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ORIGINAL ARTICLE

Evaluation of asthma control, parents' quality of life and preference between AeroChamber Plus and AeroChamber Plus Flow-Vu spacers in young children with asthma

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Abstract

Objective: The AeroChamber Plus (AC) valved holding chamber has been enhanced to include the Flow-Vu (FV) inspiratory flow indicator that provides visual inhalation feedback during use. We have investigated if FV alters asthma control and whether parents accept it. *Methods*: At visit 1, children with asthma, age 1–5 years, used an AC with their pressurised metered dose inhaler and 2 weeks later (visit 2) they were randomised to use either AC or FV. Subjects returned 6 (visit 3) and 12 (visit 4) weeks later. The Asthma Control (ACQ) and Paediatric Asthma Caregiver's Quality of Life (PACQLQ) questionnaires were scored at each visit, and their peak inhalation flow (PIF) when they used their spacer was measured. *Results*: Forty participants in each group completed the study. There was no difference in the ACQ scores from visits 2 to 4 between the two groups. The improvements in the PACQLQ scores were greater in the FV group ($p = 0.029$). The mean difference (95% confidence interval) for the change from visits 2 to 4 between FV and AC groups was 0.05 (−0.33, 0.43) and 0.39 (0.035, 0.737) for the ACQ and PACQLQ, respectively. Most parents preferred the FV ($p < 0.001$). There was no difference in the PIF rates at each visit and between the two spacers. *Conclusions*: There was no change in asthma control of the young children but that of their parents improved. Parents preferred the FV and this could be related to their improved perception of their children's asthma control by better PACQLQ scores.

Keywords

Caregiver, infants with asthma, parents, spacer, quality of life, visual indicator

History

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Introduction

Inhalation therapy remains the cornerstone for the therapeutic management of asthma [1–4]. Despite the availability of many inhaler devices with various design and formulation, the pressurised metered dose inhaler (pMDI) is still widely prescribed by the healthcare providers [5,6]. The success of the pMDI therapy, therefore, depends not only on the therapeutic active ingredients of the pMDI, but also crucially on the correct inhaler technique used by the patients themselves [5,7–10]. Indeed, both children and adults with asthma experience the same problems when using their pMDIs. However, these problems are more pronounced in children, with a greater number of errors seen in those aged under 6 years [11]. Consequently, less than 50% of those children would get the desired therapeutic outcome of their inhaled therapy [3].

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Valved holding chamber (VHC) devices, commonly referred to as spacers, are used with pMDIs to overcome the common problem of hand–lung coordination associated with the pMDI use [12–14]. When compared to the improper use of a pMDI alone, inhalation of the dose through a pMDI connected to a spacer device significantly improved the aerosol lung deposition [1,15,16] and reduced both the oropharyngeal [17] and systemic [18] inhaled corticosteroid-related adverse effects. Therefore, both national [19] and international [20] Asthma Management Guidelines recommend using spacer devices in young children receiving pMDI therapy.

Nevertheless, up to 40% of the children use their pMDI inadequately even with a spacer [21]. Verbal counselling on correct inhaler technique is effective in all age groups [22], but only 50% of the patients were using the correct pMDI technique 1–30 days after having been trained and demonstrated the correct pMDI technique [3].

Accordingly, a regular inhaler technique check-up and training is needed even after a long period of inhaler use [2,21,23]. Moreover, a multiple feedback mechanism for a sufficient inhaler use would be useful for subjects with

asthma and their caregivers, and should enhance the patients' compliance and thus asthma control [23]. Although there is some debate in the literature regarding the optimal peak inspiratory flow (PIF) with the pMDI alone or pMDI plus VHC, several studies reveal an ideal PIF of <30 l/min [10,24]. If patients cannot learn to achieve a PIF of <30 l/min, then a PIF <60 l/min is preferable. Many patients, however, inhale too fast when they use a pMDI [25,26]. It has been shown that an inhaler training tool giving an audible feedback helps the patients to maintain the trained pMDI technique with a slow inhalation [22,27]. Similarly, the AeroChamber Plus® spacer (Trudell Medical International, London, ON) helps the patients use a slow inhalation by producing a sound when the inhalation flow exceeds 60 l/min. Recently, the feedback mechanism when using the AeroChamber Plus VHC has been enhanced by the inclusion of a visual feedback mechanism to indicate inhalation; the AeroChamber Plus® with Flow-Vu® inspiratory flow indicator (Trudell Medical International, London, ON) as shown in Figure 1. This visual feedback also confirms a tight seal between the facemask of the spacer and the patient's face (round the nose and mouth), ensuring no aerosol leakage. The inset in Figure 1 which highlights the ''flow-vu'' is the only difference between the two versions of the spacer.

The main aim, therefore, of the current research study was to determine if the routine use of the recently introduced VHC, the AeroChamber Plus with Flow-Vu (FV), would alter asthma control in pre-school children with asthma, compared with the use of the currently available VHC, the AeroChamber Plus (AC). Comparison of the inhalation flow used by the children through these VHCs was also investigated. Moreover, the impact on the quality of life of those children's parents as direct caregivers was studied. The study was integrated into the routine medical care at paediatrics respiratory outpatient clinics.

Figure 1. The AeroChamber Flow-Vu Valved Holding Chamber.

Methods

Children with asthma and their parents (caregivers) attending the paediatrics respiratory out-patient clinics at NHS teaching hospitals (United Kingdom) for routine medical care and fulfilling the study's inclusion criteria were invited to take part in this research study. Children aged 1 to 5 years with partly controlled- or uncontrolled asthma according to GINA (2008) criteria and receiving parentally supervised inhalation therapy including an inhaled corticosteroid via a pMDI plus a spacer device were considered eligible for participation. The children were excluded if their inhalation treatment had been changed over the last 4 weeks prior to enrolment, were using a dry powder inhaler or a breath-activated pMDI, had limited physical or mental ability to use a spacer or follow the study procedures, or had other chronic disease conditions at study enrolment that might adversely affect their quality of life. All asthmatic children and their parents gave signed informed consent prior to enrolment. The study was approved by Bradford Research Ethics Committee, UK (Ref: 08/H1302/24), and the Research and Development department within each of the clinics involved. The study was conducted in accordance with Helsinki Declaration on Good Clinical Practice (ICH/GCP Guidelines). The children were randomised to use the AC or the FV according to a pre-study designed randomisation table.

This prospective, randomized, parallel-grouped comparative study investigated the effect of the routine use of the novel FV VHC (designed with a visual feedback reassurance mechanism of an optimal inhalation), on asthma control in asthmatic children, compared with the routine use of the currently available AC VHC. The yellow facemask versions of both VHCs were used. Changes in the children's peak inhalation flow through a pMDI plus spacer and in the health-related quality of life of their parents were assessed as well.

The first group was the FV VHC group; patients enrolled into the FV group used the novel AeroChamber Flow-Vu VHC device connected to their pMDIs. The second study group was the AC VHC group; patients enrolled into the AC group used the currently available AeroChamber device (which does not have the visual feedback indicator). The age, sex and height of each child in both groups were also recorded.

The study involved four clinic-based visits. At visit 1 (recruitment), all participants were enrolled into a 2-week run-in period, where, irrespective of the spacer device the children were using before enrolment, they were given- and verbally trained to use an AC spacer over the run-in period. At visit 2 (baseline), each asthmatic child was randomized into either the FV or AC group according to a previously constructed randomization table. All parents along with their asthmatic children were trained to use the inhalation method they had been randomized to use. The training session continued until the parent and their child satisfactorily demonstrated the correct pMDI plus spacer technique, otherwise they were withdrawn from the study and referred to their doctor/practice nurse for inhaler device assessment. However, there were no related screen failures or withdrawals among the participants throughout the study. All parents were instructed that their child's inhaled corticosteroid pMDI

should be attached to the spacer. Visit 3 occurred 6 weeks after visit 2 and visit 4 another 6 weeks later (study end – 12 week study).

At each of the four study visits, the child's peak inhalation flow (PIF) was measured using the In-Check Meter® (Clement Clarke International Ltd, Harlow, UK), mimicking the inhalation flow achieved through a pMDI connected to a spacer. The child's parent completed the first six items of the Asthma Control Questionnaire (ACQ) [28] on their child's behalf. Moreover, the parent completed the Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ) [29]. Any changes to the child's asthma medications over the study visits were also checked and recorded with the reason for the change, as appropriate. At the end of the study, the parents, in the AC and FV groups, completed a preference question, where each FV parent was asked to rate their preference between the AC and the FV using a 5-point Likert scale (5 = much better to 1 = much worse). The FV spacer was demonstrated to all AC parents and they were then asked the same preference question and rating.

Statistical analysis

All analyses were undertaken using SPSS (Version 20.0; IBM Software, Armonk, NY). Descriptive statistics were recorded at all measured time points. Main effects multivariate analyses of covariance (MANCOVA) were derived for the analysis of change scores in the AC and FV groups with respect to the ACQ and PACQLQ questionnaires, as the joint assessment of these measures was considered to be empirically meaningful. The suitability of the MANCOVA model for this analysis was verified by determination of correlations between outcomes at the measured time points. For both the ACQ and PACQLQ questionnaires, the primary analysis was the change between baseline and final readings, i.e. from 0 to 12 weeks. Changes between preliminary (−2 weeks) and baseline measures (0 weeks); and between baseline (0 weeks) and interim (6 weeks) measures were also considered as a secondary analyses.

For the ACQ scale, the outcome measure utilised was the total score, calculated as the un-weighted mean score from each of the 6 sub-scales comprising the ACQ scale. Possible scores range from 0.0 to 6.0, with lower scores indicating greater control. For the PACQLQ scale, the outcome measure utilised was the total score, calculated as the weighted average of the Activity and Emotion subscales, with higher scores indicating greater functionality. Age, height and gender were additionally included as controlling variables in all MANCOVA and ANCOVA models.

It was judged that there was no theoretical or empirical basis to assess the PIF outcome jointly with the ACQ and PACQLQ outcomes; hence separate univariate analyses of covariance (ANCOVA) were conducted on the PIF measure.

All parameters found to exhibit significant associations with the ACQ and PACQLQ variables assessed jointly were subject to additional follow-up ANCOVA procedures to provide further insight into the nature of the relationship. A discriminant function analysis was also undertaken for the key factor (group) on the primary analysis only.

The preference question response was analysed independently of other outcomes. Parental preference was compared using the Mann–Whitney U test. An overall view of parental preference was obtained using the one-sample Wilcoxon signed rank test, testing the median statistic against the test statistic of 3 (corresponding to no preference between the AeroChamber equipment with and without the addition of the Flow-Vu device).

Results

Eighty (40 in each group) children with asthma started and all completed the study as shown in Table 1. All children were receiving daily low doses (100 mcg) of beclomethasone dipropionate and as-needed inhaled salbutamol at least 4 weeks before recruitment. Both medications were delivered by pMDIs plus facemask spacers. No change in the asthma medications was recorded for all participants throughout the study period. There were no screen failures at recruitment or withdrawals among the participants throughout the study. There was no difference between the ACQ, PACQLQ and PIF outcome variables between visit 1 (recruitment) and visit 2 (study start).

A summary of the ACQ and PACQLQ scores as well as the PIF at each visit are presented in Table 2 and in Figures 2–4, respectively. For the analysis of the change in the ACQ and PACQLQ outcome measures from baseline (visit 2) to study end (visit 4), that is from 0 weeks to 12 weeks, the MANCOVA model showed when controlling for baseline scores, age, height and gender, that there was no evidence for a significant difference at the 5% significance level between the two groups when the change in ACQ and PACQLQ were assessed jointly ($\Lambda = 0.922$; $F_{2,72} = 3.05$; $p = 0.054$). Although there was a difference between the age ($p = 0.024$) and height ($p = 0.036$) between the two groups at baseline this did not influence the ACQ and PACQLQ. However, a degree of substantive significance was indicated, with the effect being classified as borderline significant. The partial η^2 statistic of 0.078 indicated an effect of low-to-medium magnitude.

Follow-up univariate ANCOVA models indicated that group was significantly related to final PACQLQ scores ($F_{1,73} = 5.75$; $p = 0.019$) and not significantly related to final ACQ scores. The within-group mean difference (95% confidence interval) for the PACQLQ between visits 2 and 4 in the FV and AC groups was 0.51 (0.279, 0.742) and 0.13 (−0.146,

Table 1. Patient demographic data.

Variable	All participants	AC group	FV group
	Frequency (%)		
Gender	$n = 80$	$n = 40$	$n = 40$
Males	51 (63.8%)	27 (67.5%)	24 (60.0%)
Females	29 (36.3%)	13 (32.5%)	16 (40.0%)
	Mean (SD)		
Age (years)*	3.09 (1.05)	3.35 (1.09)	2.83 (0.93)
Height (cm)*	95.8 (15.8)	99.5 (12.7)	92.1 (17.6)

*The difference in age ($p = 0.024$) and height ($p = 0.036$) between AC and FV groups at baseline did not influence the study outcome measures.

Table 2. Mean (SD) questionnaires scores and inhalation flow for each visit.

	Visit 1	Visit 2	Visit 3	Visit 4
ACQ				
AC	1.91 (1.11)	1.54 (0.89)	1.72 (1.15)	1.35 (0.85)
FV	1.75 (0.54)	1.78 (0.85)	1.47 (1.09)	1.54 (0.96)
PACQLQ (total)				
AC	4.97 (1.05)	5.23 (0.95)	5.17 (1.23)	5.36 (1.11)
FV	5.34 (0.90)	5.51 (1.12)	5.94 (1.03)	6.02 (1.05)
PACQLQ (activity)				
AC	5.14 (1.15)	5.33 (1.08)	5.32 (1.38)	5.46 (1.26)
FV	5.14 (0.95)	5.31 (1.30)	5.98 (1.12)	6.04 (1.10)
PACQLQ (emotion)				
AC	4.89 (1.13)	5.19 (1.08)	5.12 (1.30)	5.12 (1.30)
FV	5.43 (1.03)	5.60 (1.16)	5.92 (1.07)	6.01 (1.12)
Peak inhalation flow (l/min)				
AC	41.2 (13.3)	40.8 (12.6)	41.8 (13.3)	40.5 (13.2)
FV	37.3 (14.4)	36.8 (13.7)	37.3 (14.1)	37.9 (13.6)

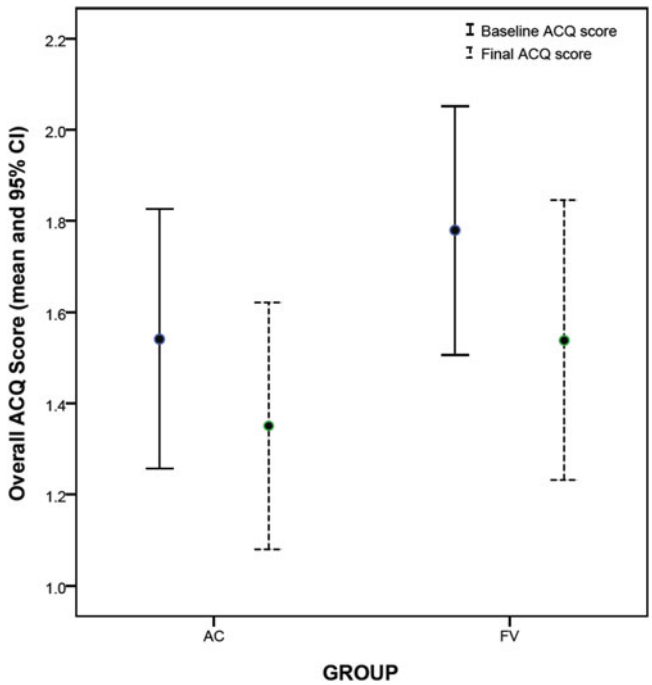

Figure 2. Mean and 95% confidence interval for ACQ scores at baseline (visit 2) and study end (visit 4).

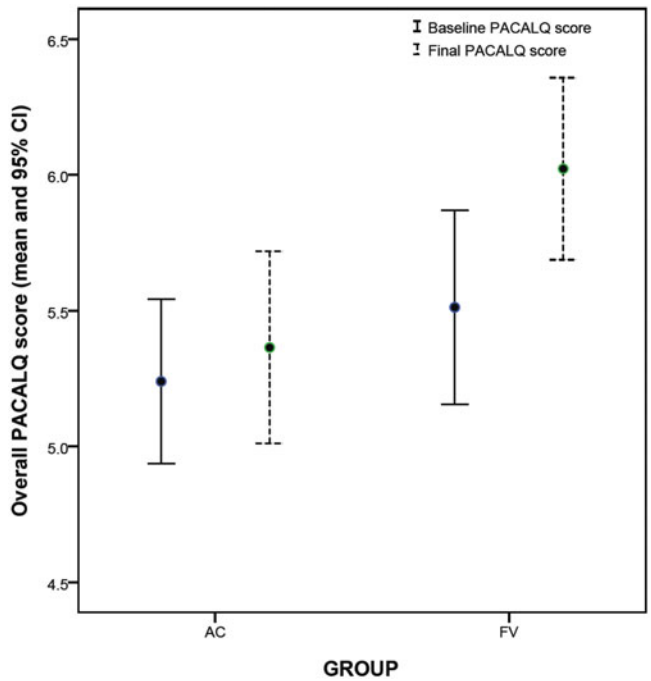

Figure 3. Mean and 95% confidence interval for PACQLQ at baseline (visit 2) and study end (visit 4).

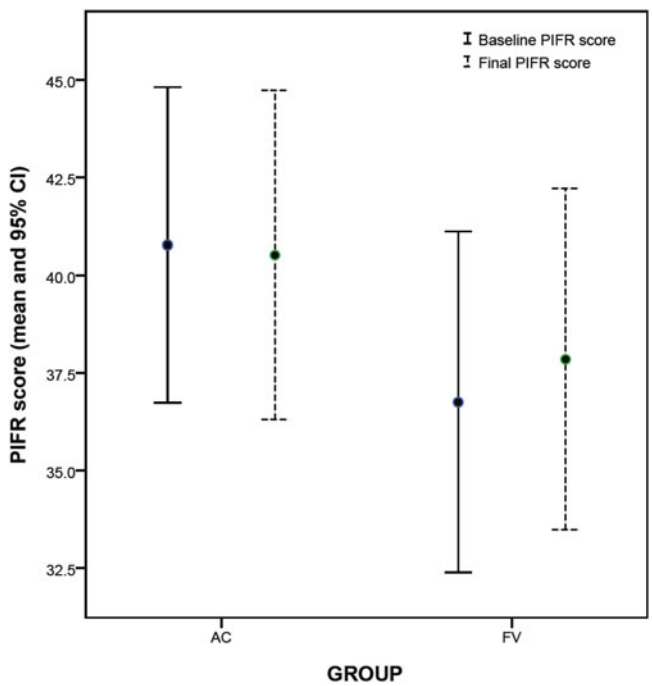

Figure 4. Mean and 95% confidence interval for peak inhalation flow at baseline (visit 2) and study end (visit 4).

0.396), respectively, and between the two groups this difference was 0.39 (0.035, 0.737) greater in the FV group. The mean difference (95% confidence interval) for the change (between visits 2 and 4) in the ACQ in the FV and AC groups was −0.242 (−0.58, 0.09) and −0.19 (−0.38, −0.03), respectively. Comparing between the two groups, the mean difference (95% confidence interval) was 0.05 (−0.33, 0.43) with no discrimination between the two groups.

A follow-up discriminant function analysis derived a single discriminant function (canonical $R^2 = 0.296$) which effectively discriminated between groups ($\Lambda = 0.912$; $\chi^2_{(2)} = 7.07$; $p = 0.029$).

The standardised discriminant function coefficients of 0.976 for the change in the PACQLQ scores and 0.078 for the ACQ scores highlight the relative importance of PACQLQ in defining the variate. Correlations between outcomes and the discriminant function revealed that final PACQLQ scores loaded heavily onto the function ($r = 0.997$) and final ACQ scores less so ($r = 0.339$).

For the analysis of change in the PIF outcome measure from visit 2 (baseline) to the final time point, the ANCOVA model showed that controlling for baseline PIF score, age, height and gender, there was no difference within each group and between the two groups ($F_{1,74} = 0.337$; $p = 0.564$).

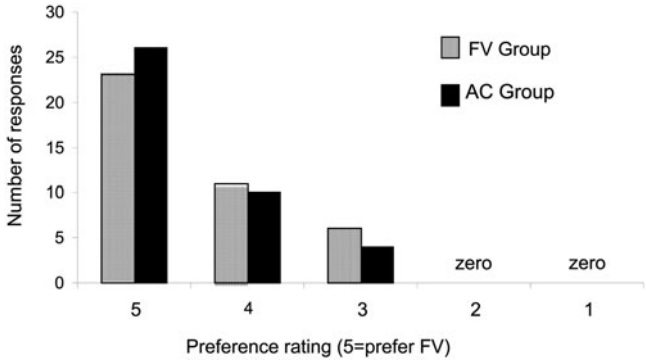

Figure 5. Likert preference score by the parents about their perception about the AeroChamber Plus Flow-Vu Valved Holding Chamber (5 = FV most preferred, 1 = AC most preferred).

Figure 5 shows that at the end of the study the majority of the FV parents had a strong preference for the Flow-Vu version of the AeroChamber. Similarly, when the AC parents were demonstrated the Flow-Vu version at the end of the study they too had a strong preference for this version. The median (range) preference of the FV and AC parents was 5 (3–5) in both groups. For these parental preference scores, a Mann–Whitney *U* test indicated a non-significant difference in preference scores between the AC and FV groups ($Z = 0.755$; $p = 0.450$). A Wilcoxon single sample signed ranks test found that the median preference score was significantly different to the ''neutral'' option 3 ($p < 0.001$) in both groups.

Discussion

Adequate technique of the pMDI alone has shown the same efficacy and safety as using a pMDI plus spacer [30]. However, patients with asthma who continue to have the problem of co-ordinating the pMDI activation with inhalation, even after repeated technique training sessions, are commonly prescribed a spacer device to use with their pressurised inhalers [13]. This has been instituted in the Asthma Management Guidelines as a recommended practice in young children aged less than 12 years where the issue of poor pMDI technique is more evident [19,20]. These recommendations toward the use of spacers have been based on the advantages that these devices provide in terms of improved lung deposition of inhaled bronchodilators [15,31] and inhaled corticosteroids [17,32], accompanied with improved safety.

Despite repeated training of children with asthma on the correct pMDI-spacer use, many children continue to have inadequate spacer technique [21,33,34]. A report by the Aerosol Drug Management Improvement Team (ADMIT) on the need to improve the inhalation technique in Europe has stated that inhalation devices, enhanced with a multiple feedback mechanism to reassure the patients and their caregivers that the performed inhalation technique via an inhaler is sufficient, should improve the overall correct inhaler use and ultimately disease control [23]. Additionally, the patients' adequate pMDI-spacer technique is infrequently checked by the busy healthcare providers [35], thus inhalation devices with good technique feedback mechanisms can be helpful to the patients and their caregivers. The AC VHC helps the patients use a slow inhalation flow rate (IFR), as the spacer whistles when the patient exceeds an inspiratory flow of 60 l/min. This audible feedback has been recently enhanced by the inclusion of a visual indicator, the Flow-Vu (FV), to confirm inhalation and a good seal between the VHC and the face of the patient. The current work, therefore, compared the routine use of the AC and FV VHC by infants with asthma in terms of asthma control along with their parents' quality of life and spacer preference. The infants' PIF via the VHC was also evaluated.

The composite of both the ACQ and quality of life tools has been previously used in children and adults with asthma [36]. It has been demonstrated that the asthma control tools were predictive of the adults and children's asthma-related quality of life questionnaires' outcomes [37]. Moreover, Stelmach et al. (2012) have shown that the use of the PACQLQ was a useful tool for monitoring asthma control in children with asthma, where a significant correlation was found between the PACQLQ and the asthma control parameters [38]. In the current work, the primary analysis identified that when the changes in the ACQ and PACQLQ questionnaire scores were analysed together there was a borderline significance between the groups that was derived almost entirely from the relationship of grouping with the Paediatric Asthma Caregiver's Quality of Life Questionnaire scores which were well discriminated by the group. The improvement in the PACQLQ was greater in the FV group, and the overall change was greater than 0.5. This could be reflected by parental preference for the AeroChamber Flow-Vu, in that it would have provided the parents with reassurance that their child was receiving a dose during their inhalation manoeuvre. A similar, but small improvement in the asthma control indicated by the ACQ occurred in both groups, but the change was less than the 0.5 decrease that is regarded as clinically significant [39]. This might be justified by the limited 12-week follow-up duration of the study that might have been insufficient to establish this difference.

Although a better lung deposition was reported with an IFR around 30 l/min through a pMDI [10,24], a definite value for an optimal, slow IFR through a pMDI is still debated in the literature [10,24,40–43]. Generally, an IFR <60 l/min is considered slow enough to result in an acceptable lung deposition and thus therapeutic effect. However, the majority of patients were previously reported to inhale at a faster rate (>100 l/min) when they used their pMDI therapy [27,44]. In the current work, the infants' mean baseline IFR, mimicking normal tidal breathing, through the study spacers at study enrolment (visit 1) was slow and well below 60 l/min for the two study groups (41.2 l/min AC group; 37.3 l/min FV group). Although the PIF of the FV group was generally slower than that of the AC group, no significant difference in the PIF was demonstrated between the two groups throughout the study period. Both the AC and FV spacers, however, did maintain the infants' inhalation manoeuvres within the desirable slow inhalation flows recommended for the pMDI device.

Despite the similarity between the current AC spacer and its new FV version in terms of maintaining the recommended pMDI-spacer inhalation flow, and thus the paediatric asthma control levels, the FV group parents have demonstrated more

preference for the FV spacer compared to the AC. The FV group parents stated that with the visual flow indicator they could tell that their children were actually taking their ''puff''; this was of a particular importance when their children were asleep while being given their inhaled medicine. This later parental reassurance is in agreement with a recent work that showed an aerosol therapy acceptance and advantageous lung deposition when the aerosol was delivered through a VHC, connected to a novel calming facemask, to sleeping infants [45]. Moreover, the FV group parents commented that they were able to confirm the exact number of breaths their children took through the spacer by counting the times the FV indicator moved. This visual drug delivery reassurance, therefore, might justify the significant improvement in the quality of life of the FV group parents. Similarly, when the AC group parents were demonstrated the FV spacer at the end of the study they also had a strong preference for this version. This parental preference attitude makes the FV preferred over the AC for their asthmatic infants.

Conclusion

The AeroChamber Plus VHC and its recently enhanced Flow-Vu version maintained the recommended pMDI-spacer IFR in infants with asthma. The novel flap structure in the FV spacer provided a visual feedback to the parents, reassuring them of sufficient therapy inhaled by their infants. Moreover, the indicator's movement enabled the parents to count the number of breaths taken by their children via the spacer as per their healthcare providers' recommendation. Therefore, those parents preferred the recent FV spacer, and this could be related to their improved perception of their infants' asthma control by better PACQLQ scores.

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Declaration of interest

WA, ST, PC and JS all have no conflict of interest. H.C. has no shares in any pharmaceutical companies. He has received sponsorship to carry out studies, together with some consultant agreements and honoraria for presentations, from several pharmaceutical companies that market inhaled products. These include AbdiIbrahim, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Innovata Biomed, Meda, Mundipharma, Omron, Orion, Sandoz, Teva, Trudell Medical International, and UCB. Research sponsorship has also been received from grant awarding bodies (EPSRC and MRC). We are grateful to Trudell Medical International, Canada, for providing an unconditional grant which was used for the use of facilities at the clinics used in the study.

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