Aprendizagem da técnica inalatória em doentes com DPOC

Educational intervention and improvement of inhaler technique in COPD patients

Duarte-de-Araújo A.^{1,2,3}, Teixeira P.^{1,2}, Hespanhol V.^{4,5}, Correia-de-Sousa J.^{1,2,6}

ARTIGO ORIGINAL | ORIGINAL ARTICLE

RESUMO

Objetivos: Avaliar se o ensino correto da técnica inalatória em doentes com DPOC a pode melhorar de uma forma sustentada e quais as caraterísticas dos inaladores e dos doentes que lhe estão associados.

Métodos: Doentes \geq 40 anos com DPOC estável e diagnosticados de acordo com os critérios do GOLD foram avaliados em duas consultas médicas com um intervalo de dez a doze meses entre elas. Inicialmente foi aplicado um questionário demográfico e clínico e o Questionário de Crenças sobre Medicamentos. Na avaliação da técnica inalatória foi usada uma tabela de passos necessários para um correto uso dos inaladores e erros críticos. Posteriormente, a todos os participantes foi feito ensino e permitido treino com inaladores contendo placebo, até ao seu uso correto. Na segunda consulta foi feita uma reavaliação da técnica inalatória.

Resultados: Avaliamos 170 participantes realizando 266 manobras inalatórias com 10 diferentes inaladores. Registou-se uma melhoria no número de erros críticos em todos os tipos de inaladores, com significado estatístico naqueles que mais facilmente informavam o doente de que a inalação fora correta. A melhoria da técnica inalatória relacionou-se significativamente com o score do CAT. No subgrupo de doentes que melhoraram sua técnica inalatória, os homens tiveram uma média do score de necessidades do BMQ significativamente maior do que as mulheres.

Conclusões: Uma significativa melhoria da técnica inalatória foi observada nos inaladores que mais facilmente informam o doente sobre a correção da técnica inalatória. Os doentes mais sintomáticos mantiveram uma correta técnica inalatória de forma mais sustentada. As crenças sobre a necessidade do uso de inaladores estão associadas a uma melhor aprendizagem da técnica inalatória nos homens com DPOC.

Palavras-chave: DPOC, Técnica Inalatória, Ensino, Aprendizagem.

ABSTRACT

Objectives: To evaluate if the application of an educational intervention in COPD outpatients, regarding the correct use of the IDs, can improve inhalation technique in a sustained way, and to assess the inhalers and patient-related characteristics that are associated with some improvement of inhalation technique.

Methods: Stable COPD outpatients diagnosed according to GOLD criteria were evaluated in two different medical visits. They were invited to demonstrate the use of their IDs, and inhaler technique was accessed by using check-lists that include correct steps and critical errors. Posteriorly a correct teaching and training were given to all participants. After 10 to 12 months patients were invited for a second medical visit, and re-evaluation of inhaler technique was done.

Results: We evaluated 170 participants performing 266 inhalation manoeuvers. There was an improvement on critical errors in all types of IDs with statistical significance in the IDs with an easy feed-back to the patient that a significant amount of medication has been inhaled. Improvement was significantly related to CAT score and in the subset of patients who improved their inhalation technique, males had an average BMQ Necessity score higher than females.

Conclusions: Significantly improvement of inhalation technique was found in the group of IDs that provided an easy feed-back to patient that a significant amount of medication has been inhaled. More symptomatic patients learn better a correct inhaler technique than the less symptomatic ones. The beliefs about the need of medication are associated to inhaler technique improvement in male COPD patients.

Keywords: COPD, Inhalation technique, Educational intervention, Sustained improvement.

¹ Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal.

² ICVS/3B's, PT Government Associate Laboratory, Braga/Guimarães, Portugal.

³ Respiratory Department, H. S^a Oliveira, Guimarães, Portugal.

⁴ Respiratory Department, Centro Hospitalar de S. João, Porto, Portugal.

⁵ Faculty of Medicine (FMUP), University of Porto, Porto, Portugal.

⁶ Horizonte Family Health Unit, Matosinhos, Portugal.

Autor para correspondência: António Manuel Silva Duarte Araújo. Serviço de Pneumologia, hospital de Guimarães. Rua dos Cutileiros, 114, Creixomil, 4835-044 Guimarães; duartearaujodr@sapo.pt; antonioaraujo@hospitaldeguimaraes.min-saude.pt

Submetido/Submitted: 22 novembro 2019 | Aceite/Accepted: 30 novembro 2019

BACKGROUND AND OBJECTIVES

Chronic Obstructive Pulmonary Disease (COPD) currently represents one of the most significant health problems at international level, and its economic and social impact is still constantly increasing¹. COPD is a chronic and incurable disease, but symptoms significantly improve with therapy. Inhalers are the way used for an effective administration of medication, and it is of paramount importance that patients use them correctly, to ensure that a full dose is received. However, inhalers misuse remains unacceptably high². A large proportion of patients refer lack of effective training from their health care professionals (HCPs) and few are systematically checked in their medical visits, regarding the inhaler technique³. Face-to-face inhalers' demonstration of the correct inhalation technique, verbal instructions, training the correct use and patients' teach-back are probably the most effective methods of teaching the correct inhalation technique (IT). As it can deteriorate over time, periodic evaluation and re-training is recommended^{4,5}. It is not yet determined if improvement, after a single education intervention, is sustained over time⁶. The primary objective of this study was to evaluate if the application of an educational intervention in COPD outpatients, regarding the correct use of inhaler devices (IDs), can improve inhalation technique in a sustained way. The secondary objective was to assess the inhalers and patient-related characteristics that are associated with a sustained improvement in IT. The variables under study, evaluated for potential association to IT improvement, were type of ID, age, gender, education level, income, Graffar Social Classification score, the Beliefs about Medicines Questionnaire (BMQ) Necessity score, smoking status, mMRC degree, CAT score, FEV1% and the number of COPD acute exacerbations (ECOPD) in the previous year.

MATERIALS AND METHODS

This is an interventional study conducted in the outpatient respiratory care of Guimarães hospital. Stable COPD patients over 40 years, diagnosed according to GOLD criteria and using inhaler devices were evaluated in two different medical visits, with a ten to twelve-months interval between visits. They were recruited consecutively and evaluated on a first medical visit between March 2016 and May 2017. No participants were enrolled in another different study, and all gave their written informed consent. The study was approved by the Guimarães Hospital Ethics Committee, the Research Ethics Committee of Minho' University and by the Portuguese Data Protection Agency. Refusal to participate and inability to understand and respond to simple questionnaires were the exclusion criteria. In the first visit, a survey of demographic and clinical data, the Graffar Social Classification questionnaire, validated for use in Portuguese population⁷, and the Portuguese version of BMQ were applied⁸. The BMQ is an eleven-item questionnaire with a five-item Necessity scale and six-item Concern scale, assessing respectively the beliefs about the medication' necessity and concerns related to side-effects, dependence and toxicity of medication. Evaluation of symptoms was done using the Portuguese versions of the COPD Assessment Test (CAT)

and the Medical Research Council Dyspnea Questionnaire (mMRC). The number of ECOPD referred in the last year was recorded. We defined ECOPD according to GOLD as an acute worsening of respiratory symptoms that results in additional therapy⁹, but also requiring an unplanned medical visit. All participants performed at least one spirometry according to ERS/ATS criteria and referenced according to the Global Lung Function Initiative prediction equations (GLI 2012)^{10,11}. Participants were invited to demonstrate the use of their prescribed ID, and demonstrations were done using inhalers containing placebo medications. Inhaler technique was accessed by using previous defined checklists of 5 steps for each ID (Table 1).

Table 1. Check-list of 5 steps and errors foreach ID

1-	Correct priming or loading (Incorrect priming or loading were considered a critical error)						
2-	Exhalation before inhalation (No-exhalation before inhalation was not considered critical)						
3-	Correct inhalation (Incorrect inhalation was considered a critical error)						
4-	Holding the breath a few seconds after inhalation (not required when using a spacer) (Not holding the breath or exhalation through the mouthpiece was not con- sidered critical)						
5-	Finalization (cleaning the mouth- piece, removing the used capsule af- ter verifying that no powder remains, checking color changing in control window, closing ID and washing the						

mouth if necessary)

They were developed according to the instructions provided by the manufactures and to previous literature¹², and include essential steps and critical errors. Errors considered critical are related to priming/loading or the inhalation maneuver, and could substantially affect drug delivery to the lungs. These included lack of inhalation through the mouthpiece for all devices, slow and not forceful inhalation for dry powder inhalers (DPI) and rapid or forceful inhalation for pressurized metered-dose inhalers (pMDI) or soft-mist inhalers (SMI). Critical errors device-dependent are listed in Table 2.

Table 2. Critical errors in different IDs

1-	Aeroliser®, Breezhaler [®] , and Handiha- ler [®] : failure to insert the capsule, failure to press and release buttons, powder re- maining in the capsule after inhalation.
2-	Diskus®: failure to open the cover, to slide the lever until it clicks, or not kee- ping inhaler horizontally
3-	Ellipta®: failure to slide cover down until a click is heard or block air vent with fingers.
4-	Genuair [®] : failure to remove the cap, to press and release the button until the control window has changed to green, not holding inhaler horizontally, and not changing control window to red after inhalation
5-	pMDI: failure to remove cap, not shaking the inhaler (suspensions only), not hol- ding the inhaler in the upright position, poorly synchronized hand actuation and inhalation, inhalation through the nose, actuation against teeth, lips or tongue.
6-	Respimat [®] : lack of cartridge in the device, failure to open the cap, twisting the base or pressing the dose-release button, poorly synchronized hand actuation and inhalation.

Table 2. Critical errors in different IDs(cont.)

- 7- Spiromax[®]: failure to hold the inhaler in upright position, failure to open mouthpiece cover until a click is heard or blocking air vent with fingers.
- 8- Turbuhaler[®]: failure to remove cover, to hold the inhaler upright when twisting the grip (tolerance ± 45°) until a click is heard.

After this assessment, face-to-face demonstration and training with placebo inhalers were given to all participants, until a correct use was achieved. Ten to twelve months later, participants were invited by mail for a second medical visit, and re-evaluation of inhalers' technique was done by the same HCP using the same check-lists. Patients using different IDs were excluded. The difference in the number of critical errors between the two visits and the difference in total number of critical errors, because many patients used two or more inhalers, were defined as outcomes. Both outcomes were expressed as qualitative (equal number of critical errors, more errors - worsening of IT, less errors - improvement of IT).

Statistical analysis was performed with SPSS Statistics for Windows software, version 23.0. Armonk, NY: IBM Corporation. For null hypothesis testing Chi-Square test and Analysis of Variance with Covariant (ANCOVA) was performed. The level of statistical significance was set at p <0.05.

Results

Sample characteristics

288 out 319 patients were invited for the second medical visit, but only 201 agree to participate. From then, 31 were excluded because they were using different IDs. We evaluated 170 participants (mean age = 66.8 years, 78.2% males) performing 266 inhalation manoeuvers. Ten different IDs were examined (Aeroliser[®], Breezhaler[®], Diskus[®], Ellipta[®], Genuair[®], Handihaler[®], pMDI, Respimat[®], Spiromax[®] and Turbuha ler[®]) in a total of 31 (11.7%) pMDI, 63 (23.7%) single-dose inhalers (sDPI) 136 (51.1%) multiple dose inhalers (mDPI) and 37 (13.9%) SMI-Respimat[®]. The main demographic, clinical and functional characteristics of patients are described in Table 3.

Table 3. Demographic, clinical and functionalcharacteristics of COPD patients

Characteristics	n = 170				
Mean age (years)	66.8				
Age \geq 65 years	102 (60.0)				
Male gender	133 (78.2)				
Education level \leq 3 school years	49 (28.8)				
Education level ≤ 6 school years	152 (89.4)				
Very low monthly income (< 530 Euros)	119 (70.0)				
Graffar social classification $4 + 5$	105 (62.5)				
mMRC grade ≥ 2	107 (62.9)				
CAT score ≥ 10	100 (78.7)				
ECOPD \geq 2 (last year)	70 (41.2)				
Post-bronchodilator mean FEV ₁ %	52.8				
GOLD 2017 stage and classification (n; %):					
I - 18 (10.6); II - 66 (38.8); III - 64 (37.6); IV - 22 (12.9)					
A - 32 (18.8); B - 69 (40.6); C - 3 (1.8); D - 66 (38.8)					

Note: Data shown as mean or n (%).

Abbreviations: mMRC, modified Research Council Dyspnea Questionnaire; CAT, COPD Assessment Test; ECOPD, chronic obstructive pulmonary disease acute exacerbations; GOLD, Global Initiative for Chronic Obs- tructive Lung Disease.

Tobacco smoking was the most common exposure identified. The mean tobacco exposure was 48.75 pack-years, and 15.4% of subjects were current smokers. The distribution of patients according to GOLD 2017 stage and classification were 10.6%, 38.8%, 37.6% and 12.9% GOLD 1 to 4, and 18.8%, 40.6%, 1.8% and 36.8% GOLD A to D.

Results by IDs

In the second visit, a technique free from any errors was observed in 145 (54.5%) demonstrations, only 2.2% more than in the first evaluation. Errors were related to priming/loading (9.8%), lack of exhalation before inhalation (12.8%), inhalation manoeuvre (11.3%), lack of holding the breath after inhalation (27.1%)and incorrect finalisation (13.9%). After teaching the correct inhaler technique, critical errors were more often related to inhalation manoeuvres than to priming/loading. Holding the breath after inhalation was the step more difficult to be learned. Misuse related to priming/ loading and misuse related to inhalation manoeuvre were respectively higher in mDPI group (13.3%) and in pMDI (38.7%, p<0.001) group. Forgetting to hold the breath after inhalation was higher in sDPI group (38.1%, p=0.031). Table 4 presents the difference on errors related to the 5 steps for a correct inhaler technique in different types of inhaler devices.

Errors related to: priming noinhaholfina-/loading exhalation ding lizalation the tion breath mDPI -3% -5.9% -8.1% +1.5%+0.8% pMDI -12.9% -22.4% -9.7% -19.9% -19.4% sDPI -12.7% -7.9% -11.2% +6.4% +1.8%Soft--8.1% -5.4% -13.5% -8.1% -8.1% mist Inhaler

Table 4. Errors variation in visit 2 related to visit 1, by groups of inhaler devices.

Data are presented as the difference between the percentage of errors in visit 2 and visit 1. An improvement in number of critical errors was observed in 50 (18.8%) and a worsening in 21 (7.9%) demonstrations. There was an observed improvement on critical errors in all types of IDs, with statistical significance in sDPI group. We found also a statistically significant improvement in number of critical errors In the group of IDs (Aeroliser + Breezhaler + Handihaler + Genuair) with an easy feed-back to the patient that a significant amount of medication has been inhaled (Table 5). Although some improvement in inhalation technique was observed in pMDI group, its misuse related to inhalation manoeuvre remains the more common reason for any inhaler misuse.

			Errors M1					McNemar test		
			No error	Error	Total	Worsened	Improved	P -value		
mDPI	_	No error	92	20	112	8.1%	14.7%			
	Error M2	Error	11	13	24			0.150		
		Total	103	33	136					
pMDI	Error M2	No error	12	7	19	3.2%	22.6%			
		Error	1	11	12			0.070		
		Total	13	18	31					
sDPI	Error M2	No error	48	10	58	1.6%	16.1%			
		Error	1	3	4			0.012		
		Total	49	13	62	8.1%	21.6%			
Softm	Error	No error	23	8	31					
	M2	Error	3	3	6			0.227		
		Total	26	11	37					
sDPI + Genuair	Error M2	No error	76	14	90	1.04%	14.6%	0.001		
Genuali		Error	1	5	6					
		Total	77	16	96					

Table 5. Variation on critical errors in the different groups of inhaler devices.

Note and abbreviations: Errors M1, Moment 1: first assessment; Errors M2, Moment 2: 2nd assessment; mDPI, multiple-dose dry-powder inhalers; pMDI, pressurized inhalers; sDPI, single-dose dry-powder inhalers; Softm, soft-mist inhalers; errors shown as number of demonstrations; Worsened/Improved described as % of demonstrations.

Results by patients' characteristics

A worsening in the total number of critical errors was observed in 20 (8.8%) patients, and an improvement in 47 (25.9%). Worsening or improvement were not significantly related to demographic characteristics as age (p=.262), gender (p=0.331), education level (p=.379), monthly income (p=0.965) or Graffar Social Classification score (p=0.144). They were also not related to airflow limitation (p=0.694). Improvement was significantly related to CAT score (CAT<10: 22.2% worsened and 22.2% improved inhalation technique; CAT \geq 10: 6% worsened and 25% improved inhalation technique, p=0.037), but not to mMRC grade (p=0.474),

smoking history (p=0.752) or COPD acute exacerbations (p=0.472). Some change in inhaler technique after an education intervention was not significantly related to BMQ Necessity score (p=0.719). However, in the subset of patients who improved their inhalation technique, male patients had an average BMQ Necessity score significantly higher than females (mean BMQ Necessity score were respectively 21.97 and 17.88, p=0.017 – figure 1).

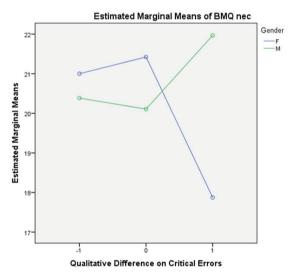


Figure 1. Necessity score by gender and difference in critical errors between the two visits.

DISCUSSION

Some improvement in inhalation technique was achieved after a single education intervention in all types of IDs, with statistical significance in the group of inhalers with an easy feed-back to the patient that a significant amount of medication has been inhaled. It appears that some devices' attributes, by improving patients' confidence on their use, improve the maintenance of a correct inhaler technique. A previous

study referred that the same devices' attributes leads to patients' confidence and improves treatment adherence in COPD patients³. A significant number of papers explore the effects of educational intervention on frequency of inhaler errors. They vary in the duration of interventions. in the tools used to assess inhalers' errors and in HCP involved in the studies, but a significant improvement in inhalation technique is usually reported. In a recent systematic review on critical inhaler errors, 11 out of 21 studies exploring the relationship between previous inhaler instructions and frequency of inhaler errors, found a positive association between previous instructions and a better inhaler technique¹³. In the present study, after teaching the inhaler technique, the misuse related to inhalation manoeuvre in the pMDI group remains the more common reason for any inhaler misuse. This is consistent with a previous study on seven different devices, where the worse technique was found in the pMDI group, with only 79% of patients using them correctly after education and training¹⁴. In our study, a significant rate of patients improved their inhalation technique; however, a worsening was also observed. The difference between technique improvement and worsening are related to the role played by the education intervention, the maintenance of training by the daily use and the over-time deterioration of inhalation technique. In COPD patients, mMRC and ECOPD are often examined outcomes related to inhaler technique. In a small experimental study, the number of ECOPD was significantly related to inhaler technique and to an education intervention, af-

ter a 3 months follow-up¹⁵. In a small cross-sectional study carried out in Portuguese asthma and COPD patients, previous education on inhalation technique was associated with lower number of inhalers' errors, however without impact on COPD stability¹⁶. In another small study published by the same Portuguese group, an education intervention regarding the inhalation technique was not related to clinical improvement in COPD patients, reevaluated 6 to 8 months later¹⁷. In our study we failed to demonstrate any significant association between improvement of inhaler technique and many demographic, clinical or functional characteristics of COPD patients. Nonetheless, this lack of statistical significance gives clinical relevance to the need of teaching the inhalation technique to all patients equally. In this sample the only significant association was the positive association between symptoms and improvement of the inhaler technique. This can be a sample characteristic; however more symptomatic patients can be more motivated to learn how to use inhalers properly. We found that male patients who improve their inhalation technique seems to be more believers in the need of medication than women. We can thus assume that men, but not women, have to believe in the need for medication to learn better and improve inhalation technique. This information is new and need to be confirmed by other studies.

To the best of our knowledge, this is the largest study carried out in Portuguese population of COPD patients, concerning the sustained improvement of the inhalation technique after a single educational intervention. However,

this study was conducted in a single institution, with patients being treated by pulmonologists, and other possible education interventions, conducted by others HCPs, were uncontrolled. This may limit the generalisation of results to other populations¹⁸. We compared the number of critical errors before and after an education intervention. The definition of critical errors when using inhalers is of great importance, because they are likely to significantly decrease delivery of medication to the lungs, and thus impair health-related outcomes. However, there is currently a lack of consensus on their definition¹³. Though it is based on previous medical literature, our definition of critical errors deserves discussion. Nonetheless. re-evaluation of inhalers' technique was done using the same check-list of steps and errors of the previous visit, and re-evaluation was done by the same HTP, to avoid inter-observer variability. Some of this data can be useful in clinical practice in planning educations interventions related to inhaler devices.

CONCLUSIONS

A correct teaching of inhaler technique improves patients' mastery to use inhalers in a sustained way. This data corroborates the observations of other authors, and draws attention to the effectiveness of educational interventions. An easy feed-back that a significant amount of medication has been inhaled, presented by some inhaler devices, improve the maintenance of a correct inhaler technique. More symptomatic patients learn better a correct inhaler technique than the less symptomatic ones. The beliefs about the need of medication are associated with the maintenance of a correct mastery in male COPD patients. Clinicians must recognise that the inhaler device is as important as the drug itself, and this means not only prescribing the right device for a particular patient, but also training the patients in their correct use.

Acknowledgments

A research letter with some data presented in this paper was published in Pulmonology. 2019; 25(1): 53-55. An abstract of this paper was presented in the 9th IPCRG World Conference, Porto 2018, 31 May-2 June, and published in 9th IPCRG World Conference Abstract Book. Another abstract of this paper was presented in the 6th International Conference on Chronic Obstructive Pulmonary Diseases, Tokyo 2018, 17-18 May, and published in J Pulm Respir Med 2018, volume 8. DOI: 10.4172/2161-105X-C1-028. In all cases only partial data was published.

Author contributions

Duarte-de-Araújo conceived and developed the study, carried out the collection of data and data interpretation, wrote the first draft and collaborated in the final writing. Pedro Teixeira carried out the statistical analysis, contributed to the section on methods and results, and collaborated in the final writing. Venceslau Hespanhol reviewed the final draft. Jaime Correia-de-Sousa reviewed all the drafts and collaborated in the final writing. All the authors approved the final manuscript.

Disclosure

The authors have no conflicts of interest to declare.

REFERENCES

 Dal Negro R, Bonadiman L, Turco P. Prevalence of different comorbidities in COPD patients by gender and GOLD stage. Multidisciplinary Respiratory Medicine. 2015; 10:24. DOI 10.1186/s40248-015-0023-2.

- Sanchis J, Pedersen S; on behalf of the Aerosol Drug Management Improvement Team (ADMIT). Systematic Review of Errors in Inhaler Use. Has Patient Technique Improved Over Time? CHEST. 2016; 150(2): 394-406.
- 3. Price D, Keininger D, Viswanad B, Gasser M, Walda S, Gutzwiller F. Factors associated with appropriate inhaler use in patients with COPD – lessons from the REAL survey. International Journal of COPD. 2018,13: 695-702.
- Sanchis J, Corrigan C, Levy M, Viejo J. Inhaler devices – From theory to practice. Respiratory Medicine. 2013; 107: 495-502.
- 5. Capstick T, Clifton I. Inhaler technique and training in people with chronic obstructive pulmonary disease and asthma. Expert Rev Respir Med. 2012; 6(1): 91-103.
- 6. Crompton G, Barnes P, Broeders M, Corrigan C, Corbetta L, Dekhuijzen R, et al. The need to improve inhalation technique in Europe: A report from the Aerosol drug Management improvement Team. Respiratory Medicine. 2006; 100:1479-1494.
- 7. Graffar M. Une méthode de classification sociale d'échantilons de population. Courrier VI 1956;6:445-59.
- Salgado T, Marques A, Geraldes L, Benrimoj S, Horne R, Fernandez-Llimos F. Cross-cultural adaptation of the Beliefs about Medicines Questionnaire into Portuguese. São Paulo Med J. 2013; 131(2): 88-94.

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD), updated 2017. Available from http://goldcopd.org/ gold-2017-global-strategy-diagnosis-management- prevention-copd/
- 10. Quanjer P, Stanojevic S, Cole T, Baur X, Hall G, Culver B, et al. Multi-Ethnic reference values for spirometry for the 3-95 year age range: The global lung function 2012 equations. Eur Respir J. 2012; 40(6): 1324-1348. Doi:10.1183/09031936.00080312.
- 11. Miller M, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Series "ATS/ERS Task Force: Standardisation of function testing". Eur Respir J. 2005;26:319-338.
- 12. Sanchis J, Corrigan C, Levy M, Viejo J. Inhaler devices From theory to practice. respiratory Medicine. 2013; 107: 495-502.
- 13. Usmani O, Lavorini F, Marshall J, Dunlop C, Heron L, Farrington E and Dekhuijzen R. critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. Respiratory Research. 2018; 19:10. DOI 10.1186/s12931-

017-0710-y.

- 14. Lenney J, Innes J, Crompton G. Inappropriate inhaler use. Assessment of use and patient preference of seven inhalation devices. EDICI. Respir Med. 2000; 94(5): 496-500.
- 15. Goris S, Tasci s, Elmali F. The efects of training on inhaler technique and quality of life in patients with COPD.J. Aerosol Med Pulm Drug Deliv. 2013;26:336-44.
- 16. Maricoto T, Rodrigues LV, Teixeira G, Valente C, Andrade L, Saraiva A. Assessment of Inhalation Technique in Clinical and Functional Control of Asthma and Chronic Obstructive Pulmonary Disease. Acta Med Port. 2015;28:702-7.
- 17. Maricoto T, Madanelo S, Rodrigues L, Teixeira G, Valente C, Andrade L, Saraiva A. Educational interventions to improve inhaler techniques and their impact on asthma and COPD control: a pilot effectiveness implementation trial. J Bras Pneumol.2016;42(6):440-443.
- 18. Hackshaw A. Small studies: Strengths and limitations. Eur Respir J. 2008; 32: 1141-1143.