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Maximizing doses from multi-dose vaccine vials using the air bubble trapping technique

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Purpose: Vaccine shortages present significant challenges for public health, necessitating strategies such as fractional dosing and the use of adjuvants to conserve doses. However, reducing vaccine wastage remains essential. One approach is the air bubble trapping technique (ABTT), which involves trapping an air bubble to minimize dead volume loss and maximize the number of doses extracted from multi-dose vials.
Materials and Methods: This study compares ABTT with standard methods using 3 syringe types. Healthcare workers prepared 0.1 mL and 0.5 mL saline doses both with and without ABTT.
Results: Results showed that ABTT produced comparable vaccine volumes to conventional techniques but required extra preparation time. ABTT reduced volume by 8.6% for 0.1 mL doses and 2.9% for 0.5 mL doses, with preparation times of 30.63 and 32.95 seconds, compared to 12.53 and 15.11 seconds without ABTT.
Conclusion: ABTT was consistent across different syringe types and levels of user experience, allowing for practical integration into vaccination workflows.

Keywords: Vaccination; Syringes; Hypodermic needle; Vaccine; Administration and dosage

INTRODUCTION

Vaccine scarcity is a frequent occurrence influenced by various factors, such as limited manufacturing capacity, stringent regulatory processes, shortages of raw materials, market withdrawals, and sudden increases in demand [1,2]. Several evaluated strategies to alleviate vaccine shortages include using fractional doses for yellow fever vaccines [3], reducing potency in MMR vaccines [4], incorporating dose-sparing adjuvants in influenza vaccines [5], and administering vaccines intradermally for mpox vaccination [6]. Additional approaches include optimizing the use of multi-dose vials with low dead-volume syringes (LDVS) and needles.

Globally, approximately 80% of vaccines are packaged in multi-dose vials [7], which reduces packaging materials and mitigates the impact of material shortages [8]. However, the use of multi-dose vials can result in vaccine wastage due to unused doses or losses during syringe preparation [9]. To address technique-related wastage, manufacturers typically overfill vials to ensure the stated number of doses can be

administered. The use of excess vaccine beyond the labeled doses is permitted and commonly practiced. For example, in a 10-dose vial, the overfill can range from 16% to 24% of the total volume [10].

Using syringes and needles with minimal dead volume can help reduce vaccine wastage. A high dead-volume syringe retains a relatively large amount of liquid in the needle and between the syringe hub and plunger after injection, compared to a LDVS, which leaves less than 35 microliters remaining after injection [11]. During the coronavirus disease 2019 (COVID-19) pandemic, LDVS with fixed needles were used to maximize the number of vaccine doses obtainable, allowing up to 6 doses to be extracted from multi-dose vials of the Pfizer-BioNTech COVID-19 vaccine [12,13]. However, shortages of these syringes also occurred during this time [14,15].

Methods used to minimize dead volume and maximize the amount of vaccine extracted from multi-dose vials, especially in settings without access to LDVS, represent potential strategies for conserving vaccines. One such method is the 'air bubble trick' [16]. This technique involves removing air from inside the needle by injecting it back into the vial, withdrawing the precise dosage along with a small amount of air, and then using this air to eject all liquid during injection [16]. Evaluation data regarding the effectiveness of this air bubble trapping technique (ABTT) is currently unavailable.

Our objective is to assess the effectiveness of ABTT through 3 main evaluations: (1) comparing the volumes obtained using ABTT vs. without ABTT across 3 different syringe types, (2) quantifying the size of the air bubble used to administer the intended dose with ABTT, and (3) measuring the additional time required for ABTT implementation.

MATERIALS AND METHODS

Participants and setting

Staff nurses and pharmacists with experience at COVID-19 vaccination sites were recruited via email from the Los Angeles County Department of Public Health's Clinic Services and Mobile Vaccination Team. With purposive and judgmental nonprobability sampling, 26 nurses and 4 pharmacists were selected from a central health center. These participants were asked to complete a survey about their job roles and vaccination experience. Using the Dreyfus Model of Skill Acquisition, participants were categorized as novice, proficient, or expert based on their years of vaccination experience [17-19]. A novice has less than 2 years of experience, a proficient individual has 2 to 5 years, and an expert has over 5 years of vaccination practice.

Materials

Three syringe and needle combinations were selected for this study: (1) 1 mL, 25 G×1" VanishPoint syringe with safety needle by Retractable Technologies, Inc., Little Elm, TX, USA (Ref. 10161); (2) 1 mL, 23 G×1" Magellan syringe with hypodermic safety needle by Covidien, Dublin, Ireland (Ref. 8881811310); and (3) 1 mL, 27 G×1/2" BD SafetyGlide syringe with safety needle by Becton, Dickinson and Company, Franklin Lakes, NJ, USA (Ref. 305945). These syringes were chosen based on their widespread use during the COVID-19 pandemic. The VanishPoint syringe/needle has a low dead volume of 0.02 mL [20]; the Magellan syringe/needle has a dead volume of 0.07 mL (Cardinal Health, email communication, June 2024); and the BD syringe/needle is reported to have a dead volume of 0.04 mL (BD Medical Information, email communication, June 2024). Normal saline, manufactured by Hospira (Lake Forest, IL, USA), was used as a substitute for the vaccine in this study.

Technique and data collection

A volume of 0.1 mL and 0.5 mL of normal saline was drawn into a syringe using a conventional technique. Subsequently, the contents were expelled from the syringe into an antistatic weighing dish and weighed using the AccuLab VIC-303 analytical scale. The time taken, in seconds, to withdraw the dose was recorded by the investigators using a stopwatch, starting from the moment the needle was inserted into the vial until the desired volume was withdrawn and expelled onto the weighing dish.

Each participant performed 20 draws per syringe: 10 standard draws (5 at 0.1 mL and 5 at 0.5 mL) without ABTT, followed by 10 draws (5 at 0.1 mL and 5 at 0.5 mL) using ABTT. During ABTT draws, the air bubble size was recorded. Participants unfamiliar with ABTT received brief training just before the experiment.

Data analysis

Descriptive statistics were conducted on personnel characteristics, specifically profession and years of vaccination experience. To assess the accuracy of time and volume measurements under each condition (ABTT vs. no ABTT), the mean and standard deviation were calculated for the 30 participants. The recorded weights were converted to volume (mL) using the density of normal saline (1.0046 g/mL). A paired-t-test was used to compare the mean volumes and times for drawing 0.1 mL and 0.5 mL between the ABTT and no ABTT conditions, with 95% confidence intervals used to evaluate significant differences. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

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Ethics

This research project was reviewed and approved by the LAC DPH Institutional Review Board (IRB), under IRB Project No. 2023-07-006.

RESULTS

Lower volumes were withdrawn with ABTT at both doses compared to doses without it (**Fig. 1**). For the 0.1 mL dose, the average volume with ABTT was 0.093 mL, compared to 0.101 mL without ABTT, a significant difference of 0.008 mL (8.6%) between the 2 groups (t(29)=–5.58, p<0.0001). Similarly, for the 0.5 mL dose, ABTT users averaged 0.482 mL, versus 0.496 mL without ABTT, a difference of 0.014 mL (2.9%), also statistically significant (t(29)=–7.28, p<0.0001). The air bubble size was recorded for each participant during ABTT use, averaging 0.04 mL for the 0.1 mL dose and 0.05 mL for the 0.5 mL dose.

Using ABTT took twice the amount of time to draw the desired dose (**Fig. 2**). On average, participants needed 30.63 seconds to draw 0.1 mL with ABTT, compared to 12.53 seconds without it, a significant difference of 18.10 seconds (59.1%) (t(29) =7.96, p<0.0001). Similarly, for a 0.5 mL dose, participants took 32.95 seconds with ABTT and 15.11 seconds without, a significant difference of 17.84 seconds (54.2%) (t(29) = 8.49, p<0.0001).

Across all 3 syringe types, drawing 0.1 mL was faster than 0.5 mL (**Fig. 3**). Syringe 1 (VanishPoint) was the slowest for both doses, averaging 24.93 seconds for 0.1 mL and 26.25 seconds for 0.5 mL. Syringe 2 (Magellan) was faster, with times of 21.52 seconds for 0.1 mL and 24.05 seconds for 0.5 mL. Syringe 3 (BD SafetyGlide) showed the fastest times, at 18.24 seconds for 0.1 mL and 21.75 seconds for 0.5 mL.

The use of ABTT resulted in longer administration times across all experience levels, dose sizes, and professions (**Table 1**). Nurses were faster and administered slightly more volume than pharmacists for both doses with ABTT. For the

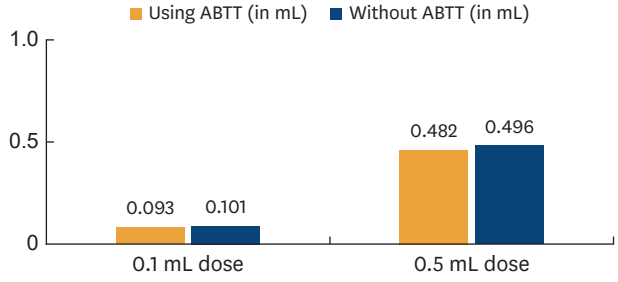

Fig. 1. Comparisons of volume (in mL) expelled using the ABTT vs. without the ABTT (No ABTT) for 0.1 mL and 0.5 mL doses. The mean differences between conditions for both the 0.1 mL and 0.5 mL doses were statistically significant, p<0.0001.
ABTT, air bubble trapping technique.

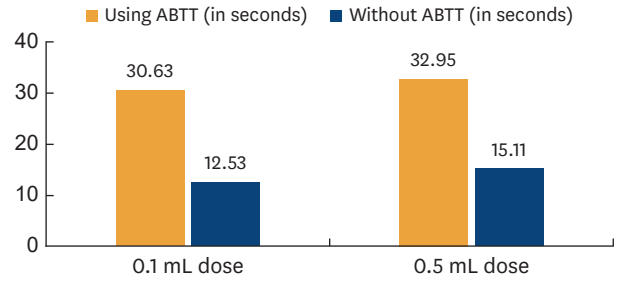

Fig. 2. Comparisons of time (in seconds) needed to draw a dose using the ABTT vs. without the ABTT (No ABTT) for 0.1 mL and 0.5 mL doses. The mean differences between conditions for both the 0.1 mL and 0.5 mL doses were statistically significant, p<0.0001.
ABTT, air bubble trapping technique.

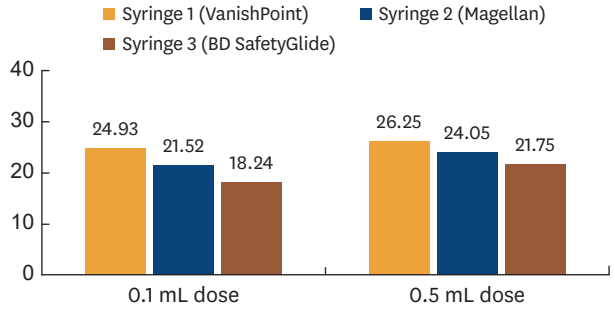

Fig. 3. Comparisons of time (in seconds) needed to draw a dose using ABTT among different syringes. Paired t-tests showed significant differences in draw times between 0.1 mL and 0.5 mL for each syringe, p<0.0058.
ABTT, air bubble trapping technique.

Table 1. Mean volume (mL) and time (seconds) across healthcare workers on ABTT vs. No ABTT for 0.1 mL and 0.5 mL dose

Variables	Volume		Time	
	ABTT	No ABTT	ABTT	No ABTT
Dose size=0.1 mL				
Nurse	0.093	0.101	30.04	12.69
Pharmacist	0.089	0.101	34.49	11.48
Experience (yr)				
<2	0.088	0.100	32.35	14.28
2–5	0.094	0.102	32.45	11.84
>5	0.095	0.102	27.55	12.17
Dose size=0.5 mL				
Nurse	0.482	0.496	32.79	15.22
Pharmacist	0.481	0.498	33.85	14.41
Experience (yr)				
<2	0.479	0.495	34.12	16.38
2–5	0.485	0.497	34.82	14.63
>5	0.479	0.496	30.13	14.83

ABTT, air bubble trapping technique.

0.1 mL dose, participants using ABTT administered slightly less volume and took longer. Similarly, for the 0.5 mL dose, the volume was marginally lower, and administration times were longer with ABTT. Those with 2–5 years of experience were the quickest without ABTT, averaging 11.84 seconds for the 0.1 mL dose and 14.63 seconds for the 0.5 mL dose. Among ABTT draws, participants with over 5 years of experience were the fastest, with times of 27.55 seconds for the 0.1 mL and 30.13 seconds for the 0.5 mL.

DISCUSSION

This study shows that the ABTT is as effective as the traditional method for drawing doses across different syringe and needle types. It is also comparable to a standalone LDVS in conserving vaccine doses, though it requires extra preparation time. The inclusion of an air bubble helps maintain volume accuracy and minimizes vaccine loss in the needle hub.

The ABTT process involves drawing an air bubble into the syringe barrel, positioning it at the plunger end, and adjusting for the correct dose before injection. In this study, the air bubble, measured between 0.04 mL and 0.05 mL, helps push the vaccine out completely during injection, recovering the amount typically trapped in the dead space. Using ABTT, withdrawing 10 doses can save approximately 0.2 mL with the VanishPoint syringe, 0.7 mL with the Magellan syringe, and 0.4 mL with the BD SafetyGlide syringe. This saved volume is crucial during vaccine shortages and public health crises. Studies show that LDVS syringes are preferred to minimize waste, but they may not always be available and often come at higher costs. For example, using VanishPoint syringes (an LDVS) costs about 21% more than non-LDVS syringes like Magellan and 35% more than BD SafetyGlide syringes. Therefore, adopting the ABTT method to minimize vaccine waste offers significant financial benefits, allowing for more doses to be drawn while reducing overall syringe costs, especially when using less expensive non-LDVS syringes.

The volume of liquid expelled using ABTT was nearly the same as without it, regardless of the dose amount (0.1 mL vs. 0.5 mL). Notably, participants with varying years of vaccination experience demonstrated consistent accuracy in volume withdrawal. In this study, the volume was calculated based on weight rather than directly measured. Thus, data was evaluated to the thousands of a milliliter (0.001 mL) for statistical analysis, revealing a significant difference between ABTT and no ABTT, although the differences of 3%–9% in variations of volume are unlikely to significantly impact immunogenicity. In practical settings, vaccine doses are generally rounded to the nearest tenth (0.1 mL). Following this standard, no significant differences in expelled volume were observed when both doses were rounded to 0.1 mL and 0.5 mL.

Using ABTT for dose withdrawal takes about twice as long as withdrawing without it, regardless of the dose size. Since this technique is relatively new, many participants were unfamiliar with it. Despite varying vaccination experience, all participants were introduced to ABTT during the COVID-19 pandemic. In this study, most healthcare workers were classified as proficient (40%), followed by experts (37%) and novices (23%). Expert individuals (over 5 years of experience) generally withdrew doses faster using ABTT compared to novices (under 2 years) and proficient (2–5 years). The faster speed of more experienced participants is likely due to their familiarity with syringes and practiced injection techniques, which enabled quicker and more accurate withdrawals and contributed to more efficient use of ABTT.

This study has several limitations. Variations in syringe and needle dead volumes may have affected performance, and testing only 3 syringe types does not capture the full variety available on the market. The small sample size of 30 participants, with a notable imbalance between nurses (n=26) and pharmacists (n=4), could introduce bias. Differences in user skill and technique may also influence the outcomes, and the time needed to complete 60 draws could lead to fatigue, potentially impacting the quality of later attempts. Additionally, the need for some participants to return to work promptly may have caused rushed draws, which could affect the results. Despite these limitations, the consistent findings across different syringes suggest the results may be applicable in a broader context.

In conclusion, optimizing vaccine use during shortages is essential for public health. Our study shows that ABTT effectively reduces vaccine wastage and maximizes the doses from multi-dose vials. Importantly, healthcare workers, regardless of their vaccination experience or the type of syringe used (LDVS or non-LDVS), performed ABTT successfully with minimal training. Further research is needed to refine vaccine preparation methods and assess the real-world application and effectiveness of ABTT.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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