Neurotoxin Waste from Drawing Product Through the Vial Stopper

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ABSTRACT

Botulinum toxin injection is the most common cosmetic surgery procedure in the world. Current technique requires reconstitution that can produce product waste resulting in significant loss of profit as well as inaccuracy of actual units injected. By random sampling of "used empty" vials, it was shown that an average of 5 units are potentially wasted by the conventional methods of drawing up the product with a needle through the stopper of an inverted vial. Depending on the pricing and dilution of the product, this can result in a profit loss of $50 to $60 per vial, which can quickly add up to tens of thousands of dollars in a busy practice. Removing the stopper, tilting the vial, and aspirating the last residual with a small gauge needle can result in significant savings. Finally, this residual was calculated at a five-percent loss, which results in an inaccuracy of actual units delivered. (*J Clin Aesthet Dermatol.* 2014;7(6):33–37.)

Neurotoxins have become the most popular nonsurgical cosmetic procedure in the world. In 2012, more than 4,125,179 botulinum toxin procedures were administered by plastic surgeons, dermatologists, otolaryngologists, and their nurse injectors, according to the American Society for Aesthetic Plastic Surgery Cosmetic Surgery National Databank. One of the main drawbacks existing today is the need for the practitioner to reconstitute the medication and draw it from the vial prior to injection. This inconvenience is accepted, but inefficient, as it results in a loss of time and money from the extra steps required. A more significant loss can result from residual neurotoxin that remains in the vial and cannot be drawn up through the stopper.

The author utilizes the common dilution of 2.5mL preserved saline to reconstitute each 100-unit vial. Mathematically, this should yield five 0.5mL syringes containing 20 units each. It is impossible to capture 100 percent of the reconstituted toxin, as there is liquid that, by capillary action, clings to the vial walls, stopper, syringe, and needle. This means that a small amount of waste is a given. In the business world, this is referred to as shrinkage. More importantly, the amount of this "waste" can vary by how the solution is removed from the vial.

The most common method of removing reconstituted product from the vial is to aspirate the liquid through the stopper. The Allergan Botox Cosmetic product brochure states the following: "a new, sterile needle and syringe should be used to enter the vial on each occasion for removal of BOTOX."[1] Alternatively, some clinicians remove the stopper and aspirate from the vial base.

Conventionally, most people draw from an inverted vial with the stopper facing the floor, which means that the surface area of the stopper and vial neck will harbor some liquid due to capillary action. When drawing from an upright vial with the stopper removed and the vial tilted 30 degrees, there is less surface area for residual liquid to adhere, plus the tilting of the vial allows one to get the last drop from the remaining puddle. A large-bore needle with a long bevel is frequently used, but may not capture the total residual puddle. Using a 32-guage needle on a 1mL syringe can aspirate the total residual. If the unstoppered vial is sitting level on its base, it may be impossible to see the residual, while tipping the vial 30 degrees will reveal any residual amount.

Since 1998, the author has followed common practices for onabotulinumtoxinA (Botox, Allergan, Inc. Irvine, California) reconstitution,[2–7] including drawing up the

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Figure 1. A 15-year sample size of used stoppered Botox vials

reconstituted drug by placing a needle through the stopper and aspirating. From time to time, the author's practice removed the vial stoppers using a conventional bottle opener to try this technique. This technique was inconvenient for the staff and made it easy to fracture the vial top and sustain a laceration, which was another reason not to "pop the top." After trying this technique, the author's staff always migrated back to the "needle through the stopper" technique.

The author has used 5,000 vials of Botox since 1998 and saved the vials in a display in the office (Figure 1). Examining this collection of vials shows that most vials contained a small amount of residual liquid. When one examines a vial with a very small amount of liquid, it is almost invisible when the vial is upright and level (Figure 2A), but if the vial is tipped, the residual becomes very apparent (Figure 2B). This is an important fact for staff to realize when assessing if any residual is present.

Looking at these thousands of vials, all of which contain residual liquid, begs the following questions: how many units are wasted and how much income is lost when residual liquid remains on the bottom of vials? In an informal effort to quantify how much residual neurotoxin remains in an average vial when drawn through the stopper, the author randomly collected "empty" vials from his collection. Fifty vials (100-unit vials) were chosen and numbered. The top was removed from each vial using a home-style bottle opener or bandage scissors (Figure 3). Care was taken to only engage the metal vial rim as not to fragment glass or displace the stopper. Each vial was tilted 30 degrees from vertical so that the residual liquid could be visualized, then the liquid was aspirated with a 1mL Luer Lock syringe and a 32-gauge needle. As stated earlier, it is important to use the smallest needle possible when aspirating the last aliquot of residual liquid as larger needles have a long bevel that cannot get to the bottom of the residual puddle and the larger diameter needle will retain a small amount of residual liquid. The residual liquid was drawn up into the syringe and purged so the liquid was at the "zero" measurement line on the syringe. Figure 4 shows a 10-vial sample, Table 1 shows the 50-vial residual volumes, Table 2 shows the descriptive statistics from the sampling, and Figure 5 shows a histogram of the sampling.

RESULTS

The results show that the author's technique of aspirating through the stopper with an 18-gauge needle will leave an average residual volume of .127mL, which corresponds to 5.08 units of residual waste per vial at a dilution of 2.5mL/vial. This represents a five-percent waste of product per vial. A smaller dilution would be more concentrated and allow even more waste.

Extrapolating the residual waste of 5.08 units per vial, the author used 615 vials last year (as a solo injector), which equals 3,124 units of unused product. At $10 per unit, the loss during that calendar year was $31,242. Adjusted for the cost of the product, the actual waste amounted to $15,621.

Applying this to an average cosmetic practice, a practitioner could waste 508 units of neurotoxin per 100 vials used. If the doctor charged $10 per unit, the lost revenue would be $5,080 (minus cost of product). A fee of $12 per unit would equate to $6,096 of lost revenue (minus cost of product). A similar scenario would exist if a dilution less than 2.5mL was used since the residual contains more units.

When the author examines his collection of 5,000 vials, the revenue loss (minus the cost of the product) would be

$127,000. This makes it well worth the effort of removing the stopper, tilting the vial, and removing all residual with a 32 gauge needle.

DISCUSSION

In 2003, Dykstra et al[8] reported a survey of 30 physicians who stated that Botox vial residual varied from 2 to 15 units. In this study, 80 vials were tested for residual Botox by three different methods of removal. Inverting the vial and withdrawing through the stopper with a 21-gauge, 1.5-inch needle was the most wasteful, leaving an average residual of 8 units. The second most wasteful method was using a 2-inch, 21-gauge needle in a noninverted vial, which left an average residual of 2.3 units (the longer needle reached the bottom of the flat vial). The most efficient means of removing residual product was removing the stopper and aspirating the noninverted vial with a 21-gauge, 1.5-inch needle, leaving an average residual of only 1 unit. These authors did not recommend the latter method due to compromise in sterility and possibility of glass shards in the vial.[8]

During routine 2.5mL reconstitution, the author's staff inverts the vial, and, using an 18-gauge needle, aspirates through the stopper into a 3mL syringe. Using a "front loading" technique (through the hub), five single 1mL syringes are loaded with 0.5mL each. When the vial is set down on a level surface, it appears to be totally empty; however, as stated earlier, tilting the vial will show any significant residual. Despite routine efforts to remove all the liquid from the vial, this study showed that significant waste (5 units per vial) was occurring.

In an informal effort to determine how other specialists reconstitute and aspirate vials, the author chose 20 random colleagues from plastic surgery, facial plastic surgery, dermatology, oral and maxillofacial surgery, and oculoplastic surgery who are high-volume, experienced neurotoxin injectors and asked them a single question via email. "How does your office remove reconstituted neurotoxin from the vial?" All 20 responded and 65 percent (13 of 20) reported using needles (18–31 gauge) to aspirate through the stopper. Only seven doctors (35%) reported removing the stopper and then aspirating the residual.

The financial advantage of removing the stopper and aspirating the neurotoxin from the base of the vial is obvious as it allows the doctor to gain 5 additional units (per this study) of product per vial. This technique could save the average practice thousands of dollars per year.

Figure 2. A flat and level vial may appear as if it has no residual liquid in it (top), while a tilted vial will better show any residual (bottom).

Figure 3. A common bottle cap opener or heavy duty bandage scissors can be used to uncap the vial. Regardless of which method is used, care must be employed to not fracture the vial neck, as laceration can result. Engaging the very end of the stopper rim is the safest and easiest means of removal without glass fracture.

Figure 4. These 10 syringes are representative of residual neurotoxin aspirated from "empty" vials.

Various factors affect the efficiency of removing liquid from a vial including the position of the vial (tilted or upright) and the size of the needle. A 32-gauge needle with a short bevel is the most efficient in removing final residual. An efficient way to remove toxin may be to aspirate through the stopper until the last visible amount is drawn up, then remove the stopper and use a 32-gauge needle on a 1mL syringe to maximize the last drops from the base of a tilted vial. This method preserves vial sterility until the last units are removed.

LIMITATIONS

This informal study with a small sample size is intended to illustrate the waste seen in a busy, solo injector practice and to alert other practitioners of the alarming results. The measurement method of residual volume is "clinical" and not laboratory grade (micropipettes, temperature control, etc.). Although the sample size described herein is moderate, it is the author's opinion that a similar residual would factor out if all 5,000 vials in this collection were examined. Additionally, it could be that the author's staff is inefficient in drawing up from vials and more wasteful than the average person. The author's observations and teachings at many other cosmetic surgery offices over the years would indicate that this is not the case and that this waste is repeatable in the average office.

CONCLUSION

Current United States Food and Drug Administration-approved botulinum toxin A preparations must be reconstituted and drawn up from vials, and waste is inevitable. Small waste from a less expensive product may be tolerable, but as illustrated, with a vial of botulinum toxin A costing $525, even a fraction of a milliliter can add up over time, especially at lower dilutions. Hopefully, technology will find a means of delivering prepared neurotoxin in loaded syringes similar to filler products. In the meantime, a conical vial or one more ergonomic for capturing maximal residual liquid would be advantageous for the end user.

This informal study shows that in a busy single doctor injectable practice, the estimated incidental waste of one brand of neurotoxin resulted in a net profit loss of $15,621 in one year at a 2.5mL dilution. A smaller dilution has proportionately more loss. A survey of 20 busy injectors from multiple specialties shows that most of the sample practitioners aspirate the neurotoxin through the intact stopper of an inverted vial. This waste quickly adds up when factored over multiple years. Extracting the final bit of residual neurotoxin by removing the vial stopper and aspirating from the tilted vial with a 32-gauge needle on a 1mL syringe is financially worth the effort.

Finally, with a five-percent waste, practitioners are only delivering 95 percent of intended units. With a single cosmetic treatment, this is minute, but in cases of treatments employing 4 to 5 vials, such as leg muscle spasticity, the miscalculation of intended units could be significant.

TABLE 1. Fifty-vial residual volumes (50 vials; 6.36mL residual; 254 units of waste)

VIAL NUMBER	RESIDUAL VOLUME	VIAL NUMBER	RESIDUAL VOLUME
1	0.01	26	0.04
2	0.09	27	0.10
3	0.13	28	0.03
4	0.21	29	0.11
5	0.07	30	0.10
6	0.10	31	0.20
7	0.20	32	0.11
8	0.10	33	0.10
9	0.11	34	0.18
10	0.13	35	0.17
11	0.20	36	0.19
12	0.09	37	0.12
13	0.08	38	0.16
14	0.13	39	0.19
15	0.28	40	0.14
16	0.12	41	0.02
17	0.21	42	0.11
18	0.20	43	0.13
19	0.04	44	0.14
20	0.19	45	0.03
21	0.10	46	0.08
22	0.19	47	0.08
23	0.10	48	0.10
24	0.12	49	0.10
25	0.18	50	0.15

TABLE 2. Descriptive statistics

AMOUNT OF RESIDUAL BOTOX (mL)	
Mean	.1270
Standard error of mean	.1270
Standard deviation	.1270
Minimum	.02
Maximum	.28
Sum (total for all vials)	6.35

REFERENCES

1. Botox [package insert]. Irvine, CA: Allergan, Inc; revised 2013.
2. Niamtu J. Aesthetic uses of botulinum toxin A. *Oral Maxillofac Surg.* 1999;57(10):1228–1233.
3. Niamtu J. The use of botulinum toxin in cosmetic facial surgery. *Oral Maxillofac Surg Clin North Am.* 2000;12(4):596–612.
4. Niamtu J. Botulinum toxin A: a review of 1,085 oral and maxillofacial patient treatments. *J Oral Maxillofac Surg.* 2003;61:317–324.
5. Niamtu J. Neurotoxin treatment: it ain't what it used to be. *Cosmet Dermatol.* 2010;23(8):346–347.
6. Liu A, Carruthers A, Cohen JL, et al. Recommendations and current practices for the reconstitution and storage of botulinum toxin type A. *J Am Acad Dermatol.* 2012;67(3):373–378.
7. Alam M, Yoo SS, Wrone DA, et al. Sterility assessment of multiple use botulinum A exotoxin vials: a prospective simulation. *J Am Acad Dermatol.* 2006;55(2):272–275.
8. Dykstra DD, Wieting JM, McGuire J, Kowalkowski T. Maximizing extraction of botulinum toxin type A from vials. *Arch Phys Med Rehabil.* 2002;83(11):1638–1640.