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Use of a disposable valved-holding chamber (spacer) in a school-based asthma trial

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To the Editor

Patients with asthma use pressurized metered dose inhalers (pMDIs) to deliver precise amounts of drug to their lungs. Poor inhaler technique, common among children, reduces drug delivery to the lungs and increases deposition in the oropharynx and the subsequent risk of minor, local complications. [1–3] Adding a spacer improves medication delivery by reducing oropharyngeal deposition.[4] A variety of spacers have been successfully used including inexpensive, low-tech toilet paper rolls and expensive, sophisticated plastic chambers.[5

Valved holding chambers (VHCs) include a low-resistance one-way valve that holds a fine cloud of medication until it is inhaled during normal tidal breathing. When used in combination with pMDIs, VHCs maximize medication deposition in the airways while minimizing deposition in the oropharynx.[1, 4] VHCs benefit children by eliminating the need to coordinate pMDI actuation and breathing. However, most VHCs are constructed of molded plastic making them bulky, inconvenient to store and transport, and relatively expensive.[6] Furthermore, they should be washed weekly.

These characteristics made plastic VHCs poorly suited for use in our Supervised Asthma Medication in Schools (SAMS) study that evaluated the effectiveness school-supervised use of a once-daily inhaled corticosteroid (ICS) regimen among children 5 – 11 years of age.

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SAMS was approved and monitored by the Institutional Review Board at the University of Arizona and the Office of Curriculum and Instruction at the Tucson Unified School District.

All students were prescribed mometasone furoate (Asmanex Twisthaler®) supplemented with as-needed use of albuterol sulfate (Proventil® HFA), both donated by Merck & Co, Inc. Because Asmanex is a dry-powder inhaler, VHCs were only used with Proventil. SAMS chose to use a paperboard VHC (LiteAire®), donated by Thayer Medical Corporation.

The LiteAire® was chosen for several of its unique properties: at $3 per unit, it is less expensive than a traditional $22 plastic VHC particularly if lost or damaged; being collapsible, it is more easily stored than a rigid VHC; and not having to be washed makes it more convenient to maintain. Each LiteAire® was prescribed for individual use and was stored in the school's health office where its use was recorded by school staff. While these units were labeled for 1- week's use, they were only replaced if visibly worn or lacked obvious functionality. To assess the appropriateness of this off-label use, 104 devices with the most frequent and/or longest use were collected for microbial and functionality testing. Fifty-six control devices that were similarly opened and stored, but never used, were also evaluated.

Microbial testing was conducted by Banner University of Arizona Medical Center using validated protocols for clinical testing. Swabs were cultured from 2 locations on each unit: inside the mouthpiece chamber (MC), the "patient side", and inside the inhaler chamber (IC), the "pMDI side." (Figure 1) Analyses of colony forming units (CFUs) were conducted using linear regression and non-parametric testing with Minitab (State College, PA) and MedCalc (Ostend, Belgium).

The number of pMDI uses (2 puffs per use) was a stronger predictor of microbial load (R^2_{adj}=0.10, p=0.0007) than duration of use (R^2_{adj}=0.02, p=0.11). Because the association was stronger on the MC "patient side" (R^2_{adj}=0.11, p=0.0004) than the IC side (R^2_{adj}=0.05, p=0.02) and because the MC results were thought to be more clinically relevant, only MC results are presented.

The 104 active LiteAire® units were used a mean of 15.6 times (SD 21.4, range 1–141); the average number of days from first use to last use was 60.9 days (SD 47.3, range 1–200). (Table 1) Overall, the average microbial load was 3.0 CFUs (SD 10.7, range 0–88) with 59% of units having no growth. While receiving similar use, units stored in sealed plastic bags/ containers (37 units) had a higher microbial load than those stored open-to-air (67 units), 5.6 (15.7) CFUs versus 1.7 (16.5) CFUs, respectively (p<0.001).

Due to its paperboard matrix, the LiteAire® can absorb moisture from the subject's breath during use and moisture is known to facilitate microbial growth. However, paperboard is made of randomly networked fibers preventing a continuous layer of water from forming and thereby discouraging microbial growth [7]. Permitting units to dry between uses by storing them open-to-air may further hinder microbial growth [8].

A number of functionality tests including those for "pop-ability" "collapse-ability", valve resistance, visual assessment, and total emitted dose (TED) without simulated breathing

were conducted by Thayer. Of the 42 units tested, 28 were active units and 14 were control units. All units passed functionality testing.

At present, LiteAire® units are FDA approved for 1 week's use; however, labeling them by the number of uses might be more appropriate given that duration of use does not appear to independently predict bacterial growth. The original labeling was based on equivalent or lower bacterial growth than existing FDA-approved plastic VHCs after purposeful inoculation of devices with *Streptococcus* and *Staphylococcus* bacteria during 28 simulated uses over a 7 day period. Because LiteAire® units are not expected to be sterile devices, we used the average bacterial growth from those units that had been used consistent with the original labeling (≤7 days and ≤28 uses) to establish an acceptable amount of growth.

When these control units were compared to units that were more heavily used, the more heavily used units had a greater microbial load, p=0.002. A receiver operator characteristic (ROC) curve analysis demonstrated that a cutoff of 39 uses identified 100% of the more heavily used units that exhibited a higher microbial load than the control units (≥2.1±7 CFUs). At this cutoff, the specificity was 93%.

Because our study was conducted in a climate with very low humidity (Tucson, Arizona), the results may not be generalizable to other locations. Because the units were used in school children 5–11 years of age, the results may not be generalizable to other populations. Because Lite-Aire® units cannot be paired with a nebulizer mask, they are not appropriate for use among younger children (e.g., preschool) who lack the strength and coordination to use an inhaler.

In summary, our data indicate that number of uses rather than duration of use best predicts microbial load and hence potential risk to the patient. Therefore, we believe the LiteAire® device can be used at least 39 times over a 6-month period without exceeding the microbial exposure associated with its original FDA approval based on 28 simulated uses over 7 days. [9] Accordingly, we believe that the LiteAire® VHC is an excellent choice when there is a need for a disposable, low cost, collapsible VHC to be used either consistently over a short period of time or irregularly over a longer period of time. Optimal settings include schools, emergency departments, outpatient clinics, pulmonary function labs, jails, or prisons. While the most common application will be to administer quick relief medication; the LiteAire® device can also be used to administer controller medication.

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Clinical Implications

Because the number of uses predicts bacterial growth better than the duration of use, the paperboard LiteAire® holding chamber can be safely used for longer than its current 1-week labeling before exhibiting unacceptable bacterial growth.

Figure 1.

A LiteAire VHC in a. its flat position, b. its ‘popped-up’ form holding a metered dose inhaler (MDI) and c. in its cut-away view showing inside the mouthpiece chamber (MC) on the left and the Inhaler Chamber (IC) on the right.

Table 1

Summary of usage data for all 160 LiteAire VHCs.

	Used Devices	Control Devices
Number of Units	**104**	**56**
Number of pMDI Uses (2 puffs per use)		
Range	1–141	0
Mean ± SD	15.6 ± 21.4	0
Median	7	0
Significance in predicting Microbial Load	R^2_{adj}=0.11, p=0.0004; SIGNIFICANT	
Number of Days		
Range	1–200	0
Mean ± SD	60.9 ± 47.3	0
Median	59	0
Significance in predicting Microbial Load	R^2_{adj}=0.02, p=0.11; NOT SIGNIFICANT	
Storage Methods		
Sealed (Count / %)	37 / 35.6%	24 / 42.8%
Open to Air (Count / %)	67 / 64.4%	32 / 57.1%
Significance in predicting Microbial Load	R^2_{adj}=0.09, p=0.002; SIGNIFICANT	
Microbial Load in MC		
Range	0–88	0–4
Mean ± SD	3.07 ± 10.73	0.14 ± 0.62
Median	0	0
Open to Air / Sealed (Mean ± SD)	1.6 ± 6.5 / 5.6 ± 15.6	0.13 ± 0.42 / 0.17 ± 0.82
<=39 uses / >39 uses (Mean ± SD)	2.1 ± 6.9 / 11.1 ± 25.9	0.14 ± 0.62 / N/A