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ORIGINAL RESEARCH

The Effect of Adding a Training Device and Smartphone Application to Traditional Verbal Counseling in Asthmatic Children

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ABSTRACT

Introduction: New training devices have been introduced to help in inhaler counseling by addressing the inspiratory flow through the metered-dose inhaler (MDI), which is the most important problem of the MDI inhalation technique. This study aims to compare the effects of MDI traditional verbal counseling and advanced counseling using training devices with a smartphone application in pediatric asthmatic patients.

Methods: A total of 201 pediatric asthmatic subjects (8–18 years) were divided into two groups: a verbal counseling group, who received only MDI verbal counseling training (n = 101), and an advanced counseling group who received counseling using a training device (Flo-Tone with Trainhaler smartphone application) in addition to the traditional MDI verbal counseling (n = 100). Every patient in the two groups attended three counseling visits, 1 month apart. At each visit, pulmonary functions [peak expiratory flow (PEF), forced expiratory volume in 1 s (FEV_1) as % of predicted] were measured. Also, patients were asked to perform their normal inhalation technique using their MDI, and mistakes were detected and recorded by the investigator. Then, patients were trained on the correct steps of the MDI inhalation technique using either verbal counseling or advanced counseling depending on their study group. In the advanced group, the Flo-Tone was connected to the mouthpiece of the MDI to blow a whistle while the patient inhaled from the MDI. That whistle was detected by the Trainhaler smartphone application and the duration of inhalation determined by the application was recorded.

Results: Both groups showed a gradual significant decrease ($p < 0.05$) in the total mean number of MDI inhalation technique mistakes from the second visit of counseling, and the improvement continued in the third visit, with a lower number of mistakes in the advanced

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group especially in inhaling at a slow rate until the lungs are a full step. Also, the advanced counseling group showed a gradual significant increase ($p < 0.05$) in lung function (PEF and FEV1% of predicted) from the second visit of counseling, particularly (FEV1% predicted) results which showed a greater and more rapid overall improvement in the advanced group compared to the limited overall improvements that occurred in the control group, while significant improvement ($p < 0.05$) of lung function was obtained at the third visit in the verbal counseling group. In the advanced group, the number of seconds measured by the smartphone application, which represents the duration of inhalation, increased significantly ($p < 0.05$) in the second and third visits.
Conclusions: The addition of training devices and smartphone applications to traditional verbal counseling of MDI inhalation technique in asthmatic children resulted in significant improvements in lung function (especially in FEV1% of predicted results), and duration of inhalation, and progressive decreases in the average number of MDI inhalation techniques errors compared to the verbal counseling group.

Keywords: Flo-Tone; Counseling; Children; Inhalation technique; MDI, FEV_1; PEF; Trainhaler application

Key Summary Points

Why carry out this study?

One of the main difficulties with pressurized metered-dose inhalers (pMDI) is that some patients find it hard to properly use pMDI.

Poor pMDI inhalation technique, especially inhalation at an incorrect inspiratory flow, causes sub-therapeutic effects because of poor lung deposition.

What was learned from the study?

Training devices with smartphone application together with traditional verbal counseling significantly corrects pMDI steps inhalation technique.

It also improves pulmonary function and leads to a significant reduction in the number of inhalation technique mistakes, compared to traditional verbal counseling only.

INTRODUCTION

Asthma aerosolized short-acting beta agonist (SABA) treatment mostly results in a quick onset of action [1–3]. However, most patients do not receive all the advantages of the inhaled medications because of their incorrect use of their inhalers [4]. Erroneous inhalation strategy can decrease the lung deposition of the inhaled medications. This increases the undesired accumulation within the oropharyngeal zone, which in return causes asthma symptoms to be uncontrolled [5–7].

Pressurized metered-dose inhalers (MDIs) are still the foremost utilized inhalation devices that specialists prefer [8, 9]. However, they require a proper inhalation technique to deliver the inhaled medication. MDI inhalation technique differs very much from that of the dry powder inhaler, especially in the inhalation flow required to deliver the dose [10–15]. Incorrect utilization of inhalers can be noted between all ages of patients, but it appears more frequently within children and older patients [16–19].Some previous studies have shown that most repeated inhalation technique mistakes were the inability in actuation coordination of MDI at the time of inhalation, maintaining the needed inhalation flow for a sufficient period, the period of holding the breath after inhalation is shorter than recommended, and missing shaking of the MDI before use to mix the contents [20–23]. The patient's ability to inhale the aerosolized drug deeply and steadily for 5 s is a key step in the inhalation process, as faster inhalation speed will decrease the portion of drug delivered to the lungs, which leads to poor asthma control [21, 24]. Conventional counseling by instructing the patients on the right steps of inhalation method verbally was found to be deficient to overcome faults in the

coordination process [25, 26]. The beneficial effects of inhalers and lung disease management can be improved by repeated regular counseling sessions [19, 27]. New training devices have emerged to help in the counseling process [19, 24, 25, 28, 29]. They produce a whistling signaling sound that can be heard and detected by the patient. This sound shows that the target range has been accomplished by the inspiratory flow through the MDI. This whistle can also be detected by smartphone applications to measure the duration of the proper inhalation flow to ensure that a sufficiently higher percentage of the drug has reached the lungs to exert its therapeutic effect [19].

This study aimed to evaluate the effect of advanced counseling using training devices with a smartphone application with traditional verbal counseling compared to traditional verbal counseling alone on pediatric asthmatics' pulmonary functions and frequency of mistakes in MDI inhalation technique.

METHODS

The study was conducted in Beni-Suef University Hospital chest clinic and School health insurance clinic, Beni-Suef, Egypt after the study protocol was approved by the Research Ethical Committee of the Faculty of Pharmacy, Beni-Suef University (REC-H-Ph-BSU-18001) and following the Declaration of Helsinki. Participants provided written informed consent. Children included in the study were asthmatic children between 8 and 18 years old who use MDIs (containing beclomethasone and salbutamol combined in the same inhaler) as a treatment and capable of performing pulmonary function tests correctly. Children were excluded from the study if they were critically ill or treated in intensive care units or had any mental handicaps that could hinder them from performing the required pulmonary function tests correctly. Pediatric asthmatics recruited in the study were randomized using an online website (https://www.randomizer.org/) into two groups; a verbal counseling group, and an advanced counseling group [Flo-tone (Clement Clarke International, UK) attached to the metered-dose inhaler + Trainhaler application (Clin-e-cal Limited, United Kingdom) and verbal counseling]. Each patient in the two groups had three consecutive visits 1 month apart. At each visit, pulmonary functions (PEF, FEV_1% of predicted) were measured using a spirometer (PIKO-1, Ferraris respiratory Europe LTD., UK) through three trials for each patient, and the highest reading was recorded.

Patients in both groups were trained on the correct inhalation technique of MDI verbally by explaining the correct steps (11 steps) as shown in Table 1. According to the ERS/ISAM task force report suggestions, the MDI inhalation technique was separated into several steps, as it was revealed before that this separation of steps may help subjects in improving their inhalation technique as it makes the MDI counseling more operative and permit us to easily notice the hard steps [30].

An investigator asked the patient to show him his own MDI inhalation technique steps using an empty MDI, and the investigator observed and detected the patient's mistakes in each step and recorded them. The investigator corrected the patient's MDI inhalation technique mistakes and illustrated the proper MDI inhalation technique steps either verbally only, in the verbal counseling group, or by using the non-medicated training devices connected to an empty MDI, as shown in Fig. 1, and its smartphone application with verbal counseling, in the advanced counseling group. Children in the advanced counseling group were instructed to inhale from their MDI connected to the training device until hearing the sound of the whistle and to trying to keep this sound for 5 s. The duration of inhalation represented by time of whistle sound continuation was measured using the Trainhaler smartphone application installed on their smartphones as shown in Fig. 1.

Statistical Analysis

Analysis of results was performed using Student's *t* test for between-group and within-

Table 1 Total number of mistakes and percentages of mistakes in MDI inhalation technique in each step for the three visits

Steps of using pMDI	Control group (101 patients)			Advanced group (100 patients)		
	visit1	visit2	visit3	visit1	visit2	visit3
1. Remove the protective cap from the mouthpiece of the MDI	0	0	0	0	0	0
2. Shake the MDI	50	32	13	75	14	7
	49.5%	31.68%	12.8%	75%	14%	7%
3. Breathe out as far as comfortable	84	50	38	95	64	22
	83.17%	49.5%	37.6%	95%	64%	22%
4. Place the MDI mouthpiece between the teeth and seal with the lips	78	69	61	77	26	6
	77.23%	68.32%	60.39%	77%	26%	6%
5. Ensure that your tongue does not obstruct the mouthpiece	0	0	0	3	1	0
				3%	1%	0%
6. Depress the inhaler to release the dose at the start of inhalation	0	0	0	0	0	0
7. Maintain a slow inhalation rate until the lungs are full	81	72	58	77	39	13
	80.2%	71.28	57.43%	77%	39%	13%
8. Remove the MDI from the mouth and hold breath for 5–10 s	73	57	23	79	43	22
	72.28%	56.44%	22.77%	79%	43%	22%
9. If more than one dose, each time wait about 30 s before the next dose	67	61	28	80	45	25
	66.34%	60.4%	27.72%	80%	45%	25%
10. Rinse mouth and if possible, brush teeth after dosing	47	36	17	56	36	19
	46.53%	35.64%	16.83%	56%	36%	19%
11. Replace cap on the MDI	0	0	0	0	0	0

group comparisons. A repeated measure analysis of variance test with least significant difference correction was used to compare the effect of treatment throughout the three visits and between groups. The Chi-square test was used for the analysis of the correct achievement of each training step between both groups (SPSS 23, SPSS, Chicago, IL, USA).

RESULTS

A total of 201 pediatric asthmatic subjects (8–18 years) were enrolled in the 3-month prospective study of education and assessment. They were randomly divided into two groups; a verbal counseling group (n = 101, 63 females), and an advanced counseling group (n = 100, 39 females). Table 2 shows the baseline characteristics of the two groups. Almost all patients in the two groups were prescribed the same medications in addition to their inhaler (MDI). All patients were on MDI therapy containing beclomethasone and salbutamol (combined in the same inhaler under the trade name of "VENTAL COMPOSITUM"). Most of the patients were prescribed antibiotic (ampicillin intramuscular injections or amoxicillin capsules or amoxicillin/clavulanic acid syrup), ketotifen

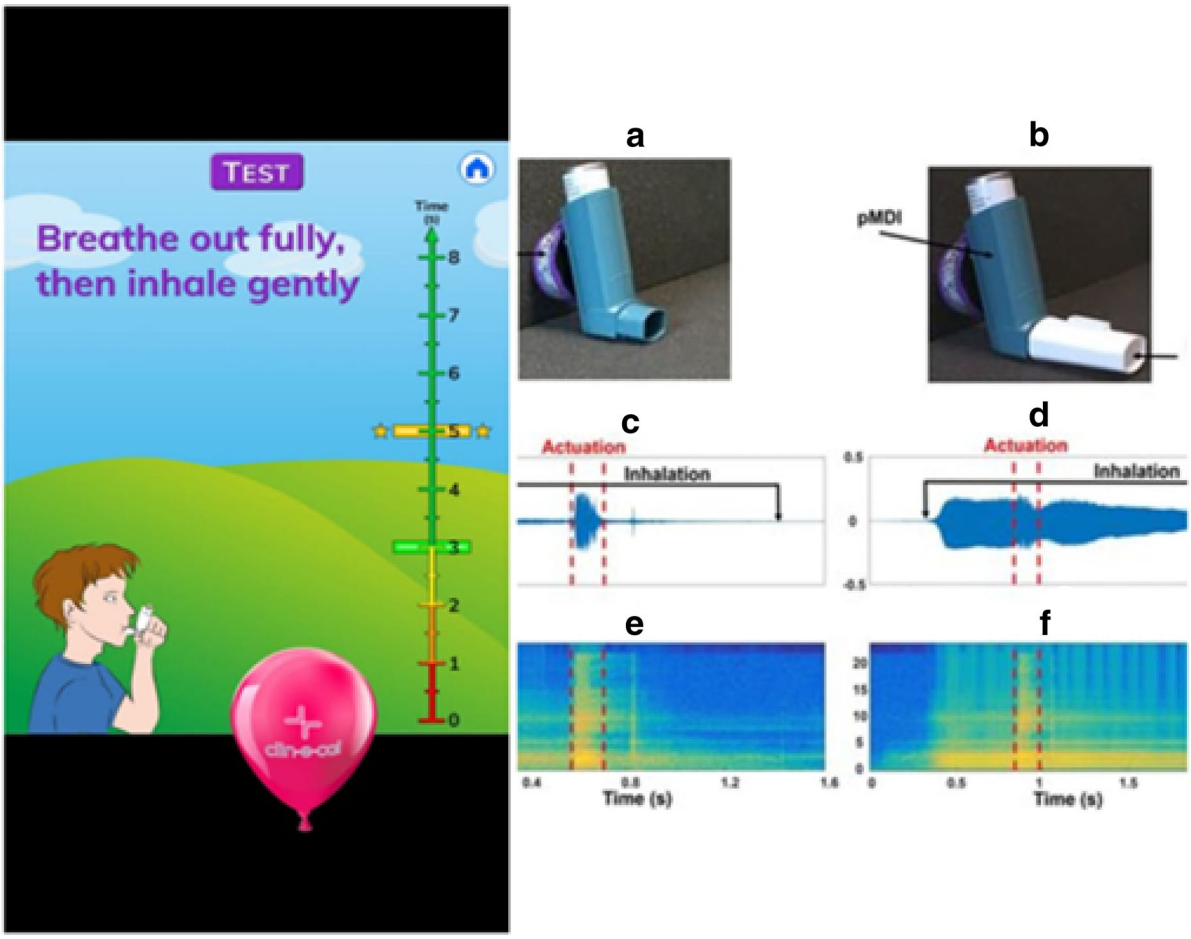

Fig. 1 MDI with and without Flo-Tone and the Trainhaler smartphone application screen showing the response to the sound produced from the Flo-Tone

syrup (as an anti-histaminic mast cell stabilizer), bromhexine syrup (as a mucolytic), prednisolone syrup (as an anti-inflammatory drug for reduction of symptoms such as wheezing), dextromethorphan hydrobromide syrup (as an antihistamine and cough suppressant), and salbutamol as a bronchodilator. In the advanced counseling group, lung functions (PEF and FEV_1% of predicted) improved significantly in the second visits, while in the verbal counseling group they improved significantly ($p < 0.05$) only in the third visit (as shown in Fig. 2 and Fig. 3). In the advanced counseling group, the improvement in mean PEF and mean FEV1% predicted was significant ($p < 0.05$) from visit 1 to visit 2 and from visit 2 to visit 3 and also from visit 1 to visit 3. However in control group, the improvement in mean PEF and mean FEV1% predicted was significant ($p < 0.05$) from visit 2 to visit 3 and from visit 1 to visit 3, and there was no significant improvement from visit 1 to visit 2 (as shown in Table 3). It can also be noticed clearly from Table 3 that the significant improvements in the values of (PEF and FEV1% predicted) lung function from each counseling visit to the following next visit in the advanced counseling group were remarkably greater than those with little improvement in the control group (especially for FEV1% predicted). Moreover, this greater improvement in lung function of asthmatic children in the advanced group was found to be detected faster and earlier, as it

Table 2 Baseline characteristics of two groups

Parameter visit	Control group [101 patients (63 females)]	Advanced group [100 patients (39 females)]
Age in years (mean and standard deviation)	13.337 (2.754)	12.19 (3.184)
Height in centimeter (mean and standard deviation)	153.396 (12.346)	147.775 (14.27)
Baseline FEV_1 in liters (mean and standard deviation)		
Visit 1	1.76 (5.89)	1.3306 (0.7021)
Visit 2	1.35 (0.72)	1.6179 (0.7311)
Visit 3	1.39 (0.6)	1.953 (0.8071)
Number of females and males	63 females 38 males	39 females 61 males
Baseline FEV_1% of predicted (mean and standard deviation)	43.16 (22.92)	51.52 (19.77)
Baseline PEF in liter per minute	140.05 (66.18)	138.47 (76.51)

was observed from the second counseling visit unlike in the other control group in which the improvement was observed later in the third counseling visit. Although calculated values of FEV1% of predicted were found to be low (specially baseline values in the first visits of patients in both groups), but a significant increase in these results was detected throughout the following consecutive counseling visits especially for the advanced group in which higher and faster lung function improvements have been noticed compared to the control group. However, low values of FEV1% predicted indicate that we are almost dealing with a group of severe asthmatic children. Study results revealed that mean (standard deviation) values of Fev1% of predicted of the advanced counseling group increased significantly and greater from 51.52 (19.77) in the first counseling visit to 76.52 (17.84) in the third counseling visit compared to control group in which mean (standard deviation) values of Fev1% of predicted increased less from 43.16 (22.92) in the first visit to 51.72 (21.69) in the third visit (as shown in Table 3). Also, for the PEF spirometric parameter, study results showed that mean (standard deviation) values of PEF increased significantly greater and more rapid in the advanced counseling group from 138.47 (76.51) in the first visit to 197.24 (79.54) in the third visit compared to the more limited and late increase in the control group from 140.05 (66.18) in the first visit to 156.45 (57.43) in the third visit (as shown in Table 3). Both groups showed a gradual significant decrease ($p < 0.05$) in the total mean number of pMDI inhalation technique mistakes from the second visit of counseling with a higher significant decrease ($p < 0.001$) in the total mean number of mistakes between visit 1 and visit 3 in the advanced counseling group compared to the verbal counseling group (as shown in Table 1 and Fig. 4). Also for the advanced group, the number of seconds measured by smartphone application, which represents the time of maintaining whistle sound from training device (duration of inhalation) increased significantly ($p < 0.05$) in the second and third visits (as shown in Table 3 and Fig. 5).

Some steps in the MDI inhalation technique were understood and operated easily without mistakes from visit 1 by all asthmatic children in the two study groups including removing the protective cap from the mouthpiece of the MDI, releasing the drug dose from the MDI at the start of inhalation, and refitting the MDI cap by the completion of inhalation technique.

Most children in both study groups had considered step 7; maintain a slow inhalation rate until the lungs are full and step 8; remove the MDI from the mouth and hold breath for 5–10 s to be the most difficult for them. Our study results showed that 81 children from 101 children in the verbal counseling group and 77 children from 100 children in the advanced counseling group failed to maintain the required rate of slow inhalation in the first

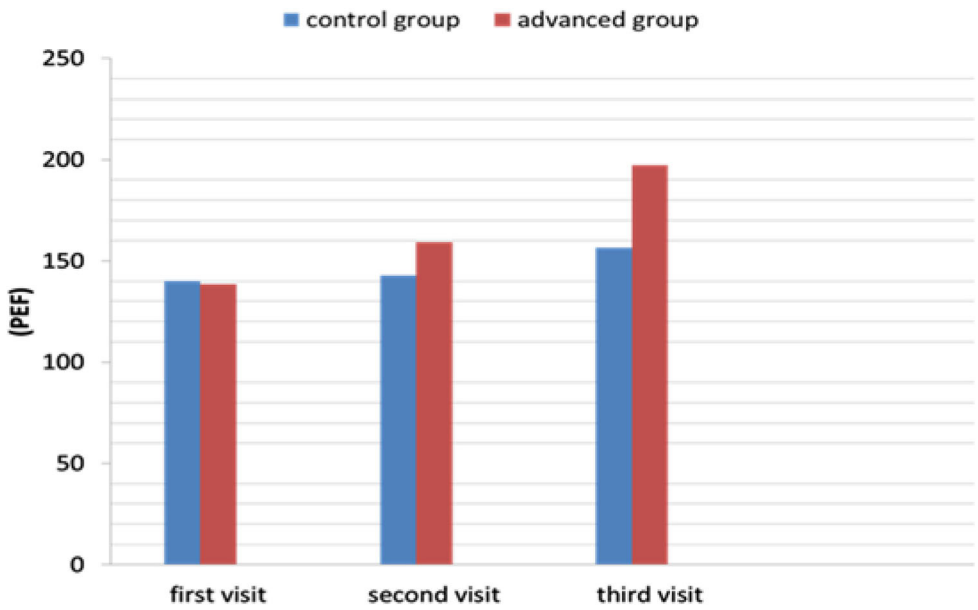

Fig. 2 Significant improvements in total mean values of PEF of both groups for the three counseling visits

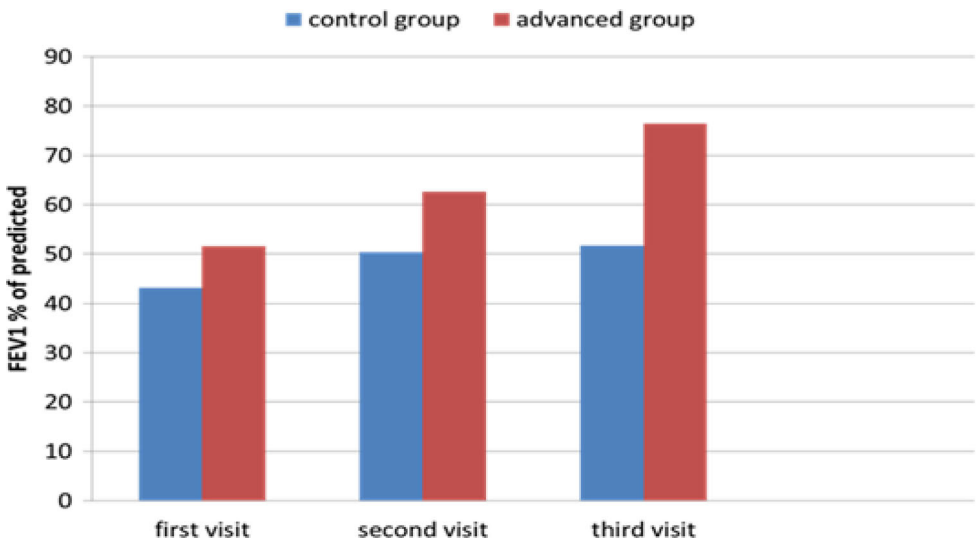

Fig. 3 Significant improvements in total mean values of FEV1% predicted of both groups for the three counseling visits

counseling visit, which is considered a critical step in the inhalation technique process; but by the third visit, only 13 children in the advanced counseling group had mistakes in this step compared to 58 children in the verbal counseling group. Some other steps of the MDI inhalation technique were performed inappropriately in both groups, particularly in the first counseling sessions. One of these steps was shaking of the MDI vigorously before using. We noted that about 50% of children in the verbal counseling group and 75% of children in the

Table 3 Mean (SD) values of PEF, Fev1% of predicted, mean number of mistakes in pMDI inhalation technique, and total number of seconds measured by Trainhaler application

Parameter visit	Control group	Advanced group
PEF (in liters per minute)		
Visit 1	140.05 (66.18)	138.47 (76.51)
Visit 2	142.86 (48.35)	159.49 (78.65)*
Visit 3	156.45 (57.43)*	197.24 (79.54)*
FEV_1% of predicted		
Visit 1	43.16 (22.92)	51.52 (19.77)
Visit 2	50.30 (26.84)	62.58 (18.44)*
Visit 3	51.72 (21.69)*	76.52 (17.84)*
Mean number of mistakes		
Visit 1	4.76 (1.06)	5.43 (1.02)
Visit 2	3.71 (1.20)*	2.69 (1.44)*
Visit 3	2.43 (1.31)*	1.15 (1.27)*
Number of seconds measured by application		
Visit 1	–	0.75 (0.57)
Visit 2	–	1.11 (0.70)*
Visit 3	–	1.65 (0.76)*

*Denotes significance $p < 0.05$

advanced counseling group failed to remember to shake the MDI or shake it properly in the first visit, however, these percentages decreased significantly by the third visit for both groups, but the decrease in percentages of mistakes was higher in the advanced counseling group. Other highly repeated children's mistakes were in failing to empty the lungs before inspiration by exhaling as far as comfortable and waiting for 30 s between repeated doses, as shown in Table 1.

DISCUSSION

This study showed that verbal counseling using an MDI training device with a smartphone application (Flo-Tone + Trainhaler smartphone application) produced a more significant reduction in the mean number of mistakes in MDI inhalation technique compared to using traditional verbal counseling only. Moreover, advanced counseling in asthmatic children showed a significant improvement in lung function parameters (PEF, FEV_1% of predicted) in asthmatic children compared to traditional verbal counseling only. Also, a significant gradual increase in the duration of inhalation in seconds was detected in asthmatic children with advanced counseling.

In childhood asthma medical care, the correct procedure for using inhalation devices is considered the cornerstone, but many children with asthma use their devices incorrectly, leading to inadequate drug deposition [31]. So asthmatic children need to be instructed comprehensively about the proper inhalation technique [32]. Despite giving asthmatic children verbal inhalation instructions, incompetent inhalation technique is commonly seen between them. Asthma guidelines recommend instructing, educating, and monitoring asthmatic patients on a regular basis [33, 34]. Around 94% of patients treated with MDIs have been found to use them wrongly, while about 84% of patients using dry powdered inhalers use their devices in the wrong way [14, 19, 25, 35]. Teaching patients the correct technique of using MDI via verbal counseling was found to have a remarkably important effect on the management of asthma. However, verbal counseling alone is not sufficient to prevent mistakes because patients keep forgetting verbal counseling by the time [5, 19, 36].

The prerequisite of achieving better and more satisfying counseling results increased the need for using additional counseling tools in conjunction with traditional verbal counseling, especially in children; perhaps because they almost need specific manners of counseling, and communication to be able to remember the proper steps of the inhalation method and to trust in the importance of their treatment adherence. According to NICE guidelines, it is recommended that asthma should be monitored regularly by using spirometry tests at each patient visit to physicians or after 3 or 6 months from asthma therapy initiation, then a

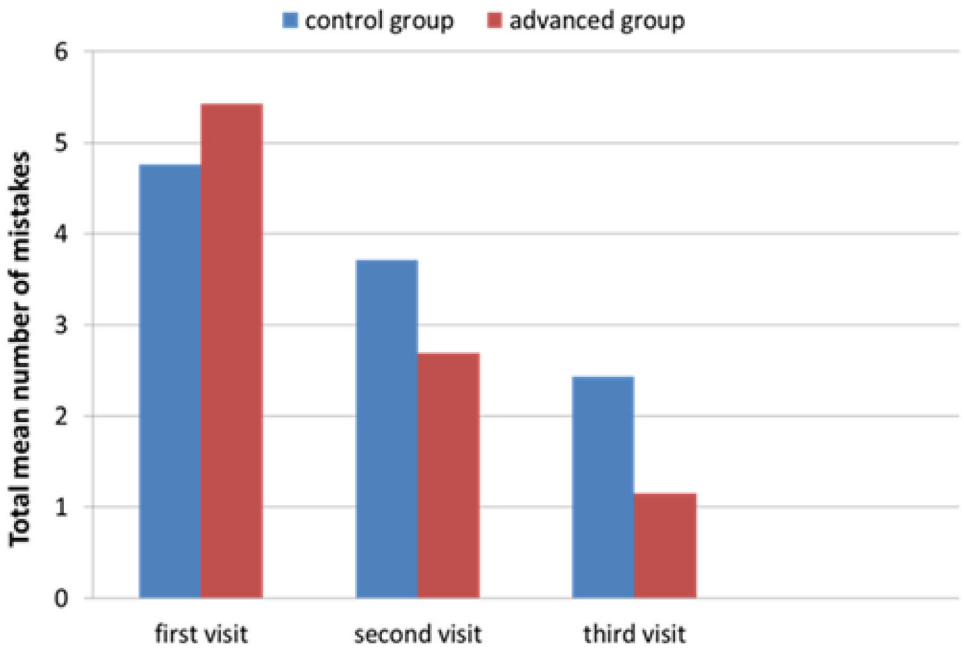

Fig. 4 Significant improvements (by decreasing) in total mean number of mistakes of both groups for the three counseling visits

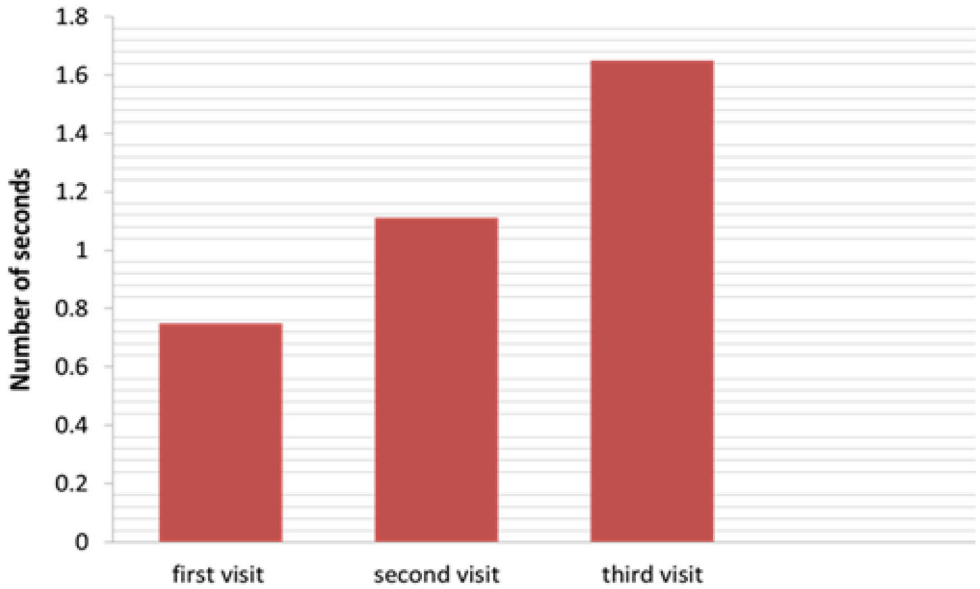

Fig. 5 Significant improvements in total mean number of seconds of inhalation duration recorded by smart phone application in advanced group for the three counseling visits

monitoring visit every 1–2 years is required as a minimum [37]. Both PEFR and FEV1 spirometric parameters can be used in asthma diagnosis and management of asthmatics, however FEV1 is a

more accurate and preferred tool than PEFR for the recognition and determination of bronchoconstriction (contractions in the bronchial smooth muscles) [38]. The most commonly used lung function test for asthma monitoring is FEV1, especially in children diagnosed with asthma, as it was found that a decrease in FEV1 is linked to increased levels of asthma severity [39]. It was revealed that asthmatic children whom FEV1 < 60% of the predicted were found to be two times more likely exposed to the risk of severe asthma attacks in the next coming year if compared with their counterpart asthmatic children who obtained FEV1 percentage of predicted more than 80% [40, 41]

The additional advantage of using advanced counseling methods in asthmatic children over conventional verbal counseling was seen in our study results. This can be shown in the significantly higher and more rapid increase ($p < 0.05$) in PEF and FEV_1% of predicted in visit 2 in the advanced counseling group, while a limited more slowly significant increase in the same measured lung functions was seen later in visit 3 in the traditional verbal counseling group. This confirms the positive additional effect of using training Flo-Tone device with Trainhaler smartphone application in collaboration with verbal counseling in the rapid improvement of asthma control. The baseline FEV_1 percent predicted in each group were only in the 47.3 and 51.52. These were extremely low FEV_1 for pediatric asthma and suggest that we had a very severe patient group. This may affect the generalizability of our findings and require further studies using more stable groups of patients. However, we could rationalize these low FEV1 values to the probable inadequate adherence to asthma medications (however, this would require assessing adherence to therapy, which is practically difficult) or also it may be due to their improper use of the MDI since the FEV1 was improved to 76.52 (17.84) in the third counseling visit. The mean number of mistakes in the steps of the MDI inhalation technique decreased significantly ($p < 0.05$) in both groups from visit 1 to visit 2 and also from visit 2 to visit 3. There was a higher significant decrease ($p < 0.001$) in the number of mistakes between visit 1 and visit 3 in the advanced counseling group compared to the verbal counseling group.

Shaking the MDI vigorously before inhalation is a fundamental step for achieving a consistent steady drug dose [42, 43]. We noted that most children in both the verbal counseling and the advanced counseling groups totally neglected to do this, or they shake inadequately in the first counseling visit but after three successive visits, the number of mistakes in this inhalation step decreased by 74% in the verbal counseling group while it decreased in advanced counseling group by 90.7%

Blowing out as far as comfortable before inhaling the drug dose from MDI is a beneficial step and helps in preparing the lungs to receive the largest possible portion of aerosolized drug dose. However, we observed a high number of mistakes in this step among children of both groups in the first visit; being completely forgotten or done incorrectly. However, by the third visit, we noted that the number of mistakes in this step decreased by 54.76% in the verbal counseling group and 76.8% in the advanced counseling group.

In step 4, "place the MDI mouthpiece between the teeth and seal with lips", we observed errors like poor sealing of the lip around the MDI, resulting in dose escaping, which can negatively affect asthma control. However, these mistakes decreased significantly between the first and third visits by 21.8% in the verbal counseling group compared to 92.2% in the advanced counseling group. It was recommended that patients inhale slowly and continuously from the MDI to get complete benefit from their inhaler [44]. We detected that step 7 was the most difficult for the majority of children in both groups to perform correctly, particularly in the first counseling visits and between the youngers. However, the number of errors in step 7 decreased from visit 1 to visit 3 by 28.4% for verbal counseling group compared to 83.12% for an advanced counseling group.

Time spacing between consequent puffs of MDI is required to prevent the inhaler valve from getting colder (as a result of successive multiple actuations), which can negatively affect the dissemination of drug particle size in the next following doses, and subsequently

drug efficacy will be decreased [45]. However, the number of mistakes in this step decreased by 58.25% at the third visit in the verbal counseling group; similarly, the improvement percentage was 68.75% in the advanced counseling group. Also, in 5–10 s of the breath-holding step, the improvement was almost similar in the verbal counseling group and the advanced counseling group with a relatively higher result in the advanced counseling group (68.5 and 72.15%, respectively). This could be because the Flo-Tone device and its Trainhaler smartphone application concentrated more on the slow inhalation and not on steps like the time spacing between consequent puffs of MDI and the breath-holding, which are of real importance in inhalation technique and need to be addressed properly in the counseling.

Asthmatic children were able to perform some steps of inhalation technique precisely from their first counseling visit, e.g., as to remove the protective cap of MDI and to replace the cap of MDI [14, 17, 19, 25].

The number of seconds recorded by using a smartphone application represents the time of inhalation. It reflects how long the asthmatic patient could maintain the whistling sound of the training device. Study results showed a significant increase ($p < 0.05$) in the measured number of seconds between the three consecutive visits. This confirms the importance and the effect of using Flo-Tone and Trainhaler smartphone application in teaching and training asthmatic children how to maintain a slow rate of inhalation by trying to keep the whistle sound up to 5 s. This provides a chance to make sure that the patient inhaled the highest possible proportion of the drug dose with the right inhalation technique, which could have a positive effect on asthma control and improvement of the patient's lung function. It was observed that most children could not achieve 5 s of continuous inhalation, especially those of younger ages. However, most of them gained the benefit of the significant gradual increase in the duration of inhalation time throughout visits. This significant increase in the duration of inhalation could be linked to the gradual significant improvements in lung function between visits.

All of the previous studies and our results supported using advanced counseling over traditional verbal counseling alone [14, 19, 24, 25]. According to Haitham Saeed et al.'s recent study, the group of patients who received advanced MDI optimum technique counseling by the aid of modern training devices and smart phone application showed a significant improvement in their measured lung function (PEF and FEV1) after the first and the second counseling visits, unlike patients in the other group who received MDI counseling verbally only and showed significant improvements in their lung functions only after the second visit [19]. These results are in keeping up with and supporting our current study results. However, it was done on asthmatic adults and not asthmatic children, as in our current study. Similarly, Nicola et al.'s previous study results, which only incorporated asthmatic patients more than 18 years old, reported that PEF lung function improved significantly in the investigation group in which an advanced training device is used from the second clinic visit while it improved in the other control verbal counseling group only in the third clinic visit, however the mean number of MDI technique mistakes decreased significantly in both groups from the second clinic visit [25]. These previously mentioned studies also encourage the addition of a whistle-producing piece (like Flo-Tone or Clip-Tone) to the MDI on regular base. This suggested that renovation of the MDI can enable asthmatic children and their parents to make sure that the inhalation technique is performed correctly. According to guidelines of asthma and COPD, inhaler counseling needs to be continuously repeated at every chance whenever possible [46, 47]. It worth mentioning that in the verbal counseling group, the patient faced a checkup of his inhalation technique once monthly with the investigator during the study visit; however, in the advanced counseling group, the patient had the Flo-Tone device attached to his MDI mouthpiece and the Trainhaler application installed on his smartphone and he could check his inhalation technique at any time he wishes. This possible contentious checkup could be the reason for the improvement in certain steps that are not

addressed by the Flo-Tone device and the Trainhaler application in the advanced counseling group compared to the verbal counseling group, so adding this whistle-producing piece to the MDI will help children's parents to observe and counsel their children's inhalation technique at home at every possible opportunity.

Limitations of the Study

The asthma control test was not included in the study because the childhood asthma control test for children up to 11 years contains some questions that need to be answered by parents or a close child-carer. This was difficult because many children attended the clinic accompanied by their relatives or neighbors, who do not know a lot about the child's medical case and could not answer childhood asthma control test questions accurately. Children under 8 years old were excluded from the study to decrease variation between subjects of study and to make sure that children included in the study were cooperative and able to perform the lung function tests correctly during counseling sessions. Breath-holding and time spacing between consequent puffs of MDI, which are critical elements of proper MDI technique, were almost improved similarly in both groups, suggesting that the training device only affected certain aspects of MDI technique and more upgrading in such training devices are needed to address steps like breath-holding and time spacing between consequent puffs of MDI.

CONCLUSIONS

The use of advanced patient counseling using the Flo-Tone with Trainhaler smartphone application together with traditional verbal counseling in teaching children the correct steps of MDI inhalation technique resulted in significant improvement in pulmonary function, a significant increase in the duration of inhalation, and a significant reduction in the number of inhalation technique mistakes, compared to using traditional verbal counseling alone, which could lead to better control of asthma symptoms.

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Data Availability. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Papi A, et al. Treatment strategies for asthma: reshaping the concept of asthma management. Allergy Asthma Clin Immunol. 2020;16(1):1–11.

2. Türkeli A, Yılmaz Ö, Yüksel H. Metered-dose inhaler-spacer use education effects on achieve asthma control in children. Tuberkuloz ve toraks. 2016;64(2):105–11.

3. Westerik JA, et al. Characteristics of patients making serious inhaler errors with a dry powder inhaler and association with asthma-related events in a primary care setting. J Asthma. 2016;53(3):321–9.

4. George CM, Schrock M. Inhalation therapy: help patients avoid these mistakes. J Fam Pract. 2011;60(12):714.

5. Elgendy MO, Abdelrahim ME, Eldin RS. Potential benefit of repeated MDI inhalation technique counselling for patients with asthma. Eur J Hosp Pharm. 2015;22(6):318–22.

6. Giraud V, Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. Eur Respir J. 2002;19(2):246–51.

7. Newman S. Inhaler treatment options in COPD. Eur Respir Rev. 2005;14(96):102–8.

8. Sanchis J, et al. Inhaler devices–from theory to practice. Respir Med. 2013;107(4):495–502.

9. Hendeles L, Colice GL, Meyer RJ. Withdrawal of albuterol inhalers containing chlorofluorocarbon propellants. N Engl J Med. 2007;356(13):1344–51.

10. Abdelrahim ME. Emitted dose and lung deposition of inhaled terbutaline from Turbuhaler at different conditions. Respir Med. 2010;104(5):682–9.

11. Ali AMA, Abdelrahim MEA. Modeling and optimization of terbutaline emitted from a dry powder inhaler and influence on systemic bioavailability using data mining technology. J Pharm Innov. 2014;9(1):38–47.

12. Boshra MS, et al. Inhaled salbutamol from Aerolizer and Diskus at different inhalation flows, inhalation volume and number of inhalations in both healthy subjects and COPD patients. Exp Lung Res. 2019;45(3–4):84–91.

13. Boshra MS, et al. Total emitted dose of salbutamol sulphate at different inhalation flows and inhalation volumes through different types of dry powder inhalers. Exp Lung Res. 2018;44(4–5):211–6.

14. Saeed H, et al. Effect of human error, inhalation flow, and inhalation volume on dose delivery from Ellipta® dry-powder inhaler. J Pharm Innov. 2019;14(3):239–44.

15. Boshra MS, et al. Inhaled salbutamol from Aerolizer and Diskus at different inhalation flows, inhalation volume and number of inhalations in both healthy subjects and COPD patients. Exp Lung Res. 2019;45:1–8.

16. Elgendy MO, Abdelrahim ME, Eldin RS. Potential benefit of repeated dry powder inhaler's inhalation technique counseling on asthmatic patients. Pulm Ther. 2015;1(1):91–101.

17. Elgendy MO, et al. Asthmatic children and MDI verbal inhalation technique counseling. Pulm Pharmacol Ther. 2020;61:101900.

18. Nicola M, et al. Effect of DPI's training-device on inhalation technique and clinical efficacy in asthmatics. Beni-Suef Univ J Basic Appl Sci. 2018;7(2):178–83.

19. Saeed H, et al. Impact of advanced patient counseling using a training device and smartphone application on asthma control. Respir Care. 2020;65(3):326–32.

20. Harb HS et al. (2021) Real-life assessment of chronic obstructive pulmonary disease patient performance with different inhalers. Int J Clin Pract e13905. https://doi.org/10.1111/ijcp.13905.

21. Harb HS et al. (2021) Determinants of incorrect inhaler technique in chronic obstructive pulmonary disease patients. Int J Clin Pract e14073. https://doi.org/10.1111/ijcp.14073.

22. Harb HS, et al. Prevalence and predictors of suboptimal peak inspiratory flow rate in COPD patients. Eur J Pharm Sci. 2020;147:105298.

23. Harb HS, et al. First-time handling of different inhalers by chronic obstructive lung disease patients. Exp Lung Res. 2020;46(7):258–69.

24. Wael W et al. The effect of Clip-tone® and its smartphone application on optimisation of metered-dose inhalers inhalation technique. Int J Clin Pract. 2021;e14088. https://doi.org/10.1111/ijcp.14088.

25. Nicola M, et al. The impact of adding a training device to familiar counselling on inhalation technique and pulmonary function of asthmatics. Adv Ther. 2018;35(7):1049–58.

26. Al-Showair RA, Pearson SB, Chrystyn H. The potential of a 2Tone trainer to help patients use their metered-dose inhalers. Chest. 2007;131(6):1776–82.

27. Shareef J, Sajitha M, Shastry C. Impact of pharmacist provided patient counseling on quality of life in patients with asthma in a tertiary care teaching hospital. Int J Pharma Res Rev. 2014;3(2):1–10.

28. Abdelrahman MA et al. (2021) Effect of verbal counselling on metered-dose inhaler proper use and lung function test amongst asthmatic patients: a meta-analysis. Int J Clin Pract e14077. https://doi.org/10.1111/ijcp.14077.

29. Ali AMA et al. (2021) In vitro and in vivo performance modelling and optimisation of different dry powder inhalers: a complementary study of neural networks, genetic algorithms and decision trees. Int J Clin Pract e13764. https://doi.org/10.1111/ijcp.13764.

30. Laube BL, et al. What the pulmonary specialist should know about the new inhalation therapies. Eur Respir J. 2011;37(6):1308–417.

31. Kamps AW, et al. Poor inhalation technique, even after inhalation instructions, in children with asthma. Pediatr Pulmonol. 2000;29(1):39–42.

32. Hendriks HJ, et al. Handling of a spacer (Babyhaler®) for inhalation therapy in 0-to 3-year-old children. J Asthma. 1998;35(3):297–304.

33. Walia M, et al. Assessment of inhalation technique and determinants of incorrect performance among children with asthma. Pediatr Pulmonol. 2006;41(11):1082–7.

34. Education NA et al. (1998) Expert panel report 2: guidelines for the diagnosis and management of asthma. National Institutes of Health, National Heart, Lung, and Blood Institute, Bethesda, MD.

35. Ganguly A, et al. Study of proper use of inhalational devices by bronchial asthma or COPD patients attending a tertiary care hospital. J Clin Diagn Res: JCDR. 2014;8(10):HC04.

36. Ammari WG, Chrystyn H. Optimizing the inhalation flow and technique through metered-dose inhalers of asthmatic adults and children attending a community pharmacy. J Asthma. 2013;50(5):505–13.

37. Health N.I.f. and C. Excellence (2017) Asthma: diagnosis, monitoring and chronic asthma management. National Institute for Health and Care Excellence (NICE), UK.

38. Gulla KM, Kabra S. Peak expiratory flow rate as a monitoring tool in asthma. Indian J Pediatr. 2017;84(8):573–4.

39. Moeller A, et al. ERS task force monitoring asthma in children. Monitoring asthma in childhood: lung function, bronchial responsiveness and inflammation. Eur Respir Rev. 2015;24(136):204–15.

40. Education NA, Program P. National asthma education and prevention program. Expert panel report: guidelines for the diagnosis and management of asthma update on selected topics–2002. J Allergy Clin Immunol. 2002;110(5 Suppl):S141–219.

41. Morosco G, Kiley J. National asthma education and prevention program: Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma-Summary report 2007. J Allergy Clin Immunol. 2007;120(5):S94.

42. Hatley RH, et al. Variability in delivered dose from pressurized metered-dose inhaler formulations due to a delay between shake and fire. J Aerosol Med Pulm Drug Deliv. 2017;30(1):71–9.

43. Kunda NK, et al. A novel approach to study the pMDI plume using an infrared camera and to evaluate the aerodynamic properties after varying the time between actuations. Int J Pharm. 2017;526(1–2):41–9.

44. Ernst P. Inhaled drug delivery: a practical guide to prescribing inhaler devices. Can Respir J. 1998;5(3):180–3.

45. Everard M, et al. Factors affecting total and "respirable" dose delivered by a salbutamol metered-dose inhaler. Thorax. 1995;50(7):746–9.

46. Pauwels RA, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med. 2001;163(5):1256–76.

47. Bateman ED, et al. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J. 2008;31(1):143–78.