Safety of Storing and Reusing Hyaluronic Acid Fillers: A Retrospective Chart Review

Patrick K. Safo, MD, PhD; Christina Wahlgren, MD; Suzan Obagi, MD

Injectable dermal fillers are an integral component of cosmetic dermatology for soft tissue augmentation. Many patients request intermittent, subtle augmentation that does not require use of the complete syringe of filler material. The ability to safely store and reuse dermal fillers is of paramount importance to the cosmetic dermatologist. We investigated potential infectious complications associated with the reuse of hyaluronic acid (HA) dermal fillers stored in a medical-grade refrigerator. We performed a retrospective review of patient records for infectious complications associated with the use of stored HA fillers (Restylane and Juvéderm Ultra Plus) from January 1, 2007, to May 31, 2009. No infections were associated with the reuse of stored HA fillers. The number of syringes reused during this time period was 83 of Restylane and 199 of Juvéderm Ultra Plus. Patients were retreated at mean days of 190 (7−456 days) and 195 (5−490 days) with stored Restylane and Juvéderm Ultra Plus respectively. Even with subsequent reuse, 12.9% of the stored Restylane and 13.6% of the stored Juvéderm Ultra Plus syringes were incompletely used and discarded after 1 year of storage or upon their expiration date. This large-size, retrospective study shows that there is minimal risk of bacterial infection associated with the use of stored HA fillers.

Stabilized hyaluronic acid (HA) gels compose the majority of dermal fillers used by practitioners for soft tissue augmentation.[1,2] The low immunogenicity, long duration of tissue correction, and reversibility of these agents with hyaluronidase have contributed to the increased use of HA fillers.[1,3,4] Because a growing number of patients request subtle tissue augmentation that requires small filler volumes, it is common to incompletely use the contents of filler syringes obtained from the manufacturer. A major concern for reuse of stored syringes is bacterial contamination of the product with increased risk for infectious complications in patients. Bellew et al[5] demonstrated an absence of cultured bacteria (aerobic and anaerobic) from 30 partially used HA filler syringes stored for up to 9 months at room temperature. Similarly, Bhatia et al[6] observed no bacterial growth in cultures from the contents of 34 HA filler syringes stored for up to 12 months at room temperature. However, there are no studies documenting the potential infectious complications associated with reuse of stored HA fillers in vivo in patients. Using a larger study population and a different

Dr. Safo is a resident and Dr. Wahlgren is a former resident at the Department of Dermatology, Cosmetic Surgery & Skin Health Center at the University of Pittsburgh Medical Center, Pennsylvania. Dr. Wahlgren is now in private practice in Seattle Washington. Dr. Obagi is Associate Professor of Dermatology, Associate Professor of Surgery-Division of Plastic Surgery, and Director, Cosmetic Surgery & Skin Health Center, University of Pittsburgh Medical Center.

The authors report no conflict of interest in relation to this article.

Correspondence: Suzan Obagi, MD, Cosmetic Surgery and Skin Health Center, Blaymore II, 1603 Carmody Ct, Ste 103, Sewickley, PA 15143 (obagimd@gmail.com).

storage temperature, we study the in vivo rate of infectious complications in patients treated with syringes of HA fillers stored for up to 12 months in a medical-grade refrigerator.

METHODS

Institutional Review Board approval was granted for this study from the University of Pittsburgh. We performed a retrospective chart review of patients injected with Restylane (Medicis Pharmaceutical Corporation) and Juvéderm Ultra Plus (Allergan, Inc) between January 1, 2007, to May 31, 2009, at the Cosmetic Surgery & Skin Health Center at the University of Pittsburgh Medical Center. Patients who were initially injected with Restylane (1.0 mL per syringe) or Juvéderm Ultra Plus (0.8 mL per syringe) were screened, and those with incompletely used filler syringes were included in the study.

Injection Technique and Storage of Filler

Patients' skin was cleansed with isopropyl alcohol 70% prior to the administration of the filler. A sterile needle (27−30 gauge, size varied depending on physician preference) was used to inject. Upon completion of treatment, any remaining filler that had not reached its expiration date was saved. The treatment needle was removed and a new, sterile needle was attached to the treatment syringe. A patient identification tag stating the patient's name and date of birth was attached to the syringe after verifying the information with the patient. The syringe was placed in a small plastic bag and a second patient label was applied to the bag. The patient's record was noted with the amount of filler remaining. The syringe was stored in a refrigerator maintained at 4°C until the next use. This refrigerator was equipped with an alarm and was checked twice daily for appropriate temperature. Biannual review of a log of stored syringes was done to discard syringes older than 1 year or that had reached the product expiration date. Patients were informed of the discarded syringe.

Reuse of Stored Syringe

At the patient's next visit, topical anesthetic was applied to the treatment area. This was then removed with isopropyl alcohol 70% after the desired duration of topical anesthetic application. The patient's name and date of birth were verified with the patient identification tag on the treatment syringe. The treatment was completed as described earlier. Again, any remaining filler was stored as described with a new, sterile needle attached to the syringe.

The charts were reviewed for patient calls or office visits for local or systemic adverse effects related to the filler injection from reused syringes.

RESULTS

During the study period, 340 syringes of Restylane and 510 syringes of Juvéderm Ultra Plus were used at our facility. Of the 340 Restylane syringes, 116 (34%) were partially used at the initial visit and were subsequently stored for reuse in 83 patients (Figure 1). The mean time to reuse stored syringes was 190 days (range 7−456 days). Of the stored Restylane syringes, 56.9%, 23.3%, and 6.9% were reinjected once, twice, or 3 times respectively for any given patient (Figure 2). In all, 12.9% of the initially stored Restylane syringes were incompletely used with a mean discarded filler volume of 0.41 ± 0.056 mL (41.2% of original syringe volume).

Similarly, 510 syringes of Juvéderm Ultra Plus were used during this study period. Of those, 199 (39%) syringes of Juvéderm Ultra Plus were partially used and saved for reuse in 136 patients (Figure 1). The mean time to reuse stored syringes was 195 days (range 5−490 days). Of the stored Juvéderm Ultra Plus syringes, 70.4%, 13.1%, and 2.5% were reused once, twice, or 3 times, respectively, for any given patient (Figure 3). In all, 13.6% of the stored Juvéderm Ultra Plus syringes were incompletely used, with a mean discarded filler volume of 0.33 ± 0.028 mL (40.1% of original syringe volume).

Chart review revealed that there were no recorded bacterial infections related to use of the stored fillers. The majority of calls from patients was within 1 week after filler injection and included local injection-site edema in 3 of 83 (3.6%) patients treated with Restylane and 2 of 136 (1.5%) patients treated with Juvéderm Ultra Plus, which resolved with application of cold compress. Two patients treated with Juvéderm Ultra Plus experienced visible filler material that was reversed with injection of hyaluronidase.

COMMENT

Hyaluronic acid fillers are the leading injectable dermal fillers used for soft tissue augmentation. Our data demonstrate that incompletely used HA filler syringes can be safely stored for reuse. The almost equal amount of filler stored (34% and 39% of Restylane and Juvéderm, respectively) is in keeping with our clinical impression that, once an adequate baseline volume is achieved, often only a small volume is required during follow-up maintenance treatments. Therefore, it is not uncommon to open a syringe of HA filler to perform a small "touch-up" and to store the remainder. The amount of Restylane stored in the future will probably diminish as it is becoming our preferred filler for treating the nasojugal groove, the brows, and the lips. All of these anatomic areas do require larger volumes of filler thus

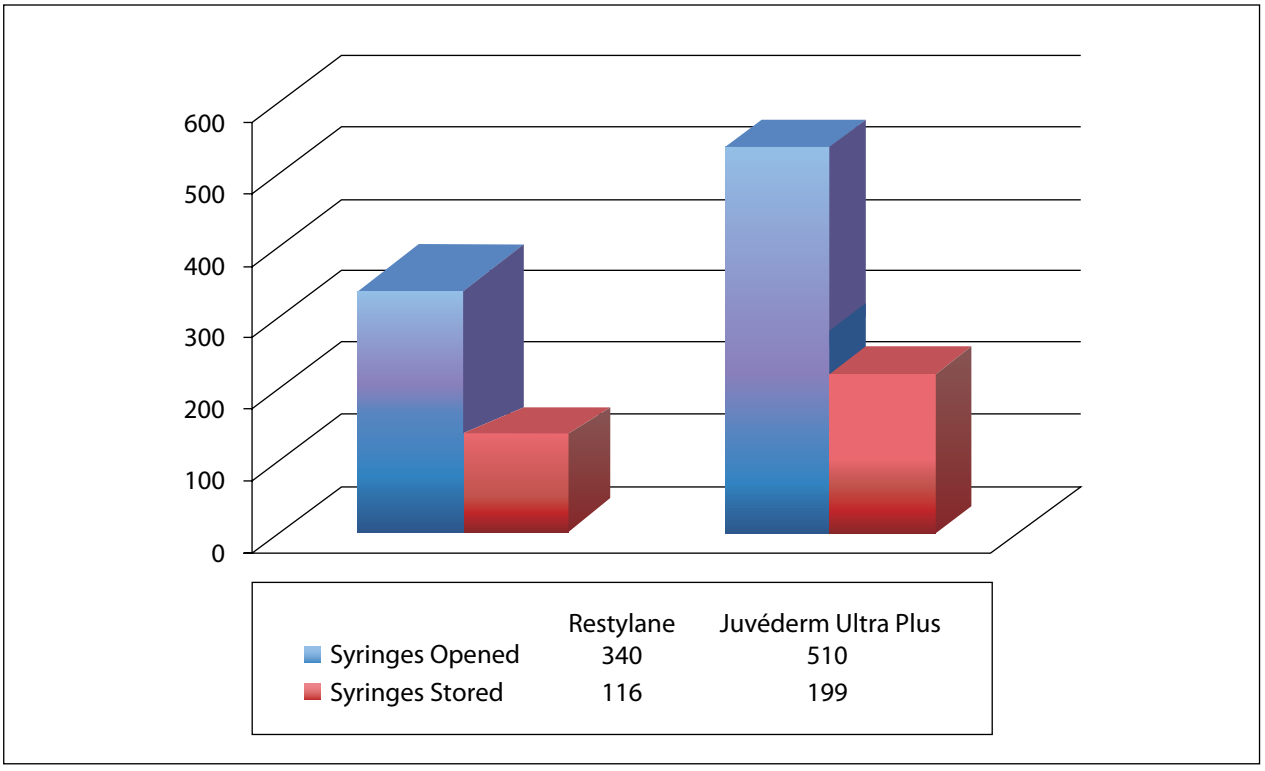

Figure 1. Number of syringes of hyaluronic acid fillers opened and stored for subsequent use.

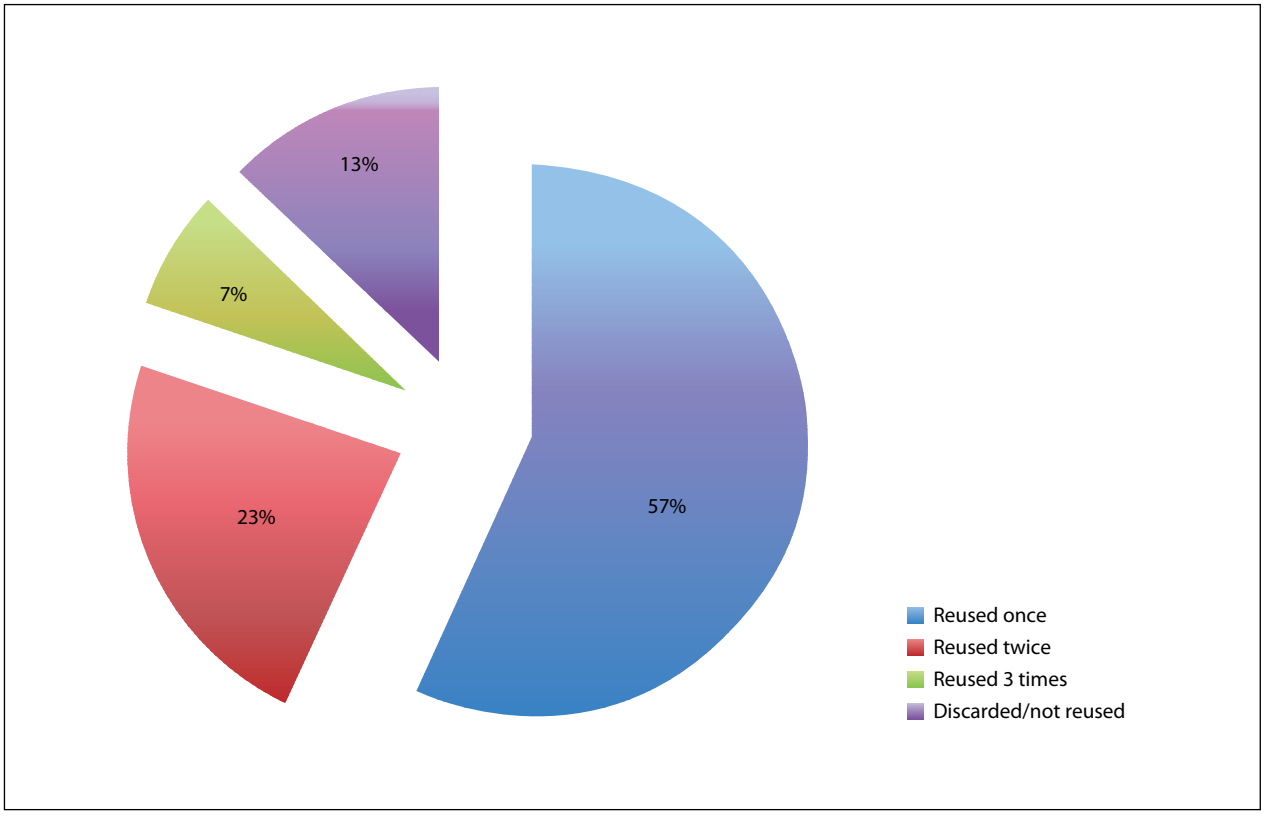

Figure 2. Restylane syringes (116) reinjected once, twice, or 3 times in 83 patients.

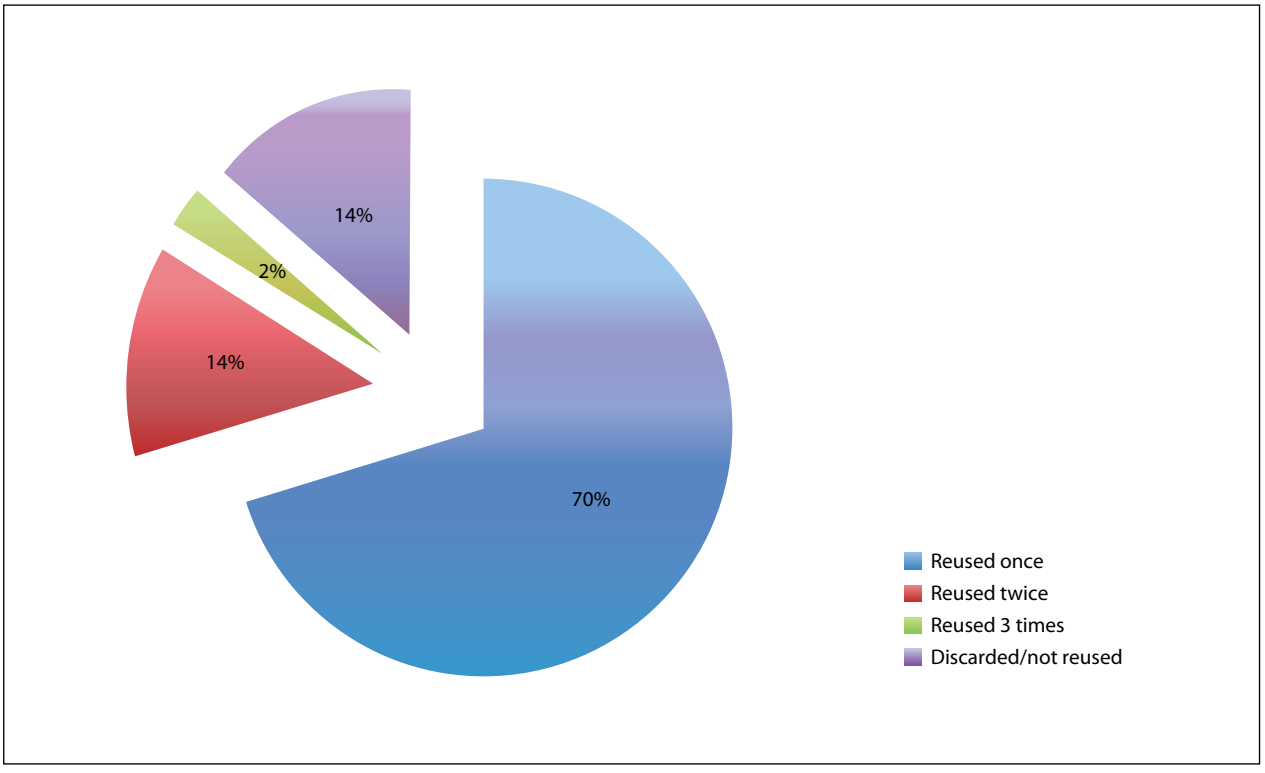

Figure 3. Juvéderm Ultra Plus syringes (199) reinjected once, twice, or 3 times in 136 patients.

making it less likely that there will be any remaining to store.

The average reuse date of 6 months in our study corresponds with recent studies by Smith et al[7] recommending reinjection of HA fillers 4.5 to 9 months after original treatment to maintain long-term tissue augmentation.[7,8] Furthermore, smaller volumes of filler are required for subsequent injections to maintain the augmentation.[7] Our ability to compare filler volume for reinjection is limited by the fact that a significant number of our patients had injections in new anatomic locations during the reuse of the stored HA syringes.

The adverse reactions related to use of HA includes erythema, edema, ecchymosis, pain, arterial embolization, sterile granuloma, hypersensitivity reaction, and bacterial infections.[3,9-11] Although the incidence of bacterial infections is rare, there is increased theoretical risk for bacterial contamination of stored syringes.[12] Indeed there is documentation of *Propionibacterium acnes* contamination of the needle tips but not the syringes of partially used collagen filler syringes stored in the refrigerator.[13] Careful storage of unused syringes and good technique does not increase the risk of bacterial infection with reuse. The absence of infectious complications in this study is in agreement with earlier studies demonstrating sterility of stored HA fillers and collagen fillers.[5,6,12-14] Furthermore, there are increasing reports of biofilm contributing to granuloma formation when using HA fillers.[15-17] We did not observe increasing granuloma formation with reuse of stored syringes.

A limitation of our study is reliance on patient-reported adverse reactions rather than follow-up in the practice. However, the vast majority of the patients who return for additional injections or other procedures did not report adverse effects. A prospective study can be done subsequently.

CONCLUSION

This study supports the safe reuse of carefully stored HA fillers for soft tissue augmentation in patients without an increased risk of bacterial infections. Reuse can be cost-effective for patients and for the practice.

REFERENCES

1. Carruthers J, Cohen SR, Joseph JH, et al. The science and art of dermal fillers for soft-tissue augmentation. *J Drugs Dermatol.* 2009;8:335-350.
2. Gold M. The science and art of hyaluronic acid dermal filler use in esthetic applications. *J Cosmet Dermatol.* 2009;8:301-307.
3. Lowe NJ, Maxwell CA, Lowe P, et al. Hyaluronic acid skin fillers: adverse reactions and skin testing. *J Am Acad Dermatol.* 2001;45:930-933.

4. Narins RS, Brandt F, Leyden J, et al. A randomized, double-blind, multicenter comparison of the efficacy and tolerability of Restylane versus Zyplast for the correction of nasolabial folds. *Dermatol Surg.* 2003;29:588-595.
5. Bellew SG, Carroll KC, Weiss MA, et al. Sterility of stored nonanimal, stabilized hyaluronic acid gel syringes after patient injection. *J Am Acad Dermatol.* 2005;52:988-990.
6. Bhatia AC, Arndt KA, Dover JS, et al. Bacterial sterility of stored nonanimal stabilized hyaluronic acid–based cutaneous filler. *Arch Dermatol.* 2005;141:1317-1318.
7. Smith SR, Jones D, Thomas JA, et al. Duration of wrinkle correction following repeat treatment with Juvéderm hyaluronic acid fillers. *Arch Dermatol Res.* 2010;302:757-762.
8. Narins RS, Dayan SH, Brandt FS, et al. Persistence and improvement of nasolabial fold correction with nonanimal-stabilized hyaluronic acid 100,000 gel particles/mL filler on two retreatment schedules: results up to 18 months on two retreatment schedules. *Dermatol Surg.* 2008;34 (suppl 1):S2-S8.
9. Van Dyke S, Hays GP, Caglia AE, et al. Severe acute local reactions to a hyaluronic acid–derived dermal filler. *J Clin Aesthet Dermatol.* 2010;3:32-35.
10. Zielke H, Wölber L, Wiest L, et al. Risk profiles of different injectable fillers: results from the Injectable Filler Safety Study (IFS Study). *Dermatol Surg.* 2008;34: 326-335.
11. Schanz S, Schippert W, Ulmer A, et al. Arterial embolization caused by injection of hyaluronic acid (Restylane). *Br J Dermatol.* 2002;146:928-929.
12. Friedman PM, Mafong EA, Kauvar AN, et al. Safety data of injectable nonanimal stabilized hyaluronic acid gel for soft tissue augmentation. *Dermatol Surg.* 2002;28:491-494.
13. Davis K, Bottone EJ, Lucas D, et al. Sterility of refrigerated injectable collagen syringes after injection of patient. *J Am Acad Dermatol.* 1992;27:959-961.
14. Culligan PJ, Koduri S, Heit MH, et al. The safety of reusing injectable collagen: a multicenter microbiological study. *Int Urogynecol J Pelvic Floor Dysfunct.* 2002;13:232-234.
15. Rohrich RJ, Monheit G, Nguyen AT, et al. Soft-tissue filler complications: the important role of biofilms. *Plast Reconstr Surg.* 2010;125:1250-1256.
16. Mamelak AJ, Katz TM, Goldberg LH, et al. Foreign body reaction to hyaluronic acid filler injection: in search of an etiology. *Dermatol Surg.* 2009;35(suppl 2): 1701-1703.
17. Christensen LH. Host tissue interaction, fate, and risks of degradable and nondegradable gel fillers. *Dermatol Surg.* 2009; 35(suppl 2):1612-1619.