Evaluasi Teknik Penggunaan Inhaler pada Pasien Asma dan PPOK di Suatu Sarana Pelayanan Kesehatan Primer : Suatu Studi Pendahuluan di Selangor Malaysia

Evaluating Inhaler Use Technique Among Asthma and Copd Patients at a Primary Health Care Unit : a Pilot Study in Selangor Malaysia

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ABSTRAK

Inhaler adalah alat yang paling disukai untuk pengobatan asma dan penyakit paru obstruktif kronik (PPOK). Penggunaan inhaler yang tidak tepat mempengaruhi efektivitas klinis dari obat yang digunakan. Suatu studi pendahuluan dilakukan untuk menentukan ketepatan teknik penggunaan inhaler pada pasien asma dan PPOK. Sebanyak 92 subjek yang didiagnosa asma dan PPOK, berusia 18 hingga 64 tahun, diamati pada studi potong-lintang ini. Subjek yang menggunakan inhaler, yang mengunungi klinik rawat jalan di suatu fasilitas pelayanan kesehatan primer di Selangor, Malaysia diminta untuk mendemonstrasikan bagaimana mereka menggunakan inhaler sementara itu formulir isian digunakan untuk menilai teknik penggunaan. Data dianalisis dengan statistik deskriptif. Dari total 92 subjek terdapat 155 inhaler digunakan. Hanya 4 dari 92 subjek (4.3%) yang menggunakan inhaler dengan benar. Rata-rata seorang pasien membuat >4 kesalahan saat menggunakan pMDI dan >2 kesalahan saat menggunakan DPI. Kesalahan yang paling umum di antara pengguna pMDI, Turbuhaler, dan Accuhaler adalah tidak mampu menahan nafas selama kurang lebih 5 detik yang mencakup ≥80% pasien. Mayoritas pasien asma dan PPOK tidak menggunakan inhaler dengan benar. Pasien yang diresepkan obat-obatan inhalasi harus dinilai ketepatan penggunaannya secara rutin pada setiap kunjungan dan dikoreksi bila diketahui terdapat kesalahan.

Kata kunci: asma, PPOK, teknik inhalasi, kepatuhan

ABSTRACT

Inhaler is the most preferable device to deliver medication in order to treat asthma and Chronic Obstructive Pulmonary Disease (COPD). Incorrect usage of inhaler influences the clinical effectiveness of the delivered drug. A pilot study was conducted to determine the appropriateness of inhaler handling technique among asthma and COPD patients. As many as 92 subjects whom diagnosed with asthma and COPD, aged between 18 to 64 years old were observed in this cross-sectional study. Consenting subjects on inhaler, who attended medical out patients clinic at a primary health care unit in Selangor, Malaysia were asked to demonstrate on how they use the inhaler while an inhaler administration checklist were used to assess each patients inhaler technique. Data was analysed using descriptive statistical methods. Of total 92 patients, a total of 155 devices were used. Only 4 out of 92 patients correctly handles the device (4.3%). In average, a patient made approximately >4 mistakes during pMDI inhalation and >2 mistakes during DPI inhalation. The most common mistake found among pMDI, Turbuhaler and Accuhaler users were unable to hold the breath for approximately 5 seconds in which comprise of ≥80% patients. In conclusion, majority of asthma and COPD patients use their inhaler inaccurately. Patients prescribed by inhalation medications should have routine assessment of their inhaler technique at every visit and corrected if found to be poor.

Keywords: asthma, COPD, inhalation technique, compliance

INTRODUCTION

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation¹. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with the variable expiratory airflow limitation². Asthma consideed as a common chronic respiratory disease affecting 1-18% population in many countries¹. Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways and the lungs to noxious particles or gases². The number of COPD cases is estimated to reach 384 million in 2010, with a global prevalence of 11.7% (95% confidence interval CI) 8.4%–15.0%³.

Medication for asthma is most commonly taken through an inhaler, which is a device that helps to get the medication straight into the lung airways where it is needed in order to increase the effectiveness and to reduce the systemic adverse reactions. There are two main groups of inhalers (pressurized metered dose inhalers /MDIs and dry powder inhalers/DPIs)⁴ and a few different names that are used. Each device is used in а different steps so it is very important to ensure the patients use inhaler appropriately. A systematic review report incorrect that inhaler technique is unacceptably frequent and has not improved over the past 40 years⁵. The condition are associated with decreased medication delivery and poor disease control6,7. One important risk factor is lack of knowledge the proper handling technique of on the inhalers by the patients who suffering from asthma and COPD patients⁸⁻¹¹. Thus, a study was constructed to assess the knowledge and practice of asthmatic device self-administration among asthma and COPD patients.

The preliminary study was aimed to describe the correctness of inhaler usage and act as a stepping stone to a larger study identifying the risk factor contribute to poor knowledge and the impact of poor inhalation technique to asthma and COPD outcome. We expect to provide recommendations regarding the handling technique of inhaler to obtain a better control and prevent the development of the disease.

METHODS Subjects

As many as 92 sample subjects recruited in the study would be those with following characteristics: (1) Patient diagnosed with asthma and COPD, (2) current user of inhaler devices, (3) repeatedly use the inhalers during last three months, (3) patient's previous visit and current visit on the same health care unit with no missed visit, (4) patients with the age of 18 to 64 years, and (6) patients who visit the pharmacy by their own and not related to the medical personnel. The exclusion criteria was the patient that does not fill up all of the item in the questionnaire.

Study design

The study was a cross-sectional study design and conducted at a primary health care unit in Selangor, Malaysia within December 2015 to March 2016.

Outcome

We collected demographical using questionnaire while the patient's knowledge about proper usage of inhaler device was identified based on the questionnaires and visual observation by the local pharmacist. The demographical data comprised of age, sex and education level. The appropriateness of inhaler usage were collected using an adopted checklist from National Asthma Council Australia¹² to determine the knowledge and practice of inhaler devices among asthma and COPD patients. The data was obtained from the patients who came to their treatment for asthma and COPD during the study period.

Statistical analysis

The number of sample was calculated based on Slovin's formula using 0.05 margin of error. Data obtained from the usage checklist was analysed using descriptive statistical methods.

RESULTS AND DISCUSSION The characteristics of subjects

Majority of the subjects was male (n=49, 53.3%) and aged 18-44 years (n=71, 77.2%). More than 40% of the subjects held diploma and degree education. However, 17 subjects (18.5%) had no formal education. A total of 155 devices were used by 92 subjects.

An inhaler containing combination of fluticasone-salbutamol was the most prefered device (n=23, 25%), followed by combination of salbutamol and salmeterol-fluticasone (n=14, 15.2%) and salbutamol-beclomethasone (n=10, 10.9%). The detailed information is (Table I).

Type of inhaler used

Overall, salbutamol inhaler (pMDI) was the most frequent medications used by subjects (44.5%) followed by fluticasone combination in pMDI (14.8%) and salmeterol + fluticasone propionate in DPI-accuhaler (9.7%) (Table II).

We found that various kind of inhaler device was used (pMDI, turbuhaler, accuhaler and handihaler) with a total of 155 devices were used. Majority of the patients were prescribed with a combination of two pMDIs (n=39, 42.4%) followed by a combination of DPIs with pMDIs (n=24, 26.1%). As many as 19 patients (20.6%) were using DPIs alone and 10 patients (10.9%) were using pMDIs alone. Turbuhaler was the most preferred device to use in cobination (n=20), followed accuhaler (n=15) and handihaler (n=9) to deliver the drug to treat asthma and COPD.

Practice of the asthmatic device among asthma and COPD patients

A large proportion of patients prescribed inhaled medications did not use their inhalers correctly. Overall, most of the patients (n=88; 95.7%) showed incorrect inhaler handling technique with either standard pressurised meterde-dose inhalers (pMDIs) or dry powder inhalers (DPIs) such as accuhaler, handihaler and turbuhaler. Only four patients (4.3%) handled the inhaler device correctly (Figure 1). Overall, DPI users (Turbuhaler, Accuhaler and Handihaler) have higher error numbers than pMDI users (97.7 vs 95.9%). Most of errors observed in patients using Accuhaler and Handihaler (100%) followed by pMDI (95.9%) and Turbuhaler (95%).

Common errors for several inhaler types (Table III) pMDI, (Table IV) Turbuhaler, (Table V) Accuhaler and (Table VI) Handihaler along with ansuggested checklist of steps for each inhaler. There are various types of the inhalers and each has its own way to handle the device. We found similar mistakes between pMDI, Turbuhaler and Accuhaler in which \geq 80% patients were unable to hold the breath for approximately 5 seconds. This was the most common mistake found in those three type of devices.

Other common errors observed in most of pMDI user were unable to continue breathe in slowly and deeply (87.7%), inability to coordinate activation with inhalation (82.2%), unable to hold the breath while removing the inhaler from mouth (72.6%) and breathe out to the inhaler instead of breath out gently away from inhaler (54.8%). 75% of Turbuhaler users were unable to place the mouthpiece between the teeth and does not form a good seal. More than half of the Accuhaler users did not keep the inhaler horizontal position while inhaling the drug (73.3%) and were unable to load the dose by holding the device in horizontal position (53.3%). All of the Handihaler use (n=9) were unable to breathe in deeply until capsule vibrate sound is heard. Most of Handihaler users also failed press the green piercing button fully (77.8%) and were unable to breathe out completely before administrating the drug (66.7%).

This study showed that the rate of inappropriateness usage of inhaler among asthma and COPD patients was more than 90% which is very high. In average, a patient made approximately >4 mistakes during pMDI inhalation and >2 mistakes during DPI inhalation. We tried to identify at which step most of the patients showed error by including various type of inhaler.

Our results shown higher percentage of patients performing incorrect inhalation

| Characteristics | n | % |
|---|----|------|
| Age | | |
| 18 – 44 | 71 | 77.2 |
| 45 – 59 | 20 | 21.7 |
| 60 - 64 | 1 | 1.1 |
| Gender | | |
| Male | 49 | 53.3 |
| Female | 43 | 46.7 |
| Education | | |
| Sijil Pelajaran Malaysia (SPM, secondary school) | 21 | 22.8 |
| STPM (STPM, pre-university education) | 1 | 1.1 |
| Foundation | 3 | 3.3 |
| Diploma | 21 | 22.8 |
| Degree | 22 | 23.9 |
| Master | 7 | 7.6 |
| No education | 17 | 18.5 |
| Inhaler used among subjects | | |
| Salbutamol (pMDI) and Fluticasone (pMDI) | 23 | 25,0 |
| Salbutamol (pMDI) and Salmeterol + fluticasone propionate (DPI accuhaler) | 14 | 15,2 |
| Salbutamol (pMDI) and Beclomethasone dipropionate (pMDI) | 10 | 10,9 |
| Budesonide + formoterol (DPI turbuhaler) | 9 | 9,8 |
| Tiotropium Br (DPI handihaler) | 9 | 9,8 |
| Salbutamol (pMDI) and Budesonide (DPI turbuhaler) | 8 | 8,7 |
| Salbutamol (pMDI) and Ciclesonide (pMDI) | 6 | 6,5 |
| Salbutamol (pMDI) | 6 | 6,5 |
| Ciclesonide (pMDI) | 4 | 4,3 |
| Salbutamol (pMDI) dan Budesonide + formoterol (DPI turbuhaler) | 2 | 2,2 |
| Salmeterol + fluticasone propionate (DPI accuhaler) | 1 | 1,1 |
| Proper usage of asthmatic device by subjects | | |
| Yes | 4 | 4.3 |
| No | 88 | 95.7 |

Table I. The Characteristics of the Subjects

n =Number of sample

Table II. Quantity of Inhaler Used Among Subjects

| Quantity of inhaler used among subjects | n | % |
|---|----|------|
| Salbutamol (pMDI) | 69 | 44,5 |
| Combination of fluticasone (pMDI) | 23 | 14,8 |
| Salmeterol + fluticasone propionate (DPI – accuhaler) | 15 | 9,7 |
| Budesonide + formoterol (DPI – turbuhaler) | 11 | 7,1 |
| Beclomethasone dipropionate (pMDI) | 10 | 6,5 |
| Ciclesonide (pMDI) | 10 | 6,5 |
| Tiotropium Br (DPI – handihaler) | 9 | 5,8 |
| Budesonide (DPI – turbuhaler) | 8 | 5,2 |

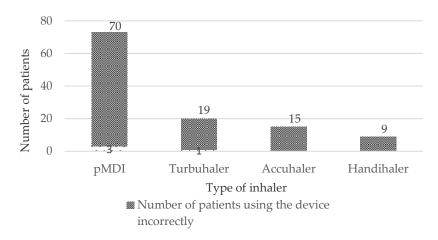


Figure 1. Number of Patients Using the Various Kind of Inhaler with Proper Usage of the Device.

| Correct handling checklist | Number of patients that incorrectly handle the device (%) | Common error |
|--|---|---|
| Remove the cap. | 0 | |
| Check the doses counter (If applicable). | 0 | |
| Hold inhaler upright and shake well. | 0 | |
| Breathe out gently, away from the inhaler. | 0 | |
| Put mouthpiece between teeth without biting and close lips to form good seal. | 3 (4.1)* | Does not form a good seal. |
| Start to breathe in slowly through mouth and at the same time press down firmly on canister. | 60 (82.2)* | Inability to coordinate activat with inhalation. |
| Continue to breathe in slowly and deeply. | 64 (87.7)* | Unable to continue breathe in slov and deeply. |
| Hold breathe for about 5 seconds or as long as comfortable. | 68 (93.1)* | Failure to hold breath for a suffici- time such as 5 seconds. |
| While holding breath, remove inhaler from mouth. | 53 (72.6)* | Unable to hold the breath wh removing the inhaler from mouth. |
| Breath out gently, away from the inhaler. | 40 (54.8)* | Breathe out to the inhaler instead breath out gently away from inhal |
| If an extra dose is needed, repeat steps 2 to 10. | 0 | |
| Replace the cap. | 0 | |

Table III. Common Errors and Suggested Checklist for pMDIs (n=73)

*Patient's mistake observed in more than one step.

| Correct handling checklist | Number of patients that incorrectly handle the device (%) | Common error |
|--|---|---|
| 1. Unscrew and remove the cover. | 0 | |
| 2. Check the dose counter. | 0 | |
| 3. Keep inhaler upright while twisting grip. | 0 | |
| 4. Twist around and then back until click is heard. | 0 | |
| 5. Breathe out gently, away from the inhaler. | 0 | |
| 6. Place mouthpiece between teeth without biting and close lips to form a good seal. Do not cover the air vents. | 15 (75)* | Unable to place the mouthpiece between the teeth and does not form a good seal. |
| 7. Breathe in strongly and deeply. | 9 (45)* | Patients do not breathe in strongly and deeply. |
| 8. Hold breath for about 5 seconds or as long as comfortable. | 19 (95)* | Patients unable to hold the breath for about 5 seconds. |
| 9. Remove inhaler from mouth. | 0 | |
| 10. Breathe out gently away from the inhaler. | 0 | |
| 11. If an extra dose is needed, repeat steps 2 to 10. | 0 | |
| 12. Replace cover. | 0 | |

| Table IV. Common | Errors and Suggeste | d Checklist for DPI | s Such as Turbuhaler (n=20) |
|------------------|----------------------------|----------------------|-----------------------------|
| Tuble IV. Common | Litois and Suggeste | a checking for Drift | Such us fulloundier (if 20) |

*Patient make mistake in more than one step.

techniques than a study from India¹³ (95.7 vs 82.3%). Our study showed that DPI users (Turbuhaler, Accuhaler and Handihaler) users have the highest error numbers than pMDI¹⁴. Conversely, the Indian study and a study in Thailand reported that MDI users have the maximum numbers of technique errors^{13,15}. However, when we pay attention on average mistakes done by patient per type of inhaler, pMDI has higher number than DPI (>4 vs >2 mistakes/patient respectively).

pMDI contains aerosol while DPI (Turbuhaler, Accuhaler and Handihaler) contains dry powder. pMDI use propellant in delivery device in which not incorporated in Accuhaler and Turbuhaler. pMDI, the early first generation inhaler, considered more difficult to use since it requires appropriate coordination technique between breath in and pressing the delivery button timing to spray out the medication. This is the reason why pMDI was recommended to be used via spacer particularly in special populations e.g. children¹⁶¹⁷¹⁸. Spacers help to collect the medicine inside to eliminate problem with breath timing. However, the spacer is not equipped with in pMDI original package. Since Accuhaler and Turbuhaler were not equipped with propellant, the patients urged to breathe in fairly hard to get the powder into their lung airway. Handihaler, mainly used for COPD, also did not equipped with propellant but the dry powder stored in a capsule. The patients should insert the capsule inside the device then push the piercing button once until it is flat against the base to make sure the

| Correct handling checklist | Number of patients that incorrectly handle the device (%) | Common error |
|---|---|---|
| 1. Check dose counter. | 0 | |
| 2. Open cover using thumb grip. | 0 | |
| 3. Holding horizontally, load dose by sliding lever until it clicks. | 8 (53.3) | Unable to load the dose by holding the device in horizontal position. |
| 4. Breathe out gently, away from the inhaler. | 0 | |
| 5. Place mouthpiece in mouth and close lips to form a good seal, keep inhaler horizontal. | 11 (73.3)* | Do not keep the inhaler horizontal position while inhaling the drug. |
| 6. Breathe in strongly and deeply. | 7 (46.7)* | Unable to breathe in strongly and deeply |
| 7. Hold breath for about 5 seconds or as long as comfortable. | 12 (80)* | Unable to hold the breath for about 5 seconds. |
| 8. While holding breath remove inhaler from mouth. | 5 (33.3)* | Exhaling into the inhaler without removing it from the mouth first. |
| 9. Breathe out gently away from the inhaler. | 0 | |
| 10. If an extra dose is prescribed (that generally recommended), repeat steps 3 to 9. | 0 | |
| 11. Close cover to click shut. | 0 | |

Table V. Common Errors and Suggested Checklist for DPIs Such as Accuhaler (n=15)

*Patient make mistake in more than one step.

powder are able to move to the lungs during inhalation.

Most of the patients performed the error within essential steps of inhaler usage such as unable to set the inhaler position prior and during inhalation, failed to inhale in the right time (e.g. synchronising actuation with inhalation), unable to inhale and hold the breath appropriately. Error during these important steps may significantly affect the amount of drug delivered to the lung that lead to suboptimal therapy outcome. Newman *et al.*, reported that among MDI users, good coordinators of actuation and inhalation produced higher aerosol dosage at lungs than bad coordinators (18.6 vs 7.2.%)^{19.4}.

All health care personnel including pharmacist involvement in asthma and COPD

patient education is important since repeated education influences the handling technique and the duration of the device usage²⁰. A study reported that providing good instruction may increase the percentage of aerosol dosage delivered to lungs (22.8 vs 7.2%)¹⁹. Optimum intact between medication and airways expected to increase the effectiveness of inhaler. Another study suggested that repeated instruction indirectly correlated with well. High levels of patient satisfaction significantly produced higher compliance leading to better quality life, less exacerbations, fewer medical care visit, and fewer sleep disturbance²¹.

Besides the aforementioned important findings, we also address some important limitations in our study. Firstly, we did not

| Correct handling checklist | Number of patients that incorrectly handle the device (%) | Common error |
|--|---|--|
| 1. Open the handihaler device. | 0 | |
| 2. Separate only one of the blisters from the blister card then open the blister. | 0 | |
| 3. Insert the capsule and close the mouthpiece firmly against the gray base until you hear a click. | 0 | |
| 4. Press the green piercing button once until it is flat (flush) against the base, then release. | 7 (77.8)* | Patient did not press the green piercing button fully. |
| 5. Breathe out completely. | 6 (66.7)* | Unable to breathe out completely before administrating the drug. |
| 6. Then, with the handihaler in your mouth, breathe in deeply until your lungs are full. You should hear or feel the capsule vibrate (rattle). | 9 (100)* | Patients unable to breathe in deeply until capsule vibrate sound is heard. |
| 7. Throw the empty capsule and close the handihaler device. | 0 | |

Table VI. Common Errors and Suggested Checklist for DPIs Such as Handihaler (n=9)

*Patient make mistake in more than one step.

include a large number of subjects so that subgroup analysis could not be conducted.

Secondly, we did not measure the outcome of the inhaler usage among patients so that we were not able to measure di association between appropriate use of inhaler and health-related quality of life of COPD patients by significantly increased patients' adherence of therapy¹⁰. This result also confirmed by Goris et al., who reported that the number of attacks, emergency applications, and hospitalizations of the intervention group provided with verbal training, demonstration movie and leaflet was lower at the follow-up than in the control group (without training)9. Patient satisfaction is important to ensure patient adherence to the handling technique as the outcome produced. Thirdly, we also did not addressed all important demographic data so that we

were not able to identify potential factors affected the inhalation technique. Based on this finding, next research will be conducted in higher number of subjects inprospective manner to measure the outcome of inhaler usage and identify those potential risk factor so that proper intervention method could be designed.

CONCLUSION

To summarize, we successfully identified the high number of incorrect use of inhaler among asthma and COPD patients. In addition, we also reported that patients tend to perform the mistakes during the essential steps. The result of this research might help the pharmacist to pay attention on several important steps while communicate their patients so that they are able to optimally educate the patients.

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REFERENCES

- 1. Asthma GIf. Global strategy for asthma management and prevention (updated 2016). 2016.
- 2. GINA G. Diagnosis of Diseases of Chronic Airflow Limitation: Asthma, COPD and Asthma-COPD Overlap Syndrome (ACOS). 2015.
- 3. GOLD. Global Strategy for The Diagnosis, Management, And Prevention of Chronic Obstructive Pulmonary Disease (2017 Report). *Global Initiative for Chronic Obstructive Lung Disease*;2017.
- Sanchis J., Corrigan C., Levy ML., Viejo JL. Inhaler devices - from theory to practice. *Respir Med.* 2013;107(4):495-502.
- 5. Sanchis J., Gich I., Pedersen S. Systematic Review of Errors in Inhaler Use: Has Patient Technique Improved Over Time? *Chest*. 2016;150(2):394-406.
- 6. Cochrane MG., Bala MV., Downs KE., Mauskopf J., Ben-Joseph RH. Inhaled corticosteroids for asthma therapy: patient compliance, devices, and inhalation technique. *Chest*. 2000;117(2): 542-550.
- Giraud V., Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *Eur Respir J.* 2002;19(2):246251.
- 8. Baddar S., Jayakrishnan B., Al-Rawas OA. Asthma control: importance of compliance and inhaler technique assessments. *J Asthma*. 2014;51(4):429-434.
- Goris S., Tasci S., Elmali F. The effects of training on inhaler technique and quality of life in patients with COPD. J Aerosol Med Pulm Drug Deliv. 2013;26(6):336-344.

- 10. Takemura M., Mitsui K., Itotani R., *et al.* Relationships between repeated instruction on inhalation therapy, medication adherence, and health status in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis.* 2011;6:97-104.
- Makela MJ., Backer V., Hedegaard M., Larsson K. Adherence to inhaled therapies, health outcomes and costs in patients with asthma and COPD. *Respir Med.* 2013;107(10):1481-1490.
- 12. NACA. Inhaler technique for people with asthma or COPD. National Asthma Council Australia; 2016.
- 13. Arora P., Kumar L., Vohra V *et al.* Evaluating the technique of using inhalation device in COPD and bronchial asthma patients. *Respir Med.* 2014;108(7):992-998.
- Loukil M., Mejri I., Khalfallah I., Ghrairi H. [Evaluation of inhaler techniques in patients with asthma and chronic obstructive disease]. *Rev Pneumol Clin.* 2018.
- Pothirat C., Chaiwong W., Phetsuk N., Pisalthanapuna S., Chetsadaphan N., Choomuang W. Evaluating inhaler use technique in COPD patients. *Int J Chron Obstruct Pulmon Dis*. 2015;10:1291-1298.
- 16. Pool JB., Greenough A., Gleeson JG., Price JF. Inhaled bronchodilator treatment via the nebuhaler in young asthmatic patients. *Arch Dis Child*. 1988;63(3):288-291.
- 17. Vincken W., Levy ML., Scullion J., Usmani OS., Dekhuijzen PNR., Corrigan CJ. Spacer devices for inhaled therapy: why use them, and how? *ERJ open research.* 2018;4(2).
- 18. Rau JL. Practical problems with aerosol therapy in COPD. *Respir Care*. 2006;51(2):158-172.
- 19. Newman SP., Weisz AW., Talaee N., Clarke SW. Improvement of drug delivery with a breath actuated pressurised aerosol for patients with

poor inhaler technique. *Thorax*. 1991;46(10):712-716.

- 20. Yildiz F. Importance of inhaler device use status in the control of asthma in adults: the asthma inhaler treatment study. *Respir Care*. 2014;59(2):223-230.
- 21. Small M., Anderson P., Vickers A., Kay S., Fermer S. Importance of inhalerdevice satisfaction in asthma treatment: real-world observations of physician-observed compliance and clinical/patient-reportedoutcomes. *Adv Ther.* 2011;28(3):202-212.