l), as seen by the naked eye. B, Hematoxylin-eosin–stained sections of the skin samples obtained on day 1 (a, d, g, j, m), day 7 (b, e, h, k, n), and day 15 (c, f, i, l, o). Scale bar = 200 μm. C, Changes in the serum levels of (a) IFN-γ, (b) IL-4, (c) IL-17, and (d) TNF-α in the study groups at different time points. Cytokine levels are measured in picograms per milligram of total protein. Data are expressed as mean (SEM, n = 3). *$P < 0.05$, †$P < 0.01$, ‡$P < 0.001$ versus nontreatment group. §$P < 0.05$, ||$P < 0.01$, ¶$P < 0.001$ versus control group.

We therefore examined the effects of 5-FU plus TA on 2,4-dinitrofluorobenzene–induced ACD in BALB/c mice. In our study, ACD mice were randomly allocated to the following 4 groups (9 mice per group): ACD control group, 5-FU group, TA group, and 5-FU/TA group. The mice in the 5-FU, TA, and 5-FU/TA groups received intralesional injections of 1 mg 5-FU, 0.4 mg TA, and a mixture of 0.5 mg 5-FU + 0.2 mg TA, respectively. The control group received intralesional injections of 1 mL normal saline. Another 9 healthy mice were assigned to a nontreatment group and left untreated. We analyzed the clinical and histopathological features in all groups and measured the serum cytokine levels (interleukin [IL] 4, interferon γ, tumor necrosis factor [TNF] α, and IL-17) at different time points (1, 7, and 15 days after treatment).

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Intralesional injection of 0.4 mg TA alone showed significant anti-inflammatory activity but also led to obvious skin atrophy and a rebound phenomenon. In contrast, both combined therapy with half-dose 5-FU and TA and treatment with TA alone reduced lesion severity (Fig. 1). This finding is in line with our previously published clinical results.[5] This effect was also supported by the results of the histopathological analysis. The intralesional injection of 0.4 mg TA inhibited the increase in epidermal thickness and capillary caliber within 7 days, but a rebound phenomenon was observed on day 15. The administration of 1 mg 5-FU significantly decreased epidermal thickness at a later time point and decreased the capillary caliber and increased the skin thickness at all time points, as compared with TA treatment. In addition, the serum cytokine measurements showed that the 5-FU–mediated inhibition of TNF-α was persistent, and the combination of TA with 5-FU could offset the weakened inhibition of TNF-α by TA alone at later stages.

In conclusion, our experiment revealed the effects of TA alone, 5-FU alone, and 5-FU/TA in a mouse model of 2,4-dinitrofluorobenzene–induced ACD. The intralesional injection of TA alone reduced inflammatory reaction and cytokine levels in the early stage but induced significant skin atrophy, rebound lesions, and elevated cytokine levels in later stages. Our results give an insight into the potential advantages of combined treatments with low-dose 5-FU/TA. Such a treatment may improve inflammatory lesions without producing skin atrophy or rebound lesions and could lower serum TNF-α and IFN-γ levels in vivo.

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Unreported Sources of Nickel Exposure in Community-Based Facilities Frequented by Children

To the Editor:

Globally, nickel is the leading cause of allergic contact dermatitis (ACD). Nickel is ubiquitous, and the published literature continues to index items most frequently associated with Ni-ACD. Unregulated nickel exposure in North America is evidenced by the significant sensitization rates seen in patch-tested cohorts, 28.1% in children (ages 0–18 years) and 18.5% in adults.[1,2]

Conservative estimates of ACD within the pediatric population suggest at least 1 million cases in the United States yearly, with roughly a quarter of those cases due to nickel.[2,3] The United States could potentially save US $5.7 billion annually in healthcare costs, extrapolating current cost-saving data from Denmark post nickel regulation, by implementing a similar regulation to that of the European Union (EU).[2]

To our knowledge, site survey testing for items releasing nickel in public locations has yet to be performed. Using the dimethylglyoxime (DMG) spot test, we sought to confirm the

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