ORIGINAL ARTICLE

A systematic review of safety and efficacy of systemic corticosteroids in atopic dermatitis

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Background: Systemic corticosteroids are often used to treat atopic dermatitis (AD). However, few studies have assessed the safety and efficacy of systemic corticosteroids in AD.

Objective: To systematically review the literature on efficacy and safety of systemic corticosteroid use (oral, intramuscular, and intravenous) in AD.

Methods: PubMed, Embase, Medline, Scopus, Web of Science, and Cochrane Library were searched. We included systematic reviews, guidelines, and treatment reviews of systemic corticosteroid use among patients of all ages with a diagnosis of AD (52 reviews and 12 studies).

Results: There was general consensus in the literature to limit the use of systemic steroids to short courses as a bridge to steroid-sparing therapies. Systemic side effects include growth suppression in children, osteoporosis, osteonecrosis, adrenal insufficiency, Cushing syndrome, hypertension, glucose intolerance, diabetes, gastritis, gastroesophageal reflux, peptic ulcer disease, weight gain, emotional lability, behavioral changes, opportunistic infections, cataracts, glaucoma, myopathy, myalgia, dysaesthesia, pseudotumor cerebri, hyperlipidemia, malignancy, thrombosis, skin atrophy, sleep disturbance, and rebound flaring.

Limitations: Baseline clinical severity, corticosteroid delivery and dose, and treatment response were reported incompletely and heterogeneously across studies.

Conclusions: Evidence is not strong enough to determine optimal delivery or duration of systemic corticosteroids in AD. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2017.09.074.)

Key words: adrenal insufficiency; atopic dermatitis; atopic eczema; corticosteroids; eczema; intramuscular; intravenous; oral; rebound flaring; systemic side effects.

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Dr Silverberg had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis, as well as for the study concept and design. Drs Yu and Silverberg take responsibility for acquisition of data and for drafting of the manuscript. Drs Yu, Drucker, Lebwohl, and Silverberg take responsibility for analysis and interpretation of the data, as well as for critical revision of the manuscript for important intellectual content.

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The American Academy of Dermatology guidelines for treatment of atopic dermatitis (AD) recommend a graded approach, beginning with skin care and trigger avoidance.[1] In mild-to-moderate AD, topical corticosteroids or calcineurin inhibitors and antiseptic measures are appropriate. Systemic therapy is recommended for persistent, moderate-to-severe AD after inadequate response to optimized topical management.[2]

A wide range of treatment strategies have been used for systemic corticosteroids (SCSs) in clinical practice (eg, different deliveries, dosing, frequencies, and durations). SCSs are commonly used as a first-line systemic treatment of AD,[3,4] typically in short courses to suppress AD activity and interrupt flares.[5]

SCSs may be a useful treatment of AD flares owing to their rapid induction of a clinical response, perceived short-term safety and tolerability, and low cost.[6] However, few studies have assessed the efficacy and safety of SCSs in AD. This systematic review sought to summarize the available evidence for using SCSs in AD.

CAPSULE SUMMARY

- Systemic corticosteroids are often used to treat atopic dermatitis, but their safety and efficacy has not been systematically reviewed.
- Most data supporting the efficacy of systemic corticosteroids are anecdotal.
- Because of significant side effects, including rebound flaring, use of systemic corticosteroids should be limited to short courses as a bridge to steroid-sparing therapies.

METHODS

Literature search

The following databases were searched through December 18, 2016: PubMed (1946- present), Embase (1947-present), MEDLINE, Scopus (1823-present), Web of Science, and Cochrane Library (1992-present). The search strategy was based on a previous Cochrane review for AD,[7] with inclusion of additional search terms related to steroid use (Supplemental Table I; available at http://www.jaad.org).

Systematic reviews, guideline statements, and treatment recommendation reviews that were published in English online, available in print, or in press were eligible for inclusion. Manuscripts were excluded on the basis of title and/or abstract review if there was no clear indication that either efficacy or adverse effects (AEs) of SCSs (oral, intramuscular [IM], or intravenous) was discussed. Studies cited in the reviews with primary data on the use and/or AEs of SCSs in AD were also reviewed.

Data extraction

S.Y. performed title/abstract review and data extraction. First author; publication year; study design; dosing and route of SCS administration; number of patients in the study; and information on efficacy, tolerability, and AEs were collected.

RESULTS

Literature search

The literature search yielded 2219 nonduplicate articles. After title and abstract review, 2147 articles were excluded; 52 reviews and 12 studies were included (Supplemental Fig 1; available at http://www.jaad.org).

Efficacy

Oral. There was a general consensus that SCSs quickly and effectively decrease clinical symptoms of AD, especially pruritus (Supplemental Table II; available at http://www.jaad.org).[5] Most data supporting use of SCSs were anecdotal, with little primary data. A case series presented 3 patients who achieved good disease control with oral corticosteroids.[8] These authors recommended use of long-term SCSs in refractory AD, especially in patients with profound psychosocial consequences. A retrospective study showed that 84.2% of patients ranked SCSs as "very successful" treatment of their AD.[9] Despite widespread use of SCSs, few randomized controlled clinical trials (RCTs) were conducted.

A double-blind, placebo-controlled, crossover RCT was performed; 4 weeks of combined oral and nasal beclomethasone dipropionate (BDP), a synthetic glucocorticoid, was compared with placebo in 26 children with severe AD. BDP resulted in a 22% decrease in mean AD severity using an unvalidated outcome, lower parent-assessed overall disease activity, and greater treatment preference toward BDP.[10,11] Oral BDP, 600 μg 3 times daily for 4 weeks followed by 1000 μg daily for 6 weeks, improved disease activity in 14 of 15 children with severe AD after 4 weeks.[12] However, 4 children failed to maintain treatment response once the BDP was tapered.

Flunisolide, a synthetic steroid analogue, was orally administered to 20 children (640 μg/d in children age <3 years and 1200 μg/d in older children) and resulted in a 49% reduction of clinical severity scores versus those with placebo after 2 weeks.[10,13] After the crossover portion at week 3,