

## Juvenile Arthritis

## Systemic adverse events following intraarticular corticosteroid injections for the treatment of juvenile idiopathic arthritis: Two patients with dermatologic adverse events and review of the literature

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## ABSTRACT

**Objectives:** Intraarticular corticosteroid injections are an important part of the treatment for juvenile idiopathic arthritis due to the ability to achieve high concentration of the medication in the affected joint, while minimizing potential systemic adverse effects. There may be some systemic absorption of corticosteroids resulting in systemic adverse events. Our aim was to demonstrate the potential of adverse events due to the systemic absorption of intraarticular corticosteroids through presentation of 2 case reports, a review of our practices and a systematic review of the literature.

**Methods:** We reviewed the intraarticular injections performed at our 3 centers in 2010 and 2011 for the prevalence of systemic adverse events. We searched PubMed for articles in English on systemic adverse effects of intraarticular corticosteroid injection in children, using numerous keywords, as well as review articles and textbooks on juvenile rheumatoid/idiopathic arthritis up to and including December 2011.

**Results:** We report the development of severe acneiform rashes in 2 adolescents with juvenile idiopathic arthritis following bilateral knee intraarticular injections of triamcinolone hexacetonide. The prevalence of systemic adverse events at our centers was in 4/179 (2.2%) injections, the 2 cases reported above, 1 case of insomnia in a 2-year-old child and 1 case of cushingoid features following injection of 21 joints. While in the literature there are some reports of general "Cushing-like" appearances, there are only very few reports of specific skin and other organ/system adverse effects resulting from systemic corticosteroid absorption.

**Conclusion:** It is important to recognize the potential of rare adverse events that are attributable to the systemic absorption of intraarticular corticosteroids in children.

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Since the 1980s, the use of intraarticular corticosteroids injections has become an important part of the treatment regimen for juvenile idiopathic arthritis (JIA), particularly in children with oligoarthritis [1]. Intraarticular injections with high-dose corticosteroids are effective locally, while minimizing systemic absorption and the risk of systemic adverse effects. There are several intraarticular formulations of corticosteroids, with differences in half-life and other pharmacokinetic and pharmacodynamic properties. Triamcinolone hexacetonide (THA) is the corticosteroid recommended by the American College of Rheumatology for the treatment of JIA, since controlled studies have shown that it produces significantly longer duration of response than other corticosteroid preparations [1–3]. Local adverse events of THA, mainly at the injection site, subcutaneous lipoatrophy,

pigmentary changes, and intraarticular/periarticular calcifications are well described, occurring in 1%–8.3% of injections [4–7].

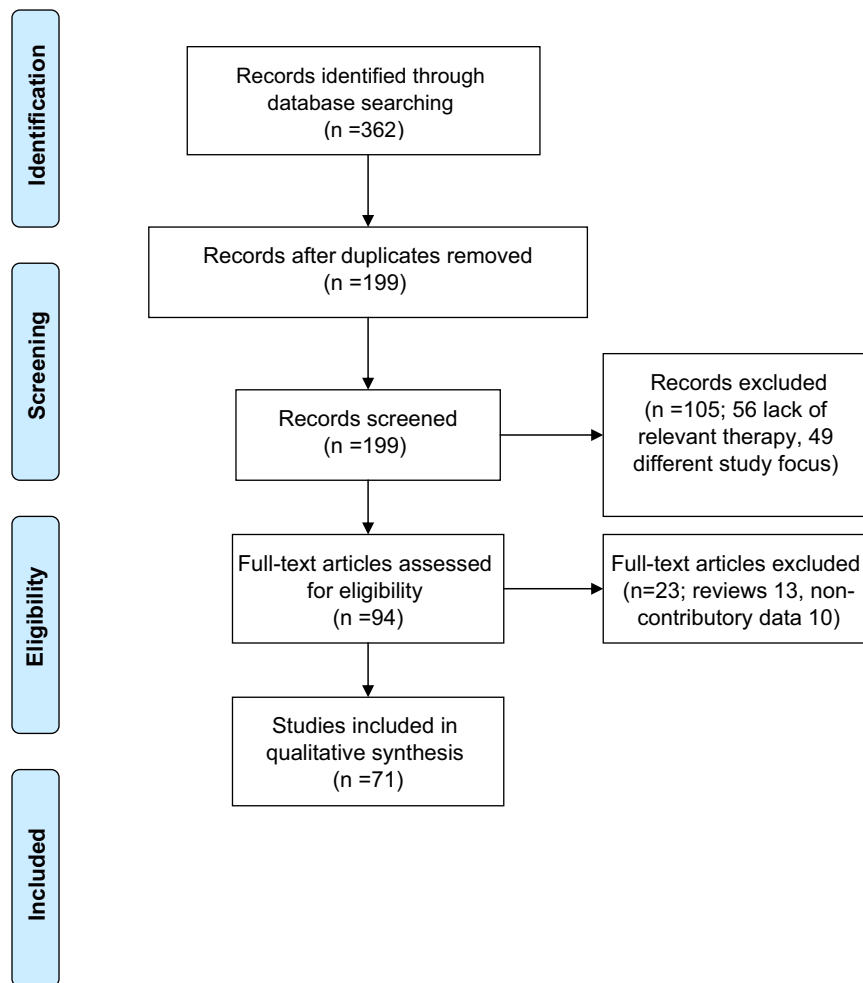
There is some systemic absorption of intraarticular corticosteroids, similar to that described in other modes of regional corticosteroid administration, for example via inhalation or through topical use [8,9]. However, there are only a few reports on systemic adverse effects [3]. We describe 2 patients with JIA who developed severe dermatologic adverse events following intraarticular injections of THA to the knees, and examine the prevalence of systemic adverse events in our practices. We also reviewed the literature on systemic adverse effects of intraarticular corticosteroid injections in children.

### Methods

We retrospectively examined the prevalence of systemic adverse events of intraarticular corticosteroid injections administered

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**Fig. 1.** PRISMA flow diagram of literature search for systemic adverse effects of intraarticular corticosteroid injection for JIA.

in 2010 and 2011 at our 3 centers (Rainbow Babies and Children's Hospital, Cleveland, OH; Dell Children's Medical Center, Austin, TX; and Shaare Zedek Medical Center, Jerusalem, Israel). Patients were located either by detailed/systematic physician records of intraarticular injection procedures or by cross-linking ICD-9 codes of juvenile arthritis (714.3\*, 696\*, 720.0\*) limited to the age of 18 years, with codes of joint injection procedures (V81.92, V76.96, V99.2). We recorded the age and gender of the patients, JIA subtype, type of corticosteroid, dose and number of joints injected, and local and systemic adverse events. Institutional Board Review approval was obtained for this data collection.

For the literature review of systemic adverse effects related to intraarticular corticosteroid injection in children, we searched PubMed for articles in English using the following search terms— intraarticular, joint injections and steroids, corticosteroids, glucocorticoids, triamcinolone acetonide, triamcinolone hexacetonide, prednisone, prednisolone, methylprednisolone, betamethasone, side effects, adverse effects, JIA, juvenile rheumatoid arthritis, and juvenile chronic arthritis. We also searched the references of review articles and textbooks on juvenile rheumatoid arthritis and JIA, especially on treatment (PRISMA flow diagram Fig. 1).

For the dermatologic adverse effects of corticosteroids we searched PubMed for articles in English using the terms: malassezia and pityrosporum, acne, steroid acne, drug acneiform rash, and eruptions.

We included articles that were published up to and including December 2011.

Photos were published with written parental consent and assent of the patient in compliance with institutional guidelines of the hospital where the patient was seen.

### Case reports

**Case 1:** A 14-year-old Caucasian female developed oligoarthritis JIA in the right ankle at 2 years of age (anti-nuclear antibody and rheumatoid factor tests were both negative). She was treated with an intraarticular injection of THA with a good response and no adverse effects. Arthritis of the left elbow at the age of 4 years and again of the right ankle at the age of 7 years were treated similarly with a good response and no adverse effects. Subsequently, she experienced mild flares of the elbow and ankle that responded to short courses of naproxen. At 12 years of age, she developed arthritis in both knees that did not respond to naproxen. Both knees were aspirated and each was injected with 40 mg of THA. One week following these injections she developed monomorphic facial and axilla cystic inflammatory acne, stria of the proximal thighs and buttocks and dysmenorrhea (Fig. 2a and b). She was treated with adapalene retinoid and clindamycin topical gels with a good, but not complete response, without scarring (Fig. 2c). Dysmenorrhea resolved after 3 months. Her arthritis

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