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Full Length Article

Effect of DPI's training-device on inhalation technique and clinical efficacy in asthmatics

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ABSTRACT

The aim of this work was to study the effect of using training device (In-Check DIAL) along with traditional dry powder inhaler (DPI) counseling on inhalation technique and pulmonary functions test (PFT) in asthmatics.

Adult asthmatics >18 years old were recruited in 3months study of investigation and training. They were divided into control and investigation groups.

DPI inhalation technique was checked and mistakes were noted and corrected at every monthly visit. Their peak expiratory flow and forced expiratory volume in 1second as percentage of forced vital capacity were checked at each visit followed by showing patients the correct inhalation technique and how to use In-Check DIAL (investigation group).

29 patients (14 females) and 57 patients (30 females) in control and investigation groups respectively completed the study. Mean number of mistakes was significantly decreased ($p < .001$) as the counseling session increased in both groups. Significant decrease in crucial mistake (inhalation quickly and forcefully until complete filling up of the lungs) that was very hard to be learned via only verbal counseling was noticed after the addition of In-Check DIAL. The improvement of the PFT results were significant from the second visit in the investigation group ($p < .05$) and from the third visit in the control group ($p < .01$). The decrease in the rate of rescue medication consumption was faster in investigation group than control group.

Using training device along with verbal counseling has proven a beneficial role in inhalation technique resulting in optimum dosage delivery and yielding reasonable improvement in PFT.

1. Introduction

The main purpose of asthma treatment is to be controlled according to the international asthma management guidelines (Asthma, 2014; Reddel and Levy, 2015), to ensure a good quality of life and minimize asthma exacerbations. This results in a well state of health and productivity; and a thorough notion of pharmaco-economic excellence (Schatz et al., 2007; Delea et al., 2008; Small et al., 2011).

Inhalers are the mainstay treatment for asthma. It is recognized that suitable inhalation technique is important for proper drug delivery to the lungs in order to achieve a reasonable treatment efficacy (Chrystyn, 2009; Roche et al., 2013). Although, misuse leads to uncontrolled state of illness and further increase in treatment costs (Bousquet et al., 2010). This remains a prevalent issue among asthmatic patients (Melani et al., 2011; Press et al., 2011; Elgendy et al., 2015a,b). There are different patterns of inhalation devices, with varying dosage forms, optimal inhalation rate and patient tolerance (Hess, 2008; Dolovich and Dhand, 2011; Laube et al., 2011; Sanchis et al., 2013; Hassan et al., 2016).

The worldwide costs related to management of asthma and chronic obstructive pulmonary disease (COPD) are colossal, for both the patients and the practitioner (Godard et al., 2002; Herjavecz et al., 2003; Leigh et al., 2003; Schramm et al., 2003; Sullivan, 2005). So undoubtedly appropriate training and proper self-management of inhalation devices by efficient counseling

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ensures patient adherence to the treatment regimen (Lareau and Yawn, 2010; To et al., 2013). Nevertheless, many patients misuse their DPIs along with committing considerable number of inhalation technique mistakes (Chrystyn et al., 2017).

The studies investigating misuse of inhalers revealed that poor technique was of high percentage among patients (Hämmerlein et al., 2011; Saji et al., 2012; Roche et al., 2013; Andreevska et al., 2014; Dantic, 2014; Shareef et al., 2014; Elgendy et al., 2015a,b). These studies also showed considerable development in correct and proper use after repeated counseling, accompanied with a subsequent lung function occurred with repeated counseling (Hämmerlein et al., 2011; Saji et al., 2012; Roche et al., 2013; Andreevska et al., 2014; Dantic, 2014; Shareef et al., 2014; Elgendy et al., 2015a,b).

In dry powder inhaler (DPI), the rate limiting step in inhalation technique is inhaling fast and forcefully to deliver optimal dose (Chrystyn et al., 2017). A lot of patients need more emphasis on that step (Chrystyn et al., 2017) Some of them become confused, performing an inhalation rate like that of metered dose inhalers (MDIs) yielding a poor dose delivery and a failure in treatment approach (Hess, 2005).

The Aerosol drug management improvement team (ADMIT) declared that training-aid devices may be helpful to counter problems of poor inhalation technique (Crompton et al., 2006). One of those devices is the multi-type training device for both MDIs and DPIs called In-Check DIAL. This device helps healthcare givers to train patients to use their inhalers properly through both measuring peak inspiratory flow rate and simulating the resistance pattern of the specific inhaler of interest.

For this reason, the aim of this study was to investigate the effect of using In-Check DIAL training device along with conventional counseling on inhalation technique of DPI and pulmonary functions and compare this to sole conventional repeated counseling.

2. Patients and methods

Patients, over 18 years old newly diagnosed with asthma on basis of a medical history investigation, physical examination and spirometry testing, were included in this study. Patients were appointed from Beni-suef University educational hospital outpatient clinics. The local ethical approval permission was obtained.

The patients were randomly divided into investigation and control groups. They both received verbal counseling with the addition of In-Check DIAL (Clement Clarke, UK) as training device in the investigational group only.

All patients had three interviews, one month apart, with the investigator at which they underwent full sheet investigation including elaborate history and diagnosis at the first visit, followed by demonstrating steps of using the hand held spirometer (ONE-FLOW, Clement Clarke, UK) to the patient before measuring of the pulmonary function tests [peak expiratory flow rate in L/min (PEF), forced expiratory volume in one second as percentage of forced vital capacity (FEV_1/FVC%)]. patients were then asked to show their DPI inhalation technique. Meanwhile the investigator recorded mistakes in inhalation technique of DPI and correct their false steps. The patients were asked about their short acting rescue treatment doses frequency (Bateman et al., 2008; Boulet et al., 2015; Elgendy et al., 2015a,b).

Eventually, the investigator trained the patients on use of the In-Check DIAL (investigation group only) in addition to verbal counseling (both groups) of DPI until assurance of correct use as shown below.

DPI inhalation technique steps (Elgendy et al., 2015a,b)

Step 1. Remove the protective cap of the DPI.

Step 2. Prepare the DPI dose according to the patient pamphlet.

Step 3. Exhale comfortably as much as possible.

Step 4. Put the mouthpiece of the DPI device between the teeth then seal with thelips.

Step 5. Make sure the tongue does not plug the mouthpiece.

Step 6. Inhale deeply as fast and deep as possible.

Step 7. Ensure a fast inhalation rate till filling up the lungs.

Step 8. Remove the device from the mouth then hold breath for 5–10 s.

Step 9. If more than only one dose is needed, wait for about 30 s before the next dose.

Step 10. Rinse mouth, and brush the teeth after dosing if possible.

Step 11. Reattach the cap of the DPI device after use.

3. Inclusion criteria

Asthmatic patients capable of performing the pulmonary function test properly, treated with a DPI and older than eighteen years were recruited in this study.

4. Exclusion criteria

Hospitalized patients in an intensive care unit; patients of any mental deficiency affecting their cognition or learning ability and anyone unable to perform the pulmonary function test properly was excluded from this study.

5. Data modeling

Data modeling was performed using Design Expert 7.0.0 (Stat-Ease Inc., Minneapolis, MN, USA) to make a graphical co-relation between the input and the output variables from the investigation group. The inputs were age and visits and they were abbreviated as following; for age 18–40 years old (0.1), from 40 to 60 years old (0.2) and older than 60 years old (0.3), and for visits, first visit (1), second visit (2) and third visit (3).

5.1. Statistical analysis

Analysis was carried out using the two way analysis of variance (ANOVA) on SPSS 20 software program (SPSS Inc., Chicago, USA) for the effect of gender and age on main variables, within-group comparison of PEF, FEV_1/FVC percentage and mean number of mistakes committed at each visit at $p < .05$ followed by Post hoc ANOVA using the Tukey system.

Also comparing the total number of mistakes in every step in the three visits was performed using Cochran and McNemar tests

6. Results

29 (14 females) asthmatic subjects were recruited in the control group and 57 (30 females) in the investigation group with mean (SD) age 47.3 (16.9) and 49.9 (17.8) respectively. Their data analysis revealed no significant difference in the PEF, FEV_1/FVC percentage and the mean number of mistakes of the DPI inhalation technique between males and female subjects.

The mean (SD) values of PEF, FEV_1/FVC% and number of mistakes of the DPI inhalation technique at each visit for the investigation and control groups are shown in Table 1. The improvement in the PEF and FEV_1/FVC% and the decrease in the mean number of mistakes in investigation group was significant from visit 1 to 2 ($p < .05$) and 1 to 3 ($p < .001$). Also, the decrease in the mean number of mistakes in control group was significant from visit 1 to 2 ($p < .001$) and 1 to 3 ($p < .001$). However, the improvement in the PEF

Table 1
The Mean (SD) values of PEF, FEV_1/FVC% and number of mistakes of the DPI inhalation technique at each visit for the control and investigation groups.

	First visit	Second visit	Third visit
PEF (L/min) control group	108.46 (52.61)	147.81.1 4 (39.42)	199.31 (35.46)
PEF (L/min) intervention group	108.42 (53.61)	155.52 (36.37)	196.31 (32.424)
FEV_1/FVC (%) control group	53.43 (16.64)	64.1 (10.51)	74.43 (8.12)
FEV_1/FVC (%) intervention group	52.0 (15.64)	69.52 (9.31)	74.96 (8.22)
Mean number of mistakes control group	5.28 (1.39)	1.58 (0.66)	0.29 (0.59)
Mean number of mistakes intervention group	5.2 (1.18)	1.26 (0.76)	0.29 (0.49)

and FEV_1/FVC% in control group was only significant from visit 1 to 3 ($p < .001$). There was no significant difference between control and investigation groups in PEF, FEV_1/FVC% and mean number of mistakes.

The percentages of correct attainment of each step of the DPI inhalation technique in investigation and control groups during the three visits are shown in Fig. 1 A and B. Steps 2, 3, 4, 6, 7, 8 and 10 were shown to be having higher rate of failure at the first visit in both groups. However, they were improved, similarly in both groups, over the next two visits. Only step 6 and 7 were improved, with much higher rate, in visit 2 and 3 in investigation group compared to control group. As shown in Fig. 2, the lowest improvement rate was in step 7 in the control group which began by a percentage of 31% then 48% and finally 55% at the third visit, where investigation group started by a percentage of 38% then 96% and finally reached 100% at the third visit.

Regarding the administration of the short acting rescues doses (Bateman et al., 2008; Boulet et al., 2015) for both of control and investigation group; at visit 1, all patients often tend to take rescue doses more than twice (partly controlled). At visit 2 the percentage of patients taking rescue doses equals or less than twice a week (well controlled) in control group reached 75%, while in intervention groups reached 79%. Afterwards in the period from visit 2 to visit 3 the percentage for the control and investigation groups were 91% and 92% respectively.

The resulted data were divided into three age groups as shown in Tables 2 and 3. The three age groups were 18–40 years old (Group 1), >40–60 years old (Group 2) and >60 years old (Group 3).

At visit 1, age group 1 has highest and age group 3 had the lowest PEF and FEV_1/FVC but the difference were gradually decreased as the visits increase. The lowest number of mistakes at visit 1 was found in age group 2. There was no mistake specific to age, gender or educational level.

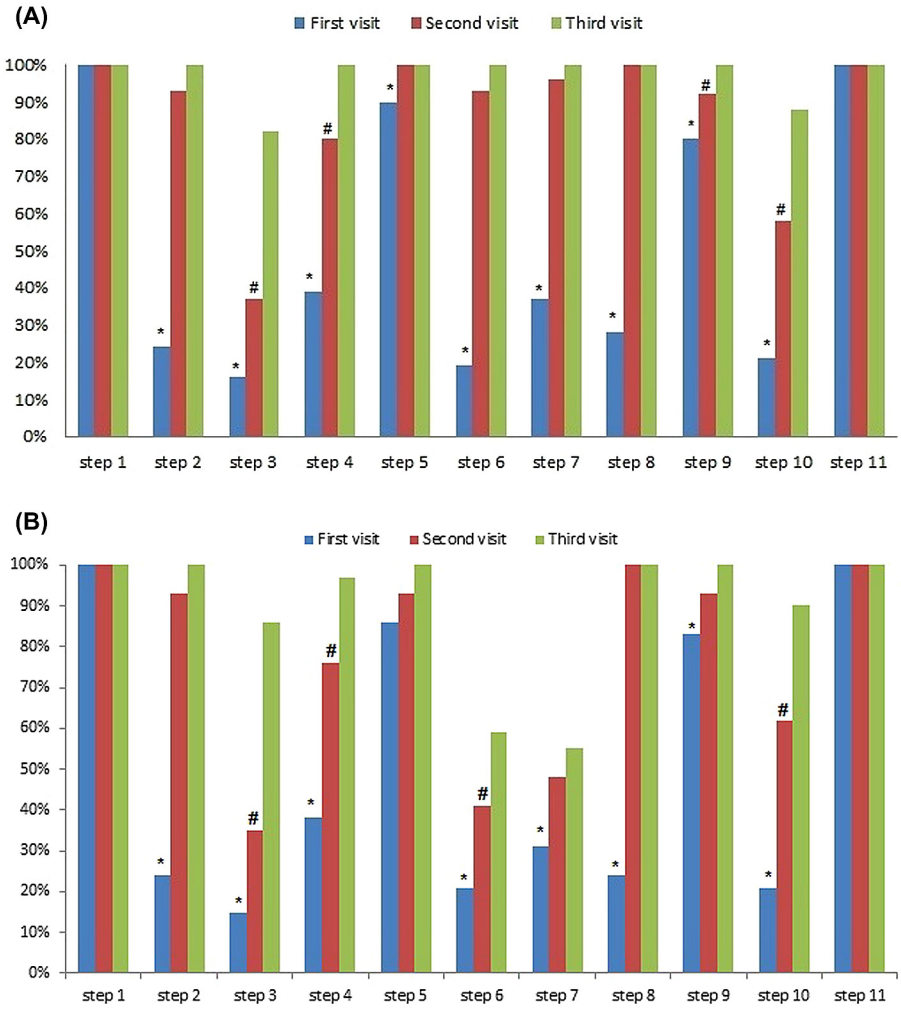

Fig. 1. Percentage of correct achievement of each step of DPI at all the visits in the (A) investigated group and (B) control group; *significant difference between visit 1 and 2, while #significant difference between Visit 2 and 3.

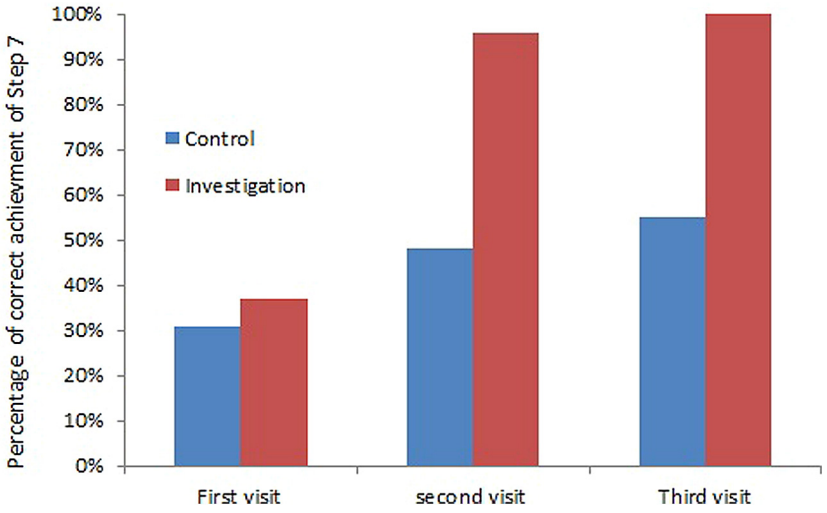

Fig. 2. The percentage of correct achievement of step 7 (Ensure a fast inhalation rate till filling up the lungs.) in relation to consecutive visits.

Table 2
The Mean (SD) values of PEF, FEV_1/FVC% and number of mistakes of the DPI inhalation technique at each visit for the control groups.

	First visit	Second visit	Third visit
PEF GP1C (L/min)	133.2 (47.8)	176.9 (55.39)	215.9 (43.18)
PEF GP2C (L/min)	114 (44.1)	159.94 (28.98)	198.181 (18.5)
PEF GP3C (L/min)	78.2 (15.8)	106.6 (13.8)	184 (11.73)
FEV_1/FVC GP1C (%)	63.1 (15.99)	72.6 (10.54)	75.5 (10.19)
FEV_1/FVC GP2C (%)	48.5 (12.6)	66.18 (8.14)	73.09 (8.3)
FEV_1/FVC GP3C (%)	48.7 (14.98)	53.52 (8.0)	74.7 (5.4)
Mean number of mistakes GP1C	5.6 (1.37)	0.63 (0.61)	0.067 (0.23)
Mean number of mistakes GP2C	5.09 (1.41)	1.6 (0.9)	0.084 (0.29)
Mean number of mistakes GP3C	5.176 (0.39)	2.53 (0.51)	0.74 (0.53)

Table 3
The Mean (SD) values of PEF, FEV_1/FVC% and number of mistakes of the DPI inhalation technique at each visit for the intervention group.

	First visit	Second visit	Third visit
PEF GP1 (L/min)	132.7 (47.8)	176.9 (55.39)	216.9 (43.18)
PEF GP2 (L/min)	110.0 (44.1)	159.94 (28.98)	198.181 (18.5)
PEF GP3 (L/min)	78.2 (15.8)	127.6 (13.8)	172.0 (11.73)
FEV_1/FVC GP1 (%)	61.5 (15.99)	73.4 (10.54)	75.5 (10.19)
FEV_1/FVC GP2 (%)	48.5 (12.6)	67.18 (8.14)	73.09 (8.3)
FEV_1/FVC GP3 (%)	46.7 (14.98)	68.52 (8.0)	76.41 (5.4)
Mean number of mistakes GP1	5.3 (1.37)	0.83 (0.61)	0.055 (0.23)
Mean number of mistakes GP2	5.09 (1.41)	1.4 (0.9)	0.09 (0.29)
Mean number of mistakes GP3	5.176 (0.39)	1.53 (0.51)	0.82 (0.53)

According to the data modeling, the overall dual effect of both age and frequency of visits on PEF, FEV_1/FVC and the mean number of mistakes are represented in Fig. 3A–C, respectively (response surface plots). Significant models for PEF, FEV_1/FVC and mean number of mistakes were reflected by Model F-values = 142.63, 31.03 and 218.96 respectively ($p < .001$). Also, there was only a 0.01% chance that the noise was a cause of these F-values, thus indicating the validity of the models for prediction of further data and validation of current results as shown in Fig. 3D.

7. Discussion

Similar to previous studies, no significant difference was found in number of mistakes between both educated and non-educated subjects (Hämmerlein et al., 2011). These findings might be because the patients were newly diagnosed and had no any past experience about the DPI (Hämmerlein et al., 2011).

The number of mistakes for inhalation technique steps decreased significantly ($p < .001$) at the upcoming visits by the effect of both counseling and In-Check DIAL as training device. Mistakes were not committed for logical steps e.g. both steps 1 "Removing the cap" and 11 "Reattach the cap of the DPI device after use" (Elgendy et al., 2015a,b).

Previous studies also revealed great improvement and decrease of total number of mistakes while applying the DPI inhalation technique using the continuous traditional verbal counseling process (Newman, 2005; Lavorini et al., 2008; Saji et al., 2012). A significant improvement between visits 1 and 2 ($p < .001$) was observed followed by further improvement in the third visit ($p < .001$). So, continuous counseling of patients has already proved to be beneficial and important for a correct inhalation technique (Newman, 2005; Lavorini et al., 2008; Saji et al., 2012). However, step 6 "Inhale deeply as fast and deep as possible." and step 7 "Ensure a fast inhalation rate till filling up the lungs.", in a previous study as well as the results of the control group, was observed to be very difficult steps for patients to be achieved or learned by only counseling (Elgendy et al., 2015a,b). While in this study a more promising progress in all patient age was observed in the investigation group. Higher percentages of right achievement of steps 6 and 7 in visits 2 and 3 were observed using the training device (In-Check DIAL) suggesting a beneficial role of the In-Check DIAL on such crucial steps (Elgendy et al., 2015a,b). Coaching of patients using the training device made those steps easily taught compared to control group or previous study applying the counseling method alone (Elgendy et al., 2015a,b). This was reflected in the significant improvement in the PFT in the investigation group which occurs in

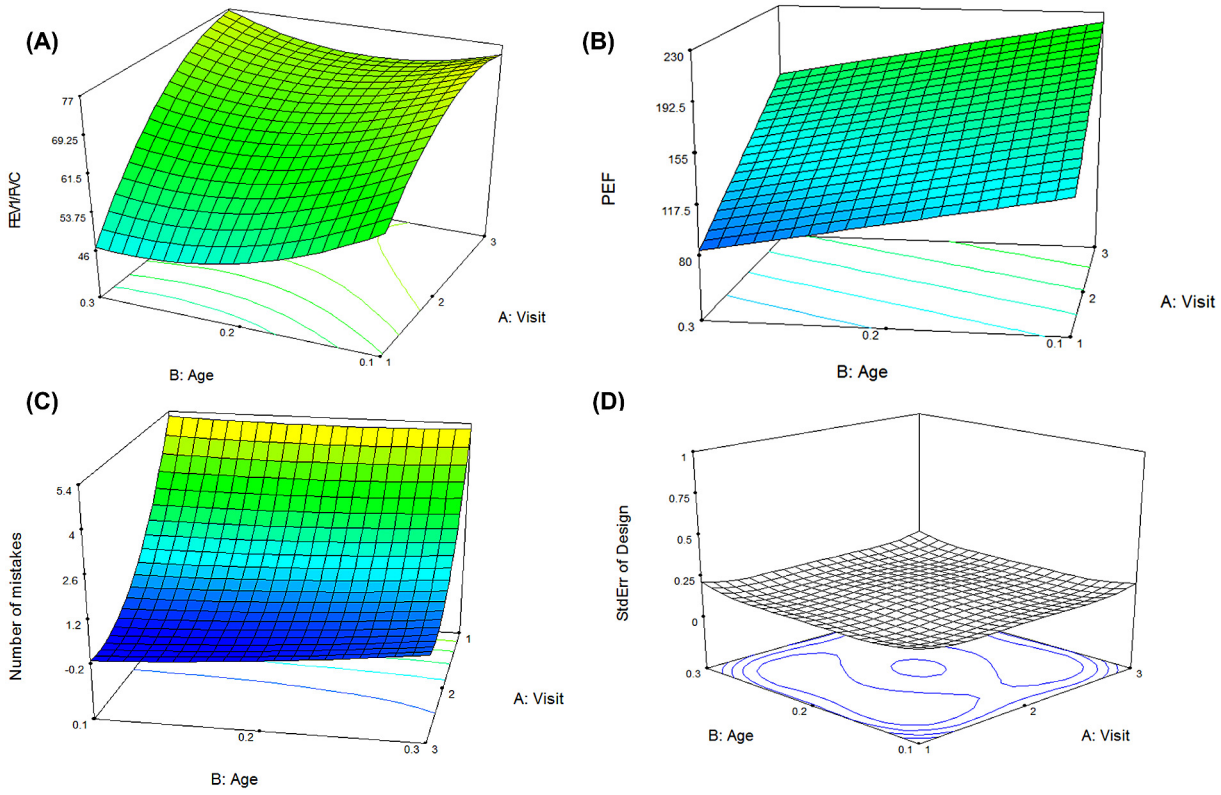

Fig. 3. A response surface plot of the relation between different visits and ages and their effect on (A) FEV_1/FVC%, (B) PEF and (C) mean number of mistakes; (D) The standard error value of models.

the second visit ($p < .05$) showing how crucial steps 6 and 7 are to the DPI user. This improvement was not found in the control group until the third visit. The In-Check DIAL improvement of steps 6 and 7 could also help in controlling the asthmatic patients faster for better quality of life since the percentage of stable patient (patients taking rescue doses equals or less than twice a week) in the second visit were higher in investigation group than control group.

The effect of the training aid could be of a very important benefit especially for the elderly patients with their low inspiration ability (Sharma and Goodwin, 2006) They might acquire more practice by the training device to achieve more easily the required inspiration of the DPI (Abdelrahim, 2010; Abdelrahim et al., 2013; Ali and Abdelrahim, 2014). Hence the uses of the training device along with the traditional counseling is much better, especially in the complete filling of lungs with the desired drug dose in contrast to using the traditional counseling method alone.

Similar to previous studies the age had effects in the present study (Elgendy et al., 2015a,b). Even though age group 3 (patients older than 60 years old) showed a significant decrease in the mean number of mistakes while going further in the counseling visits; they still had a relative higher mean number of mistakes compared to the other two groups at the end of the coaching period. That may be related to the possible inferior learning ability of old patients (Voelcker-Rehage, 2008). Also, PEF and FEV_1/FCV of different age groups for both control and intervention groups in each visit were significantly greater in age group 1 than in the other two groups ($p < .05$). This may be due to the normal physiological deterioration of lung functions with aging (Janssens, 2005; Ruivo et al., 2009).

The combined effects of continuous counseling and age are graphically simplified by the modeling results which revealed that both continuous counseling made a gradual improvement in patient's quality of life and status. Also there was a profound impact of age groups on the patient cognitive properties to memorize the DPI inhalation technique and the counseling instructions properly. Thus, modeling provided an additional way that could simply help the health care provider to know the need of certain patient according to his age and number and status (Saeed et al., 2017). Both the high F-values and low the noise of the models resulted have helped to anticipate the expected improvement in patients' status according to both age and number of counseling sessions provided to them (Ali and Abdelrahim, 2014; Hussein et al., 2017; Rabea et al., 2017) Further studies are required to implement such a tool in counseling anticipation and suggestion.

8. Conclusion

Using the In-Check DIAL in patient DPI training in addition to the traditional verbal counseling has ensured a positive useful role in training and instructing asthmatic patients about dose delivery for the DPI. It also minimized the frequency of errors related to the dose delivery. It resulted in a suitable clinical efficacy compared to traditional verbal counseling alone.

References

Abdelrahim, M., Assi, K., Chrystyn, H., 2013. Dose emission and aerodynamic characterization of the terbutaline sulphate dose emitted from a Turbuhaler at low inhalation flow. Pharm. Dev. Technol. 18 (4), 944–949.
Abdelrahim, M.E., 2010. Emitted dose and lung deposition of inhaled terbutaline from turbuhaler at different conditions. Respir. Med. 104 (5), 682–689.
Ali, A., Abdelrahim, M., 2014. Modeling and optimization of terbutaline emitted from a dry powder inhaler and influence on systemic bioavailability using data mining technology. J. Pharm. Innovation 9 (1), 38–47.
Andreevska, K., Petkova, V., Jordanova, S., Grekova, D., Madjarov, V., Dimitrova, M., et al., 2014. Effect of education on patients with chronic obstructive pulmonary disease. WJPPS 3 (3), 01–09.

Asthma, T. B. G. o. t. M. o. 2014. The British Guideline on the Management of Asthma [Online]. Retrieved 6 March 2017.
Bateman, E., Hurd, S., Barnes, P., Bousquet, J., Drazen, J., FitzGerald, M., et al., 2008. Global strategy for asthma management and prevention: GINA executive summary. Eur. Respir. J. 31 (1), 143–178.
Boulet, L.-P., FitzGerald, J.M., Reddel, H.K., 2015. The revised 2014 GINA strategy report: opportunities for change. Curr. Opin. Pulmonary Med. 21 (1), 1–7.
Bousquet, J., Mantzouranis, E., Cruz, A.A., Aït-Khaled, N., Baena-Cagnani, C.E., Bleecker, E.R., et al., 2010. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. J. Allergy Clin.Immunol. 126 (5), 926–938.
Chrystyn, H. 2009. Effects of device design on patient compliance: comparing the same drug in different devices. Davis Healthcare International.
Chrystyn, H., van der Palen, J., Sharma, R., Barnes, N., Delafont, B., Mahajan, A., et al., 2017. Device errors in asthma and COPD: systematic literature review and meta-analysis. npj Primary Care Respir. Med. 27, 1.
Crompton, G., Barnes, P., Broeders, M., Corrigan, C., Corbetta, L., Dekhuijzen, R., et al., 2006. The need to improve inhalation technique in Europe: a report from the Aerosol Drug Management Improvement Team. Respir. Med. 100 (9), 1479–1494.
Dantic, D.E., 2014. A critical review of the effectiveness of 'teach-back'technique in teaching COPD patients self-management using respiratory inhalers. Health Educ. J. 73 (1), 41–50.
Delea, T.E., Stanford, R.H., Hagiwara, M., Stempel, D.A., 2008. Association between adherence with fixed dose combination fluticasone propionate/salmeterol on asthma outcomes and costs. Curr. Med. Res. Opin. 24 (12), 3435–3442.
Dolovich, M.B., Dhand, R., 2011. Aerosol drug delivery: developments in device design and clinical use. Lancet 377 (9770), 1032–1045.
Elgendy, M.O., Abdelrahim, M.E., Eldin, R.S., 2015a. Potential benefit of repeated dry powder inhaler's inhalation technique counseling on asthmatic patients. Pulmonary Therapy 1 (1), 91–101.
Elgendy, M.O., Abdelrahim, M.E., Eldin, R.S., 2015. Potential benefit of repeated MDI inhalation technique counselling for patients with asthma. Eur. J. Hospital Pharm. 22 (6), 318–322. ejhpharm-2015-000648.
Godard, P., Chanez, P., Siraudin, L., Nicoloyannis, N., Duru, G., 2002. Costs of asthma are correlated with severity: a 1-yr prospective study. Eur. Respir. J. 19 (1), 61–67.
Hämmerlein, A., Müller, U., Schulz, M., 2011. Pharmacist-led intervention study to improve inhalation technique in asthma and COPD patients. J. Eval. Clin. Pract. 17 (1), 61–70.
Hassan, A., Rabea, H., Hussein, R.R.S., Salah Eldin, R., Abdelrahman, M.M., Said, A.S.A., et al., 2016. In-vitro characterization of the aerosolized dose during non-invasive automatic continuous positive airway pressure ventilation. Pulm. Ther., 1–12
Herjavecz, I., Boszormenyi Nagy, G., Gyurkovits, K., Magyar, P., Dobos, K., Nagy, L., et al., 2003. Cost, morbidity, and control of asthma in Hungary: The Hunair Study. J. Asthma 40 (6), 673–681.
Hess, D.R., 2005. Metered-dose inhalers and dry powder inhalers in aerosol therapy. Respir. Care 50 (10), 1376–1383.
Hess, D.R., 2008. Aerosol delivery devices in the treatment of asthma. Respir. Care 53 (6), 699–725.
Hussein, R.R.S., Ali, A.M.A., Salem, H.F., Abdelrahman, M.M., Said, A.S.A., Abdelrahim, M.E.A., 2017. In vitro/in vivo correlation and modeling of emitted dose and lung deposition of inhaled salbutamol from metered dose inhalers with different types of spacers in noninvasively ventilated patients. Pharm. Dev. Technol. 1–10 22 (7), 871–880.
Janssens, J.-P., 2005. Aging of the respiratory system: impact on pulmonary function tests and adaptation to exertion. Clin. Chest Med. 26 (3), 469–484.
Lareau, S.C., Yawn, B.P., 2010. Improving adherence with inhaler therapy in COPD. Int. J. Chron. Obstruct. Pulmon. Dis. 5, 401–406.
Laube, B.L., Janssens, H.M., Jongh, F.H., Devadason, S.G., Dhand, R., Diot, P., et al., 2011. What the pulmonary specialist should know about the new inhalation therapies. Eur. Respir. Soc. 37, 1308–1417.
Lavorini, F., Magnan, A., Dubus, J.C., Voshaar, T., Corbetta, L., Broeders, M., et al., 2008. Effect of incorrect use of dry powder inhalers on management of patients with asthma and COPD. Respir. Med. 102 (4), 593–604.
Leigh, J.P., Yasmeen, S., Miller, T.R., 2003. Medical costs of fourteen occupational illnesses in the United States in 1999. Scand. J. Work Environ. Health 29 (4), 304–313.
Melani, A.S., Bonavia, M., Cilenti, V., Cinti, C., Lodi, M., Martucci, P., et al., 2011. Inhaler mishandling remains common in real life and is associated with reduced disease control. Respir. Med. 105 (6), 930–938.
Newman, S., 2005. Inhaler treatment options in COPD. Eur. Respir. Rev. 14 (96), 102–108.
Press, V.G., Arora, V.M., Shah, L.M., Lewis, S.L., Ivy, K., Charbeneau, J., et al., 2011. Misuse of respiratory inhalers in hospitalized patients with asthma or COPD. J. Gen. Internal Med. 26 (6), 635–642.
Rabea, H., Ali, A.M.A., Salah Eldin, R., Abdelrahman, M.M., Said, A.S.A., Abdelrahim, M.E., 2017. Modelling of in-vitro and in-vivo performance of aerosol emitted from different vibrating mesh nebulisers in non-invasive ventilation circuit. Eur. J. Pharm. Sci. 97, 182–191.
Reddel, H.K., Levy, M.L., 2015. The GINA asthma strategy report: what's new for primary care? NPJ Primary Care Respir. Med. 25, 15050.
Roche, N., Chrystyn, H., Lavorini, F., Agusti, A., Virchow, J.C., Dekhuijzen, R., et al., 2013. Effectiveness of inhaler devices in adult asthma and COPD. EMJ Respir. 1, 64–71.
Ruivo, S., Viana, P., Martins, C., Baeta, C., 2009. Effects of aging on lung function. A comparison of lung function in healthy adults and the elderly. Revista Portuguesa de Pneumologia (English Edition) 15 (4), 629–653.
Saeed, H., Elberry, A.A., Eldin, A.S., Rabea, H., Abdelrahim, M.E.A., 2017. Effect of nebulizer designs on aerosol delivery during non-invasive mechanical ventilation: a modeling study of in vitro data. Pulm. Ther. 3 (1), 233–241.
Saji, M., Alhas, J., Siraj, S., 2012. Study on the impact of patient counseling on the quality of life and pulmonary function of asthmatic patient. Int. J. Pharm. Pharm. Sci. 4 (Suppl 5), 300–304.
Sanchis, J., Corrigan, C., Levy, M.L., Viejo, J.L., 2013. Inhaler devices–from theory to practice. Respir. Med. 107 (4), 495–502.
Schatz, M., Mosen, D.M., Kosinski, M., Vollmer, W.M., Magid, D.J., O'Connor, E., et al., 2007. The relationship between asthma-specific quality of life and asthma control. J. Asthma 44 (5), 391–395.
Schramm, B., Ehlken, B., Smala, A., Quednau, K., Berger, K., Nowak, D., 2003. Cost of illness of atopic asthma and seasonal allergic rhinitis in Germany: 1-yr retrospective study. Eur. Respir. J. 21 (1), 116–122.
Shareef, J., Sajitha, M., Shastry, C., 2014. Impact of pharmacist provided patient counseling on quality of life inpatients with asthma in a tertiary care teaching hospital. Int. J. Pharm. Res. Rev. 3 (2), 1–10.
Sharma, G., Goodwin, J., 2006. Effect of aging on respiratory system physiology and immunology. Clin. Interv. Aging 1 (3), 253.
Small, M., Anderson, P., Vickers, A., Kay, S., Fermer, S., 2011. Importance of inhaler-device satisfaction in asthma treatment: real-world observations of physician-observed compliance and clinical/patient-reported outcomes. Adv. Therapy 28 (3), 202–212.
Sullivan, S. 2005. The burden of uncontrolled asthma on the US health care system. Managed care (Langhorne, Pa.) 14(8 Suppl): 4–7; discussion 25–27.
To, K.W., Lee, W.M., Choi, K.C., Doris, Y., Janita, C., Iris, L., 2013. Educational and supportive interventions for improving adherence to inhalation therapy in people with chronic respiratory diseases: a systematic review protocol. JBI Database Syst. Rev. Implem. Rep. 11 (1), 329–345.
Voelcker-Rehage, C., 2008. Motor-skill learning in older adults—a review of studies on age-related differences. Eur. Rev. Aging Phys. Activity 5 (1), 5–16.