

ADHERENCE

Optimizing the Inhalation Flow and Technique Through Metered Dose Inhalers of Asthmatic Adults and Children Attending a Community Pharmacy

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Objective. Despite training, many patients continue to misuse their metered dose inhaler (MDI). Research Ethics Committee approval was obtained to evaluate two different methods to help patients use a slow inhalation flow when they use their MDI. **Methods.** Asthmatic children ($n = 17$) and adults ($n = 39$) prescribed an MDI had their inhaler technique assessed. Those who achieved the recommended inhalation flow rate (IFR) of <90 l/min through their MDI formed the reference group (named (control—CT)). Others that had a poor inhaler technique with an IFR ≥ 90 l/min were randomized into either the verbal counseling (VC) group, who received verbal training on the correct MDI use with emphasis on using a slow IFR or into the 2ToneTrainer (2TT) group, who received the VC and a 2Tone Trainer to take home and use. 2TT is a training aid with audible feedback when the required slow inhalation flow is used. The participants were assessed on two occasions, 0 (baseline) and 6 weeks later. **Results.** For the asthmatic adults, the median IFR at visit 1 was 68, 200, and 240 l/min for the CT, VC, and 2TT groups, respectively. Whereas on visit 2, the median IFR was 88, 48.5 ($p < .001$), and 65 ($p < .001$) l/min for the CT, VC, and 2TT groups, respectively. Improvements in asthma quality of life were achieved in VC and 2TT groups. The asthmatic children showed a similar trend. **Conclusions.** Training by VC and a training aid helps patients use a slow IFR with an MDI and improves asthma-related quality of life.

Keywords 2ToneTrainer, asthma control, inhalation flow rate, inhalation technique, quality of life, verbal counseling

INTRODUCTION

The metered dose inhaler (MDI) is the most commonly prescribed inhaler device among those available for managing respiratory conditions (1, 2). The deceptive simplicity of the MDI technique may result in a suboptimal therapeutic outcome of the inhaled medications as many patients misuse their pressurized inhalers (1–7).

Many research studies have confirmed the importance of coordinating the actuation of the MDI canister with inhalation through the inhaler (1, 8, 9), a challenge that many patients face when using their MDI (10, 11). However, a slow and deep inhalation flow through the MDI has been found to be much more critical, in terms of aerosol lung deposition, than a perfect hand–lung coordination, provided that the patient is inhaling at the time of aerosol release (12, 13). A definite value for a slow inhalation flow rate (IFR) through an MDI is still debated in the literature; however, an IFR < 90 l/min is considered slow enough to result in an acceptable lung deposition and thus therapeutic effect (14–17). The majority of patients were reported to inhale at a faster rate (> 100 l/min) when they used their MDI therapy (18, 19).

Training patients on the correct MDI technique improves their inhaler use (20–23). However, patients do forget the correct inhaler use with time after the training session (21, 24), which mandates repeated inhaler technique reinforcement and training (2, 22, 25). An MDI technique training tool, the 2Tone Trainer (2TT) (Canday Medical Ltd., UK),

has been introduced. 2TT is an MDI-like tool without a canister that has been designed to give an audible feedback depending on the inhalation speed achieved when the user inhales through the tool. In order to do so, the 2TT has two sets of sensitive reeds fitted inside; the first one vibrates only when the IFR is between 30 and 60 l/min (the ideal IFR through the MDI) producing a mono-tone sound (low pitch). If the IFR exceeds 60 l/min (too fast), the second set of reeds is triggered producing a two-tone noise (high pitch), alarming the user to slow down their inspiration speed. When practicing the 2TT, patients should change their inspiratory efforts to maintain the mono-tone sound throughout the whole inhalation maneuver (i.e., inhale slowly and deeply), and then simulate this effort when they use their real MDI. Within the setting of a secondary care outpatient clinic, 2TT was found to help decrease IFR through MDIs with clinically significant improvements in asthma quality of life (18).

The aim of the current study was to investigate if methods to train patients to use a slow IFR with their MDI, within a primary care setting of patients attending a community pharmacy, would improve and maintain good MDI use. Reflections on the asthma-related clinical and quality of life outcomes were also evaluated. The study was incorporated into the normal pharmacist's role in patients' counseling at a community pharmacy setting.

METHODS

Patients with asthma who collected their MDI prescriptions from community pharmacies were directly invited

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to take part in this study. Any 4- to 55-year-old asthmatic patient, prescribed at least one MDI without a spacer device including a preventer (corticosteroid) MDI, was eligible for enrolment. Patients were excluded if they experienced an acute exacerbation of asthma or received oral prednisolone within 4 weeks prior to recruitment, had other illnesses adversely affecting their respiratory system, had hearing problems, and/or were unable to distinguish between the one and two tones produced by the 2TT tool. Eligible patients, who agreed to take part in the study, signed an informed consent form (the parents/guardians in the case of asthmatic children gave the informed consent) prior to performing any study-related procedures. The study was carried out according to the good clinical practice (ICH/GCP) and was approved by the Bradford Research Ethics Committee-United Kingdom (Ref: 05/Q1202/36).

The current research was designed as a parallel-grouped clinical study. Participants were recruited into two main groups: an intervention group and a reference group (hereafter named as control group (CT) for simplicity). Allocation of subjects into either the CT or intervention groups was according to their inhaler technique (see Figure 1). Those with correct MDI technique (defined as good hand-lung coordination and an IFR < 90 l/min) formed the CT group, whereas those identified with poor technique (defined as poor hand-lung coordination and an IFR ≥ 90 l/min) formed the intervention group. The intervention group was subdivided into two groups in which the allocation of the participants was based on a previously constructed randomization table; those who were verbally counseled (VC group) on the most desirable MDI technique (26) and those who received the same verbal counseling and were also given the 2ToneTrainer tool (2TT group)

The most desirable MDI technique
1) Remove the cap from the mouthpiece.
2) Shake the inhaler.
3) Breathe out slowly, as far as comfortable to empty your lungs.
4) Place the mouthpiece of the inhaler between your lips.
5) Close your lips around the mouthpiece creating a seal.
6) Start to breathe in slowly, through your mouth and immediately press the aerosol canister to release a dose (puff).
7) Breathe in slowly until your lungs are full of air (as far as you can), the breath in step should take you about 5 seconds.
8) Remove the inhaler from your mouth and seal your lips.
9) Hold your breath for 10 seconds.
10) Breathe out slowly.
11) Repeat steps 1 to 10 after 30 seconds if another dose is necessary.

FIGURE 1.—The most desirable MDI technique.

to practice (see Figure 2—the study flow diagram). Emphasis of the verbal training (in both VC and 2TT groups) was to achieve a slow IFR by encouraging patients to increase the length of their inhalation period (26).

The study consisted of two visits with 6 weeks apart as a follow-up period. At visit 1, the demographic data were taken, asthma medications were recorded, and the FEV₁ was measured using a portable spirometer. Then, each participant completed the Juniper's Asthma Quality of Life Questionnaire (AQLQ) according to their age group as follows: adults (18–55 years) completed the Mini-AQLQ (27); children (7–17 years) completed the PAQLQ (28), whilst the PACQLQ (29) was completed by their parents; finally, the parents of the children aged 4–6 years completed the PACQLQ only. Moreover, the participants/parents answered the three asthma control key questions of the British Royal College of Physicians (RCP) (30, 31). Then, the participants had their peak inhalation flow (PIF) through an MDI measured using the In-Check meter (Clement Clark International, UK) and had their MDI technique assessed using a placebo MDI, based on which the

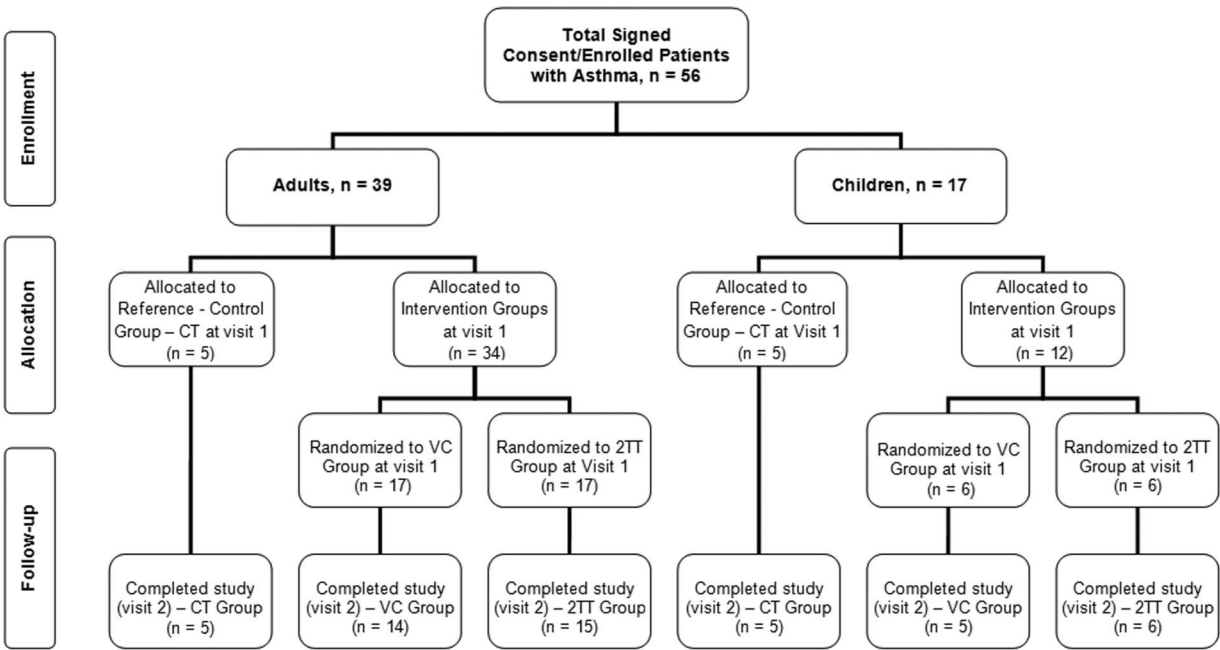


FIGURE 2.—Consort flow diagram of the study.

TABLE 1.—Demographic data of the asthmatic adults and children at study enrolment (visit 1).

Characteristics	Adult asthmatic patients				Children asthmatic patients			
	CT group	VC group	2TT group	Total adults	CT group	VC group	2TT group	Total children
Number (n)	5	17	17	39	5	6	6	17
Mean (SD) age, years	42.6 (13.2)	42.4 (7.2)	38.5 (10.8)	40.7 (9.7)	7.2 (3.1)	11.2 (2.4)	11.7 (2.4)	10.2 (3.2)
Sex (M/F)	0/5	7/10	4/13	11/28	3/2	4/2	4/2	11/6
Mean (SD) height, cm	167.1 (4.7)	169.2 (9.9)	168.4 (9.5)	168.5 (9.1)	129.2 (16.6)	147.0 (12.1)	158.2 (19.7)	145.7 (19.5)
Mean (SD) FEV ₁ % predicted	89.9 (9.1)	90.5 (18.2)	96.6 (19.8)	93.1 (17.9)	102.8 ^b (10.1)	92.2 (16.8)	88.9 (18.0)	93.0 (16.1)
Asthma severity ^a (n)	Mild	4	13	14	3	5	5	13
	Moderate	1	3	2	0	0	1	1
	Severe	0	1	1	0	1	0	1

Notes: ^aAsthma severity classification was based on GINA (2008) guidelines.

^bTwo children in the CT group were ≤5 years old and had no spirometry results.

subjects were allocated into the CT, VC, or 2TT groups as described earlier. Patients in the VC and 2TT groups received verbal training on the correct MDI technique with emphasis on achieving a slow IFR by encouraging them to prolong the length of their inhalation period over at least 5 seconds (26). The PIF was also measured immediately after the verbal counseling to ensure an IFR < 90 l/min was attained. In addition, the 2TT group received and was trained on the 2TT tool to maintain the mono-tone sound (corresponding to an IFR 30–60 l/min). The 2TT patients were instructed to practice using this tool twice daily just before taking their real MDI and to simulate the inspiratory effort needed to maintain the mono-tone sound when using their actual inhaler. The CT group was followed up without any intervention.

At visit 2, the participants' asthma medications were checked to make sure no changes in treatment had been made over the study follow-up period, then the same measurements/quality of life questionnaires were repeated.

STATISTICAL ANALYSIS

The statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS for Windows, Version 15) software. Firstly, histograms and normality distribution tests (the Kolmogorov–Smirnov and Shapiro–Wilk tests) were applied; the FEV₁ % predicted, Mini-AQLQ, and PAQLQ scores were normally distributed, while the PIF and PACQLQ scores were not normally distributed. Accordingly, comparison of measurements within the same study group (visit 1 vs. visit 2) was performed

using the related (paired)-samples *t*-test (for parametric data) and the Wilcoxon test (for nonparametric data). Comparison of measurements between different study groups was performed using the independent-samples *t*-test (for parametric data) and the Mann–Whitney *U* test (for nonparametric data). For categorical (nominal) data, correlations/comparisons were made using cross-tabulation and the chi-square (χ^2) test.

RESULTS

A total of 56 asthmatic patients (39 adults and 17 children) were enrolled into this study, and 50 patients (34 adults and 16 children) completed the two study visits as per protocol. The six patients that did not complete provided information that they were unable to attend the second visit. Figure 2 shows the progress of patients through the study. The demographic data, FEV₁ % predicted, asthma severity classification (based on GINA 2008 criteria), and study group allocations are summarized in Table 1.

Table 2 shows that there was no change in the FEV₁ values of the adults and children between visits 1 and 2. Table 3 shows no significant difference in the FEV₁ % predicted for pairwise comparisons between the study groups at either visit 1 or visit 2. Figures 3 and 4 describe the individual IFR and quality of life of the adults with summaries in Table 4 with categorization of the IFR values in Table 5. Similar data for the children are presented in Tables 4 and 6, as well as Figures 5 and 6. Comparison between the changes, from visits 1 and 2, for the IFR between the groups revealed a significant reduction ($p < .001$) in the IFR within the VC and 2TT groups.

TABLE 2.—Mean (SD) FEV₁ % predicted for all study groups at visits 1 and 2.

Adult asthmatic patients			Children asthmatic patients		
Study group	FEV ₁ % pred, visit 1	FEV ₁ % pred, visit 2	Study group	FEV ₁ % pred, visit 1	FEV ₁ % pred, visit 2
	mean (SD)	mean (SD)		mean (SD)	mean (SD)
CT (n = 5)	89.9 (9.1)	86.5 (8.6)	CT ^a (n = 3)	102.8 (10.1)	103.3 (6.4)
VC (n = 14)	90.4 (20.1)	87.2 (20.4)	VC (n = 5)	90.4 (18.1)	94.1 (4.8)
2TT (n = 15)	96.5 (21.1)	96.3 (17.6)	2TT (n = 6)	88.9 (18.0)	90.9 (14.3)

Note: ^aTwo children in the CT group were ≤5 years old and had no spirometry results.

TABLE 3.—Pairwise comparison between the study groups for the FEV₁ % predicted and IFR at visits 1 and 2.

Study group (study visit)	Mean difference (95% CI)/ <i>p</i> -value for the FEV ₁ % predicted		Mann–Whitney <i>U</i> test: <i>U</i> -value (<i>p</i> -value) for the IFR	
	Adults	Children	Adults	Children
CT vs. VC (visit 1)	−0.496 (−20.4; 19.4)/ <i>p</i> = .959	12.35 (−16.0; 40.7)/ <i>p</i> = .328	0.0 (<i>p</i> < .01) ^a	0.0 (<i>p</i> = .008) ^a
CT vs. 2TT (visit 1)	−6.6 (−27.3; 14.2)/ <i>p</i> = .514	13.9 (−13.2; 40.9)/ <i>p</i> = .265	0.0 (<i>p</i> < .01) ^a	0.0 (<i>p</i> = .004) ^a
VC vs. 2TT (visit 1)	−6.1 (−21.8; 9.7)/ <i>p</i> = .435	1.52 (−23.2; 26.3)/ <i>p</i> = .893	79.0 (<i>p</i> = .265)	14.0 (<i>p</i> = .892)
CT vs. VC (visit 2)	−0.747 (−20.9; 19.4)/ <i>p</i> = .939	9.18 (−0.46; 18.8)/ <i>p</i> = .059	26.5 (<i>p</i> = .456)	9.0 (<i>p</i> = .516)
CT vs. 2TT (visit 2)	−9.9 (−27.3; 7.5)/ <i>p</i> = .249	12.4 (−8.6; 33.4)/ <i>p</i> = .205	30.5 (<i>p</i> = .565)	14.5 (<i>p</i> = .961)
VC vs. 2TT (visit 2)	−9.1 (−23.6; 5.4)/ <i>p</i> = .207	3.22 (−12.0; 18.5)/ <i>p</i> = .645	82.5 (<i>p</i> = .334)	12.5 (<i>p</i> = .684)

Note: ^aDifference is statistically significant (otherwise not).

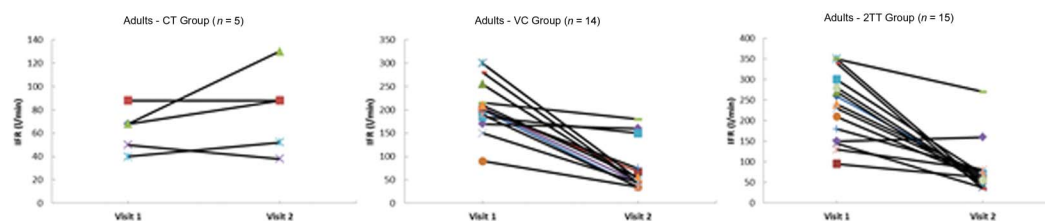


FIGURE 3.—Individual changes in IFR between visits 1 and 2 (adult groups).

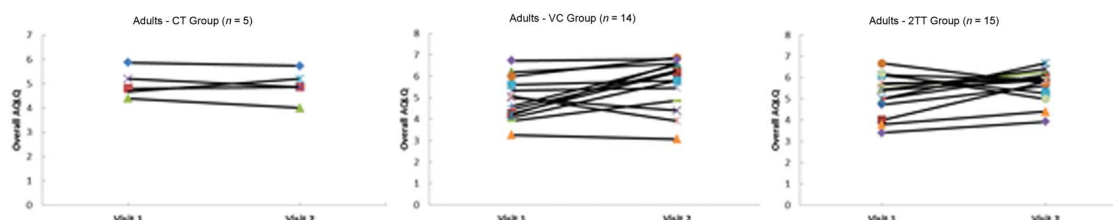


FIGURE 4.—Individual changes in overall AQLQ scores between visits 1 and 2 (adult groups).

TABLE 4.—Median (25%; 75% quartiles) of IFR at visits 1 and 2.

Adult asthmatic patients				Children asthmatic patients			
Study group	IFR (l/min), visit 1	IFR (l/min), visit 2	Δ IFR (l/min) ^a	Study group	IFR (l/min), visit 1	IFR (l/min), visit 2	Δ IFR (l/min) ^a
CT (n = 5)	68.0 (45.0, 78.0)	88.0 (45.0, 109.0)	12.0 (−6.0, 41.0)	CT (n = 5)	50.0 (42.5; 62.5)	70.0 (54.0; 100.0)	18.0 (0.0; 50.0)
VC (n = 14)	200.0 (181.2, 225.0)	48.5 (42.5, 93.7)	−143.5 (−176.2, −50.0)***	VC (n = 5)	110.0 (93.5; 200.0)	60.0 (35.0; 90.0)	−80.0 (−120.0; −33.5)***
2TT (n = 15)	240.0 (150.0, 300.0)	65.0 (45.0, 80.0)	−165.0 (−225.0, −80.0)***	2TT (n = 6)	130.0 (97.7; 172.5)	78.0 (50.0; 81.2)	−58.5 (−107.5; −19.2)***

Notes: ^aΔ: denotes the change in IFR between visits 1 and 2.

****p* < .001.

Pairwise comparisons between the study groups for the IFR are presented in Table 3; no significant difference was found in the IFR between the VC and 2TT groups at either visit 1 or visit 2.

The mean differences (95% confidence interval) of the Mini-AQLQ and its domains between visits 1 and 2 are summarized in Table 7. Similar comparison of the PAQLQ is presented in Table 8. Pairwise comparisons between the

study groups at visits 1 and 2 for the Mini-AQLQ and PAQLQ are presented in Tables 9 and 10, respectively.

For the parents' PACQLQ, the results showed that within the CT and VC groups no significant difference (*p* > .05) between visits 1 and 2 was found in the overall PACQLQ and its domains. Differences between visits 1 and 2 in the overall PACQLQ and activity limitation domain scores were significant (*p* = .031) within the

TABLE 5.—Patients (*n*, %) in the IFR categories (asthmatic adults).

Study group	IFR (l/min) category	Visit 1 (<i>n</i> , %) (baseline)		Visit 2 (<i>n</i> , %)
CT group (<i>n</i> = 5)	30–60	2	(40.0%)	2 (40.0%)
	61–89	3	(60.0%)	2 (40.0%)
	≥90	0		1 (20.0%)
VC group (<i>n</i> = 14)	IFR (l/min) category	Visit 1 (<i>n</i> , %)		Visit 2 (<i>n</i> , %)
		Before VC	After ^a VC	
	30–60	0	11 (78.6%)	9 (64.3%)
	61–89	0	3 (21.4%)	2 (14.3%)
2TT group (<i>n</i> = 15)	IFR (l/min) category	Visit 1 (<i>n</i> , %)		Visit 2 (<i>n</i> , %)
		Before VC	After ^a VC	
	30–60	0	11 (73.3%)	6 (40.0%)
		Before VC	After ^a VC	
	61–89	0	4 (26.7%)	7 (46.7%)
		Before VC	After ^a VC	
	≥90	15 (100%)	0	2 (13.3%)

Note: ^aCategorization of the IFR through an MDI measured immediately after verbal counseling at visit 1.

TABLE 6.—Patients (*n*, %) in the IFR categories (asthmatic children).

Study group	IFR (l/min) category	Visit 1 (<i>n</i> , %)		Visit 2 (<i>n</i> , %)
CT group (<i>n</i> = 5)	30–60	4	(80%)	1 (20%)
	61–89	1	(20%)	3 (60%)
	≥90	0		1 (20%)
VC group (<i>n</i> = 5)	IFR (l/min) category	Visit 1 (<i>n</i> , %)		Visit 2 (<i>n</i> , %)
		Before VC	After ^a VC	
	30–60	0	4 (80%)	3 (60%)
	61–89	0	1 (20%)	1 (20%)
		Before VC	After ^a VC	
	≥90	5 (100%)	0	1 (20%)
2TT group (<i>n</i> = 6)	IFR (l/min) category	Visit 1 (<i>n</i> , %)		Visit 2 (<i>n</i> , %)
		Before VC	After ^a VC	
	30–60	0	4 (66.7%)	2 (33.3%)
	61–89	0	2 (33.3%)	4 (66.7%)
		Before VC	After ^a VC	
	≥90	6 (100%)	0	0

Note: ^aCategorization of the IFR through an MDI measured immediately after verbal counseling at visit 1.

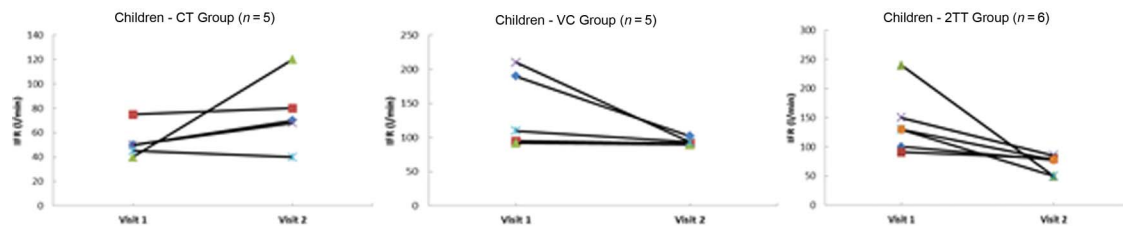


FIGURE 5.—Individual changes in IFR between visits 1 and 2 (children groups).

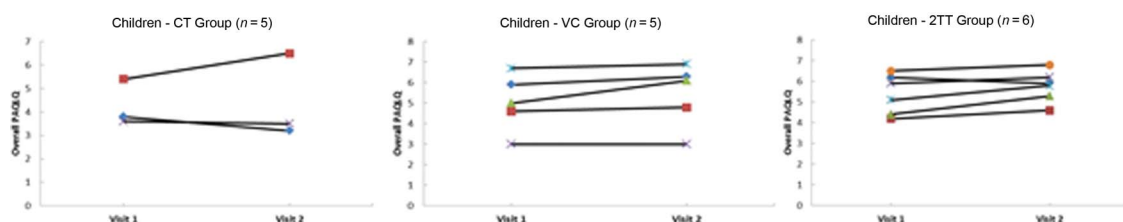


FIGURE 6.—Individual changes in overall PAQLQ scores between visits 1 and 2 (children groups).

TABLE 7.—Comparison of the Mini-AQLQ scores between visits 1 and 2 within each study group (adults).

Mini-AQLQ domains	Mean difference (95% CI)		
	Study group		
	CT group	VC group	2TT group
Overall AQLQ	0.053 (−0.41; 0.52)	−0.748 (−1.37; −0.12)*	−0.409 (−0.91; 0.09)
Symptoms	0.200 (−0.43; 0.83)	−0.729 (−1.46; −0.002)*	−0.573 (−1.20; 0.05)
Activity limitation	0.500 (−0.08; 1.08)	−0.339 (−1.01; 0.33)	−0.050 (−0.56; 0.46)
Emotional function	−0.333 (−0.84; 0.17)	−1.143 (−1.80; −0.48)**	−0.622 (−1.32; 0.07)
Environmental stimuli	−0.400 (−0.85; 0.05)	−0.929 (−1.73; −0.12)*	−0.400 (−1.12; 0.32)

Notes: * $p < .05$, ** $p < .01$ (otherwise the difference was nonsignificant).

TABLE 8.—Comparison of the PAQLQ scores between visits 1 and 2 within each study group (asthmatic children).

PAQLQ domains	Mean difference (95% CI)		
	Study group		
	CT group	VC group	2TT group
Overall PAQLQ	−0.159 (−2.33; 2.01)	−0.391 (−0.95; 0.16)	−0.362 (−0.78; 0.06)
Symptoms	−0.800 (−2.18; 0.58)	−0.500 (−0.79; −0.21)*	−0.367 (−0.93; 0.20)
Activity limitation	0.333 (−4.28; 4.95)	−0.800 (−2.22; 0.62)	−0.333 (−0.94; 0.27)
Emotional function	0.333 (−2.62; 3.28)	0.0 (−0.72; 0.72)	−0.375 (−.62; −0.13)*

Note: * $p < .01$ (otherwise the difference was nonsignificant).

TABLE 9.—Pairwise comparison of the Mini-AQLQ at visits 1 and 2 between the study groups.

Mini-AQLQ	Mean difference (95% CI)/ p -value (2-tailed)—visit 1			Mean difference (95% CI)/ p -value (2-tailed)—visit 2		
	CT vs. VC	CT vs. 2TT	VC vs. 2TT	CT vs. VC	CT vs. 2TT	VC vs. 2TT
Overall	0.077 (−0.91; 1.07) $p = .871$	−0.262 (−1.21; 0.69) $p = .568$	−0.339 (−1.07; 0.39) $p = .350$	−0.724 (−1.90; 0.45) $p = .212$	−0.724 (−1.50; 0.05) $p = .065$	0.00 (−0.74; 0.74) $p = .999$
Symptoms	0.326 (−0.77; 1.42) $p = .540$	0.147 (−1.19; 1.48) $p = .820$	−0.179 (−1.12; 0.76) $p = .700$	−0.603 (−1.90; 0.70) $p = .341$	−0.627 (−1.56; 0.31) $p = .176$	−0.024 (−0.87; 0.82) $p = .954$
Activity limitation	−0.100 (−1.15; 0.95) $p = .843$	−0.150 (−1.06; 0.76) $p = .734$	−0.050 (−0.75; 0.65) $p = .885$	−0.939 (−2.06; 0.18) $p = .095$	−0.700 (−1.76; 0.36) $p = .182$	0.239 (−0.55; 1.03) $p = .541$
Emotional function	0.262 (−1.07; 1.60) $p = .685$	−0.356 (−1.82; 1.11) $p = .616$	−0.617 (−1.65; 0.41) $p = .230$	−0.548 (−1.78; 0.68) $p = .360$	−0.644 (−1.65; 0.36) $p = .195$	−0.097 (−0.92; 0.73) $p = .812$
Environmental stimuli	−0.286 (−1.77; 1.20) $p = .690$	−1.00 (−2.33; 0.33) $p = .132$	−0.71 (−1.72; 0.29) $p = .155$	−0.814 (−2.46; 0.83) $p = .312$	−1.000 (−2.13; 0.13) $p = .079$	−0.186 (−1.16; 0.78) $p = .698$

TABLE 10.—Pairwise comparison of the PAQLQ at visits 1 and 2 between the study groups.

PAQLQ	Mean difference (95% CI)/ p -value (2-tailed)—Visit 1			Mean difference (95% CI)/ p -value (2-tailed)—visit 2		
	CT vs. VC	CT vs. 2TT	VC vs. 2TT	CT vs. VC	CT vs. 2TT	VC vs. 2TT
Overall PAQLQ	−0.76 (−3.0; 1.5) $p = .448$	−1.12 (−2.7; 0.46) $p = .138$	−0.37 (−2.0; 1.2) $p = .616$	−0.98 (−4.0; 2.0) $p = .447$	−1.33 (−3.3; 0.63) $p = .152$	−0.34 (−2.0; 1.3) $p = .651$
Symptoms	−0.99 (−3.4; 1.4) $p = .352$	−1.25 (−3.2; 0.66) $p = .165$	−0.26 (−2.0; 1.5) $p = .750$	−0.69 (−3.3; 1.9) $p = .543$	−0.82 (−2.7; 1.0) $p = .331$	−0.12 (−1.7; 1.5) $p = .867$
Activity limitation	−0.03 (−2.1; 2.1) $p = .976$	−0.50 (−1.8; 0.76) $p = .380$	−0.47 (−2.0; 1.1) $p = .507$	−1.16 (−4.0; 1.7) $p = .354$	−1.17 (−3.3; 1.0) $p = .246$	−0.006 (−1.4; 1.4) $p = .992$
Emotional function	−0.92 (−3.4; 1.6) $p = .407$	−1.35 (−3.0; 0.32) $p = .098$	−0.44 (−2.1; 1.2) $p = .558$	−1.25 (−5.0; 2.5) $p = .448$	−2.06 (−4.4; 0.3) $p = .075$	−0.81 (−2.8; 1.2) $p = .382$

2TT group, whereas they were not significant for the emotional function domain ($p > .05$).

The participants' responses to the asthma control RCP "3 questions" at visits 1 and 2 showed no significant differences ($p > .05$) for all study groups.

All participants had their MDI technique checked, using a placebo inhaler, according to the most desirable MDI technique steps (total 11 steps; see Figure 1), at both visits 1 and 2. For the asthmatic adults, the median (quartiles) of the incorrect steps at visit 1 was 3 (1; 3.5) for the CT group, 5.5 (5; 7) for the VC group, and 5 (3; 6) for the 2TT group. Whereas at visit 2 the median (quartiles) of the incorrect MDI steps was 2 (1; 2.5) for the CT group, 0 (0; 1) for the VC group, and 1 (0; 2) for the 2TT group. For the asthmatic children, the median (quartiles) of the incorrect MDI technique steps at visit 1 was 2 (1.5; 4) for the CT group, 8 (6.5; 8) for the VC group, and 6 (5.5; 7.25) for the 2TT group. Whereas at visit 2 the median (quartiles) of the incorrect steps was 3 (2; 4.5) for the CT group, 1 (0; 3.5) for the VC group, and 1.5 (0; 2.25) for the 2TT group. For both the adults and the children, the statistical analysis showed nonsignificant differences ($p > .05$) in the incorrect MDI steps between visits 1 and 2, within the CT group. While the improvement in the MDI technique was statistically significant ($p < .01$) for the VC and 2TT groups. Moreover, no significant difference ($p > .05$) in the incorrect MDI steps was found at visit 2 among the CT, VC, and 2TT groups.

DISCUSSION

Inhalation is the principal route for drug delivery in asthma treatment (2, 32, 33). The efficiency of the MDI, in terms of lung deposition, is influenced by many factors and the patient's MDI inhalation technique is a critical one (3, 11). Due to differences in study design, the results of studies into poor MDI technique demonstrate wide variations ranging up to 92% (8, 10, 18, 34, 35).

It is crucially important that patients inhale slowly and deeply when using their MDI (26) because high IFRs reduce lung deposition and increase the fraction of the aerosol dose in the oropharynx by inertial impaction (3, 12, 13). An optimal IFR through the MDI is still controversial. Dolovich et al. (1981) have suggested an $\text{IFR} < 60$ l/min for an optimal lung deposition. Indeed, the relative bioavailability of salbutamol to the lung was greater at a slower IFR (10 l/min) than at a higher flow (50 l/min) (15). Similarly, Newman et al. (16) showed that the total lung deposition decreased from 11.2% to 7.2% when the IFR was increased from 37 to 151 l/min. Moreover, a gamma scintigraphy study demonstrated that the best lung deposition when using an MDI was achieved with an IFR of 90 l/min (17). Pharmacokinetic studies have also shown that a slow and deep inhalation through an MDI, followed by a 10-second breath-holding, would result in the maximal lung deposition (15, 36). These studies, therefore, confirm that lung deposition when using an MDI is flow-dependent and those

IFRs < 90 l/min are the most recommended. However, the greater percentage of patients inhale at a faster rate (> 100 l/min) through their MDI (18, 19), and the findings of the present study were no exception.

Various methods have been suggested to improve the patients' MDI use (22, 23, 37). It has been shown that patient counseling significantly improved the MDI technique from 31% before counseling to 72% immediately after (20). Moreover, training asthmatic children and their parents improved the percentage of adequate MDI users from 8% before training to 81% after (21). Similar methods, to those in this study, were used with adults with asthma attending a hospital out-patient clinic (18). These adult asthmatics decreased their flows after training and when they used the 2TT. In contrast to this study, the improvements were greater in the 2TT group compared to the VC group.

The lung function test alone may not reflect the actual asthma control level (38) and correlates poorly with the patients' quality of life (28, 39). In the current study, and in agreement with the published literature (18), the change in the FEV_1 % predicted between visits 1 and 2 was not significant in both the VC and 2TT groups (asthmatic adults and children) and did not reflect the significant improvement in the patients' MDI use. This may be due to a ceiling effect and our lack of knowledge of the medications used by patients. Moreover, the FEV_1 % predicted and its change over the study follow-up period did not significantly correlate with the employed quality of life instruments.

Achieving optimal asthma control is the ultimate goal of both the national and international Asthma Management Guidelines (40, 41). Inadequate patient education on the correct inhaler use leads to poor asthma control (42, 43), which is subsequently interpreted into quality of life impairments (44, 45). For the asthmatic adults in the VC group, the mean difference between visits 1 and 2 in the overall Mini-AQLQ score and its domains significantly exceeded the clinically significant change of 0.5, except for the activity limitation domain. For the adults in the 2TT group, the changes in the symptoms and emotional function quality of life domains were above the clinically significant difference; however, the change in the overall quality of life was not statistically significant. For the asthmatic children, although the mean changes in the scores of the overall PAQLQ and its domains indicate an improvement in quality of life, only changes in the symptoms domain (VC group) and in the emotional function (2TT group) were statistically significant. For the asthmatic children's parents, the differences in the overall PACQLQ and the activity limitation domain were significant for the 2TT group only. The improved asthma-related quality of life from using a slow flow with no change in the FEV_1 strengthens the suggestion (18) that the outcomes are due to better penetration of corticosteroids into the peripheral airways.

Unlike the findings of a previously published research (18), the lack of significant changes in quality of life as a reflection to the significant improvement in the patients'

MDI technique and inhalation flow can be explained by the study limitations. These include the small sample size, the relatively short follow-up period, and a ceiling effect. The majority of the enrolled patients had mild, stable asthma at enrolment, which might have reduced the possibility of spotting any significant changes in their responses to the quality of life instruments. The study reflects patients attending a community pharmacy to collect their prescription unlike the previous study where the patients attended a hospital outpatient clinic.

In the UK during 2005, the New Pharmacy Contract between the Pharmaceutical Services Negotiating Committee, the Department of Health, and NHS employers introduced a remunerated Medicine Use Review service that focuses on the correct use of medicines (46). This was further consolidated by the New Medicine Service in 2011 and targeted MURs (that includes asthma and COPD) (47). This study suggests that using this government initiative to train patients in a community pharmacy to use their MDI should provide healthcare benefits.

CONCLUSIONS

In conclusion, patients should be trained to use a slow inhalation flow and the results consolidate the consensus recommendation to use this inhalation maneuver with an MDI. A slow flow can be achieved by both verbal counseling and training aid and improves asthma-related quality of life. An MDI technique training aid might add some extra cost, while the verbal training to prolong the inhalation period is simple to explain by encouraging the patient to ensure that they can count slowly to five while they inhale via their MDI.

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DECLARATION OF INTEREST

Wesam Ammari has no conflict of interest. Henry Chrystyn 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,

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