Original Research Article

Effectiveness of administration of bronchodilator by spacers, home-made spacers and nebulizers in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: In chronic obstructive pulmonary disease (COPD), bronchodilator therapy using dry powder inhaler (DPI) or a measured dose inhaler (MDI) is more convenient at a lower cost than nebulizer therapy. Mistakes in the use of MDI often occur due to lack of coordination but with the addition of spacers, drawbacks in the use of this MDI can be overcome so that it does not require coordination. Commercial spacers are relatively expensive and not available anywhere while home-made spacers made from bottles of mineral water are very cheap and can be made alone. Study aimed to evaluate the effectiveness of each device, namely a spacer, a home-made spacer and nebulizer.

Methods: This study is an experimental study of 62 COPD patients who received bronchodilators using spacers, home-made spacers, and nebulizers. Spirometry is performed for each sample before and after bronchodilator administration to assess FEV1, KVP and changes in VAS dyspnea. The difference in the effectiveness of bronchodilators for various devices in COPD patients was statistically analyzed using the ANOVA test.

Results: There were significant differences in the values of VEP1, KVP and VAS dyspnoea after bronchodilator administration through the spacer, home-made spacer and nebulizer (p<0.001), (p=0.002), (p<0.001). The increase in% VEP1 with a nebulizer device was higher than that of a spacer (p=0.001) and the increase in% VEP1 with the nebulizer device was also significantly significant compared to home-made spacer (p<0.001). The increase in% KVP with the nebulizer device was higher than that of home-made spacer (p<0.001), as well as between spacers and home-made spacers and this was significant (p=0.038). The decrease in VAS dyspnoea in patients using nebulizer device than the spacer (p<0.001). Decreasing VAS dyspnoea with nebulizer devices is higher compared to home-made spacers, also gives significant results (p<0.001). There were no differences in the decrease in VAS dyspnoea between spacers and home-made spacers.

Conclusions: The administration of bronchodilators by use of three devices (spacers, home-made spacers and nebulizers) can significantly increase the values of FEV1, KVP and VAS dyspnoea. On the use of spacers and home-made spacers, the increase of pulmonary physiological values is not significantly different.

Keywords: COPD, Home-made spacers, Nebulizers, Spacers

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of death in the world. More than 3 million people die from COPD in 2012 accounting for 6% of all global deaths.1

In chronic obstructive pulmonary disease, bronchodilator therapy by use of dry powder inhaler (DPI) or a measured...
dose inhaler (MDI) is more convenient and cost effective than nebulizer therapy. MDI is the most commonly used device with techniques that depend because MDI requires proper hand-lung coordination.2

Generally, the mistake that occurs in patients who use MDI is that most of them breathe too fast, failure to hold breath for 5-10 seconds (52.2%) and failure of inspiration slowly in 46.4%.3,4

Nebulizers are used for acute therapy in the emergency department and in hospitals but are also available for home use. In the use of nebulizers there is no special time or coordination needed; it only requires minimal effort from the patient.2

The use of spacers eliminates the need for coordination of actuation of aerosols with inspiration and also decreases oropharyngeal deposition. Commercial spacers are still expensive and may not be available anywhere, making it difficult to replace them in the event of loss or damage. Home-made spacers made from bottles of mineral water are very cheap and can be made at home, so they are easy to replace. However, there is a lack of data on comparing the efficacy of home-made spacers with commercial spacers.5

Many studies on bronchodilator therapy by use of DPI, MPI with spacers and nebulizers to treat COPD have concluded that the use of these devices is equally effective, as measured by changes in forced expiratory volume in 1 second (FEV1). In contrast, several studies have shown that nebulizers are superior to MPI based on improvements in spirometry and symptom values.2

The use of a spacer will eliminate the need to coordinate actuation of aerosols with inspiration and also reduce oropharyngeal deposition. Commercial spacers are still expensive and may not be available anywhere, so it is difficult to replace them in the event of loss or damage. Home-made spacers made from bottles of mineral water are very cheap and can be made at home, so they are easy to replace.5

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Based on the background above, the comparison of the clinical success of bronchodilator therapy administered by spacer, home-made spacer and nebulizer to FEV1 is still controversial and there is no significant difference. However, home-made spacers may be a more economical alternative compared to administration by spacer or nebulizer, so the researchers want to conduct research to ensure the effectiveness of each additional tool as a bronchodilator delivery and are expected to provide more efficient and meaningful results.

METHODS

The design of this study is a clinical trial with a quasi-experimental design comparing FEV1 and VAS dyspnea in COPD patients with bronchodilator test measures performed by use of spacers, home-made spacers and nebulizers.

The study was conducted at the department of pulmonology and respiration medicine of the faculty of medicine of the University of Sumatera Utara/ Central General Hospital of Haji Adam Malik of Medan from Maret 2018 to Mei 2018. The research subjects were taken from the population of outpatients in the pulmonology polyclinic of the central general hospital of Haji Adam Malik Medan. Determination of research subjects was carried out according to consecutive non-random sampling method with a total sample of 62 patients. The inclusion criteria were COPD patients between 40-80 years old, smoker or ex-smoker with history of 10 packs cigarette per-years, and not in exacerbation. The exclusion criteria were patients who were using oxygen and in exacerbation, patients with asthma, neuromuscular disorders and malignancy.

All subjects who fulfilled the inclusion criteria will be subjected to a history and physical examination and then a spirometry and VAS dyspnea examination. Each patient will use each of the three devices at different times in 3 periods at weeks 1.2 and 3. Before the use of bronchodilators performed with spirometry, the results of VEP1 and KVP values were recorded.

Administration of a bronchodilator short-acting β2-agonist, salbutamol, is performed by pMDI with additional devices of 750 mL spacers, home-made spacers from 600ml mineral water bottles, and nebulizers. Patients using pMDI with spacer and home-made spacers will get 4 puffs (400µg) salbutamol, and when the patient uses a nebulizer, salbutamol 2.5mg will be given. After 15 minutes of bronchodilator administration the spirometry examination was performed of FEV1 and KVP as well as assessment of VAS dyspnea.

Prior to the test, all of the subjects were instructed on the proper use of the VAS. The VAS scores for dyspnea were recorded after each bronchodilator measurement.2,6 The VAS line is a 10-cm-long horizontal line that ranges from 5 to ±5cm. On the left side, the label represents VAS = -5 (very much improved). In the middle, VAS = 0(no change). To the far right, VAS = ±5 (much worsened).2

To assess the difference in effectiveness of each additional device of spacers, home-made spacers and nebulizers as delivery of bronchodilator administration, ANOVA test is used if the data is normally distributed or by the Kruskal Wallis test if the data is not normally
distributed to evaluate FEV1, KVP, and signed rank Wilcoxon test is used to compare VAS scores.

**RESULTS**

Of the 62 research subjects analyzed, there were 59 (95.2%) males and 3 (4.8%) females. The most age COPD patients were 60-69 years old (51.6%). The Brinkman index was in the severe degree (80.6%) and the most body mass index of the patients was the norm weight (30.6%) (Table 1).

There were significant differences in the values of VEP1, KVP and VAS dyspnea after bronchodilator administration through the three devices, (p<0.001), (p=0.002), (p<0.001) (Tables 2, 3 and 4).

The increase in% VEP1 with a nebulizer device was higher than that of a spacer, and this was significantly significant (p=0.001). The increase in% VEP1 with the nebulizer device was also significantly significant compared to home-made spacer (p<0.001) as evidenced by the Post-Hoc test (Table 5).

### Table 1: Characteristics of patients with COPD for whom the difference in effectiveness of each additional device of spacer, home-made spacer and nebulizer are assessed.

| Characteristics | N (62) | % |
|-----------------|--------|---|
| Sex             |        |   |
| Male            | 59     | 95.2 |
| Female          | 3      | 4.8 |
| Age             |        |   |
| 50-59 years     | 11     | 17.8 |
| 60-69 years     | 32     | 51.6 |
| 70-79 years     | 19     | 30.6 |
| Brinkman Index  |        |   |
| Mild            | 3      | 4.8 |
| Moderate        | 9      | 14.5 |
| Severe          | 50     | 80.6 |
| Body mass index (BMI) |      |   |
| Underweight     | 5      | 8.1 |
| Normoweight     | 19     | 30.6 |
| Overweight      | 16     | 25.8 |
| Obesity         | 16     | 25.8 |
| Severe obesity  | 6      | 9.7 |

*) Significant by the ANOVA test

### Table 2: Differences in the value of FEV1 dyspnea by devices of spacer, home-made spacer and nebulizer.

| Device          | ΔFEV1(L) | SD    | p-value | Δ% FEV1(L) | p-value |
|-----------------|----------|-------|---------|------------|---------|
|                 | Mean     |       |         | Mean       |         |
| Spacer          | 0.087    | 0.0443| <0.001* | 3.677      | 1.6544  |
| Home-made spacer| 0.074    | 0.0489| <0.001* | 3.251      | 1.8571  |
| Nebulizer       | 0.113    | 0.0591|         | 4.938      | 2.4510  |

*) Significant by the ANOVA test

### Table 3: Differences in the values of KVP dyspnea by devices of spacers, home-made spacers and nebulizers.

| Device          | ΔKVP(L) | SD    | p-value | Δ% KVP(L) | p-value |
|-----------------|---------|-------|---------|-----------|---------|
|                 | Mean    |       |         | Mean      |         |
| Spacer          | 0.096   | 0.1089| 0.002*  | 3.508     | 4.0456  |
| Home-made spacer| 0.045   | 0.1340|         | 1.588     | 4.5358  |
| Nebulizer       | 0.134   | 0.1651|         | 4.637     | 5.6535  |

*) Significant by the ANOVA test

### Table 4: Differences in the value of VAS dyspnea by devices of spacer, home-made spacer and nebulizer.

| Device          | ΔVAS dyspnea | SD    | p-value |
|-----------------|--------------|-------|---------|
|                 | Mean         |       |         |
| Spacer          | -2.919       | 0.5216|         |
| Home-made spacer| -2.854       | 0.5385| <0.001* |
| Nebulizer       | -3.661       | 0.4771|         |

*) Significant by the ANOVA test

The increase in% KVP with the nebulizer device was higher than that of home-made spacer (p<0.001), as well as between spacers and home-made spacers and this was significant (p=0.038) with the Post-Hoc test (Table 5). Post-Hoc test also found a significant association between the decrease in VAS dyspnea in patients using nebulizer device than the spacer (p<0.001). Decreasing VAS dyspnea with nebulizer devices is higher compared to home-made spacers, this also gives significant results (p<0.001). There were no differences in the decrease in VAS dyspnea between spacers and home-made spacers (Table 5).
**DISCUSSION**

The majority of the subjects in this study were male, as many as 59 (95.2%). This is associated with higher smoking habits in men than women. Men are more active outside the home than women, thus increasing the risk of exposure to biomass in the environment, such as pollution in the workplace and pollution on the road.7

Most research subjects belonged to the age group of 50-69 years which amounted to 32 (51.6%). The high prevalence of COPD is found in older people. Based on GOLD (2017), the highest prevalence of COPD is found in people aged >60 years. Most research subjects have a high Brinkman index, which are as many as 50 people (80.6%).1 Studies in H. Adam Malik Hospital and Pirngadi Hospital both in Medan also indicate that the average Brinkman index of COPD patients is 738 (severe). High consumption of cigarettes will induce release of TNFα by alveolar macrophages which is followed by increased production of matrix metalloproteinase (MMP). This MMP will then initiate the destruction of smoker's airways. Thus, the greater the Brinkman index of a person, it reflects the longer and more levels of cigarette consumption and the greater the destructive effects that occur.7 The majority of research subjects belong to norm weight BMI as many as 19 (30.6%). The least common BMI was in underweight subjects, which were as much as 5 (8.1%). This is not in line with the research conducted by Ran PX et al, where compared to healthy people, the body mass index of COPD patients was significantly lower.8

Devices used in delivering inhalation drugs are as important as drugs.9 Inhalation therapy using a spacer device will increase drug delivery and lung deposition when used by measured dose inhalers by reducing the need for coordination between actuation and inhalation so as to allow more time for propellant evaporation, thereby allowing a greater proportion of drug particles to be inhaled and stored in the lungs. Home-made spacers made from bottles of drink or mineral water and even from empty salt bottles are used as alternatives to commercial spacer making, with good efficiency like other devices but cheaper.10,11 A nebulizer converts drug solutions into aerosols for inhalation which thus allows higher drug doses to be sent than standard inhalers.9

The increase in FEV1 by nebulizer in this study was higher than that of a spacer and this was significantly significant. However, there was no significant difference in% KVP between the spacer and the nebulizer. This study also shows that an increase in% FEV1 by nebulizer devices is significantly higher compared to home-made spacers, as is the increase in% KVP. This is in line with several studies that show that nebulizers are superior to MDI based on improvements in spirometry values and symptoms.2 The administration of high doses of salbutamol by nebulization leads to faster improvement in lung function which results in a faster improvement of shortness of breath.12

The reduction in VAS dyspnea by nebulizer in this study was higher than that of spacer, this was statistically significant. The reduction in VAS dyspnea by nebulizer devices was also significantly higher compared to home-made spacers. However, there were no significant differences in the decrease in VAS dyspnea between spacers and home-made spacers.

The study of Poole PJ et al, also showed that improvement in VAS was seen five minutes after administration of salbutamol by nebulizer, which was 1.04 cm, whereas by MDI it was 0.47cm. However, in the 45th minute there were no significant differences between the two devices.12

Inhalation therapy is the basis of COPD treatment and is often given by one of three devices, namely MDI/ spacer, DPI, and nebulizer.13 The efficacy of this route depends on several factors, such as the correct inhalation technique, compliance, and particle size. Availability of devices, clinical conditions, age of the patient, and the ability of the patient to use the device appropriately, use of various drugs, costs, time of administration of drugs, duration, comfort and choice of patients and doctors are factors that can be considered in selecting bronchodilator delivery devices.14

**CONCLUSION**

Bronchodilator by use of three tools (spacer, home-made spacer and nebulizer) can increase FEV1 values, KVP and VAS dyspnea which are significant (p <0.05). And between spacers and home-made spacers the increase in pulmonary physiological values that occur is not significantly different.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

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Table 5: Post-Hoc test of ∆% FEV1.

| Device                      | ∆%VEF1 (p-value) | ∆KVP (p-value) | ∆VAS dyspnoea (p-value) |
|-----------------------------|------------------|----------------|-------------------------|
| Spacer vs nebulizer         | 0.001*           | 0.129          | <0.001*                 |
| Spacer vs home-made spacer  | 0.241            | 0.038          | 0.485                   |
| Home-made spacer vs nebulizer | <0.001*        | <0.001*        | <0.001*                 |

*) Significant
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