The infection rate of intralesional triamcinolone and the safety of compounding in dermatology for intradermal and subcutaneous injection: A retrospective medical record review

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Background: Intralesional injection of sterile medications remains a mainstay in dermatology, enabling a tailored, low-cost, in-office therapy. After the 2012 United States outbreak of fungal meningitis from contaminated intrathecally administered corticosteroids, there has been increased regulation of in-office compounding, regardless of the administration route. Studies demonstrating the safety data of in-office corticosteroid compounding for intradermal or subcutaneous use are lacking.

Objective: To assess the incidence of infection caused by compounded in-office intralesional triamcinolone.

Methods: A retrospective medical record review identified patients who received in-office intralesional corticosteroid injections in 2016. Medical documentation within 30 days of injection was reviewed for suspected infection.

Results: The records of 4370 intralesional triamcinolone injections were assessed, of which 2780 (64%) were compounded triamcinolone with bacteriostatic saline. We identified 11 (0.25%) suspected localized infections, with 4 of the 11 in the compounding cohort. Of these, 7 of 11 occurred after injection of an "inflamed cyst." No hospitalizations or deaths occurred. No temporal or locational relationships were identified.

Limitations: This study was limited to 2 academic institutions. A 30-day postinjection time frame was used.

Conclusion: In-office compounding for intralesional dermal and subcutaneous administration is safe when sterile products are used by medical practitioners. There is no increased risk of compounded triamcinolone relative to noncompounded triamcinolone. (J Am Acad Dermatol 2020;83:1044-8.)

Key words: chart; compounding; delivery; dermatologist; dermatology; drug; infection; injection; injections; intradermal; intralesional; medical; professional; rate; retrospective; review; safe; safety; steroid; steroids; subcutaneous; triamcinolone.

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Contamination of injectable drug products has led to increased regulation of compounded medications, affecting all practitioners' ability to perform in-office, tailored treatments. This has increased costs and narrowed options for patients. The 2012 fungal meningitis outbreak, the most noteworthy compounding incident, was secondary to contamination of more than 3000 products by an outsourced compounding pharmacy, the New England Compounding Center. Of the 753 total cases, there were 64 deaths.[1] In response, Congress passed the Drug Quality and Security Act (DQSA) in 2013.[2,3] Title I of the DQSA pertains to drug compounding and gave the United States Food and Drug Administration (FDA) more authority to regulate and monitor compounded drugs. Importantly, the DQSA does not differentiate between low-risk sites (intradermal and subcutaneous) vs medium- or high-risk sites of injections (intra-articular, intrathecal, and intravitreal).

CAPSULE SUMMARY

- Intralesional steroid injections are commonly used in dermatology practice; however, there is little safety data available for these procedures.
- Intralesional, in-office compounded triamcinolone injections were found to have an infection rate of 0.25%, with most of these occurring after injections of "inflamed cysts," with no subsequent hospitalizations or deaths.

In-office compounding of sterile medications for intradermal and subcutaneous injection is integral in dermatology. There is a lack of evidence that this type of compounding poses a significant risk to patients. To our knowledge, from 2006 to 2018, no FDA-issued recalls, market withdrawals, or safety alerts were identified regarding in-office compounding. In comparison, during the same time period, the FDA issued 28 recalls of medications from compounding pharmacies due to a lack of sterility assurance.[4,5]

However, studies are lacking assessing the specific infection rate of in-office subcutaneous or intradermal injection of compounded sterile medications in dermatology. Thus, the purpose of this study was to assess the incidence of infection caused by compounded in-office intralesional triamcinolone with bacteriostatic saline for subcutaneous and intradermal injection.

MATERIALS AND METHODS

The Henry Ford Hospital Institutional Review Board approved the study (protocol approval number 11848). A retrospective medical record review was performed for Henry Ford dermatology patients who received in-office intralesional corticosteroid injections from a dermatologist or dermatology physician's assistant during the period January 1, 2016, to December 31, 2016. Patients were identified using Current Procedural Terminology (American Medical Association, Chicago, IL) code 11900, intralesional injection of triamcinolone. From this cohort, a manual medical record review confirmed documentation of corticosteroid injection by a member of the Department of Dermatology. Four clinic sites in Michigan were included (Detroit, Farmington Hills, Troy, and Dearborn). Subsequently, a separate approval was obtained from the George Washington University Hospital Institutional Review Board, and a retrospective medical record review was performed for George Washington University patients who received in-office intralesional corticosteroid injections from a dermatologist or dermatology physician's assistant during the period January 1, 2017, to December 31, 2017.

The intralesional corticosteroid injection included noncompounded and compounded sterile triamcinolone acetonide. Noncompounded concentrations were 40 mg/mL and 10 mg/mL. Compounding was performed with bacteriostatic saline to achieve a final concentration of 20 mg/mL, 5 mg/mL, or 3.3 mg/mL. All of the triamcinolone and bacteriostatic saline used (at all sites) were multiuse (no single-use triamcinolone and bacteriostatic saline). The time frame between preparation and use had a range of minutes to hours.

Patient details

Medical documentation within 30 days of injection was reviewed for suspected infection. Exclusion criteria consisted of patients at 1 month postoperative and patients receiving oral antibiotics before injection. The patients' medical records were reviewed to obtain demographic data, including age, sex, condition treated, number of lesion(s) injected, injection site(s), amount and concentration of corticosteroid injected, relevant comorbid conditions, and current immunosuppressive medications.

Data indicating an infection within a 30-day post-injection period were collected and included the type of infection, number of days since the corticosteroid injection, intervention(s) prescribed/recommended, relevant workup ordered (eg, imaging, bacterial or fungal culture data, complete blood count with differential), and outcome. There was

Abbreviations used:

DQSA: Drug Quality and Security Act
FDA: Food and Drug Administration

no standard time limit from when the compounded medication was prepared to time of use.

Statistical analysis

A Fisher exact test was used for statistical analysis, with a *P* value for significance set to .05.

RESULTS

A total of 4370 intralesional triamcinolone injections were assessed. The compounded cohort comprised 64% of assessed medical records, as 2780 of 4370 injections were compounded with bacteriostatic saline.

The treated diagnoses included alopecia, scar, keloid, cyst, acne, hypertrophic scar, inflamed cyst, acne keloidalis nuchae, hidradenitis suppurativa, psoriasis, lichen simplex chronicus, lupus, prurigo nodularis, pseudofolliculitis barbae, folliculitis, and pyoderma gangrenosum (Table I). The most common diagnosis treated was alopecia.

Of the 4370 intralesional injections, 11 suspected localized infections (0.25%) were identified, and 7 of the 11 suspected infections occurred after injection of an "inflamed cyst." Of the 11 suspected infections, 4 were in the compounded cohort and 7 were in the noncompounded cohort. The compounded group had an infection rate of 0.14% (4 of 2780 patients), and the noncompounded group had an infection rate of 0.44% (7 of 1590 patients). A Fisher exact test showed a *P* value of .111 between the two groups. Thus, there was no significant difference between the compounded and noncompounded groups. All of the suspected infections within the compounded cohort occurred after injection of an "inflamed cyst" (Table II). In the noncompounded cohort, the other suspected infections occurred in keloid, acne keloidalis nuchae, and follicular entrapment (Table III).

There were no hospitalizations and no deaths. Neither temporal nor locational relationships were identified.

Table I. Injections of intralesional triamcinolone by diagnosis

Diagnosis	Number injected
Alopecia	1394
Keloid	1048
Cyst	288
Acne	224
Hypertrophic scar	179
Inflamed cyst	165
Acne keloidalis nuchae	124
Hidradenitis suppurativa	118
Psoriasis	65
Prurigo nodularis	54
Lichen simplex chronicus	47
Lupus	40
Pseudofolliculitis barbae	16
Folliculitis	12
Pyoderma gangrenosum	11
Other	585

Table II. Suspected infections in noncompounded cohort by diagnosis

Diagnosis	Number of suspected infections
Inflamed cyst	3
Keloid	2
Acne keloidalis nuchae	1
Follicular entrapment	1
Alopecia	0
Acne	0
Cyst	0
Hypertrophic scar	0
Hidradenitis suppurativa	0
Psoriasis	0
Prurigo nodularis	0
Lichen simplex chronicus	0
Lupus	0
Pseudofolliculitis barbae	0
Folliculitis	0
Pyoderma gangrenosum	0
Other	0

DISCUSSION

Compounding of sterile medications is integral in dermatologic practice. This compounding allows physicians to deliver individualized, low-cost therapy in the office. However, there is little evidence regarding the safety of this practice. Regulation of in-office compounding increased after the 2012 fungal meningitis outbreak that led to 64 deaths.[1] This outbreak was traced to an outsourced compounding pharmacy and was not due to in-office compounding.

Studies assessing in-office multiuse vials have reported worldwide contamination rates ranging from 0.4% to 6%, with contaminants including spore-forming bacteria and *Staphylococci*.[6-10] Reports detailing infection after multiuse vials include hepatitis C, *Mycobacterium*, and *Serratia marcescens*.[5,6,11,12]

Table III. Suspected infections in compounded cohort by diagnosis

Diagnosis	Number of suspected infections
Inflamed cyst	4
Keloid	0
Cyst	0
Acne	0
Hypertrophic scar	0
Alopecia	0
Acne keloidalis nuchae	0
Hidradenitis suppurativa	0
Psoriasis	0
Prurigo nodularis	0
Lichen simplex chronicus	0
Lupus	0
Pseudofolliculitis barbae	0
Folliculitis	0
Pyoderma gangrenosum	0
Other	0

Researchers within allergy and otolaryngology have demonstrated the safety of in-office immunotherapy preparation under clean technique. In the allergy literature, 2 prospective (136 in-office vials and 320 in-office immunotherapy injections) and 2 retrospective (26,795 and >130,000 subcutaneous allergen in-office immunotherapy injections) studies revealed negative vial cultures and no infections.[13-15] To our knowledge, infection rates of compounded medications for dermatologic use have not been assessed. Studies assessing intralesional steroid injection efficacy did not note infection.[16-19]

The study used a retrospective medical record review to assess the infection rate after intradermal injection. The infection rate was 0.25%, and 64% of suspected infections occurred in lesions that were diagnosed as "inflamed cysts" before the intralesional injection. These lesions may have been infected before the injection. Thus, assessing the true infection rate is difficult. Nonetheless, the overall low infection rate demonstrates that in-office compounding for intralesional dermal administration is safe when used appropriately. Appropriate use includes sterile products and use by medical professionals.

A major limitation to this study is the time frame. Although a 30-day postinjection period would typically capture bacterial infections, it may not uncover atypical bacterial or fungal infections. Further, a sample size of more than 4370 medical records may not be large enough to capture very uncommon adverse events.

CONCLUSION

This study did not demonstrate an increased risk of compounded triamcinolone relative to noncompounded triamcinolone. This is important to demonstrate the safety of compounded medications relative to noncompounded. The infection rate identified in this study may be due to multiuse vials rather than the act of compounding. All of the triamcinolone and bacteriostatic saline used (at all sites) were multiuse (no single use triamcinolone and bacteriostatic saline). Although a discussion about in-office medication safety is welcomed, it is important to recognize differences in injection routes. Continuing in-office compounding for intralesional dermal injections remains in the patients' best interest.

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