MDI with DIY Spacer versus Nebulizer for Bronchodilator Therapy in Children Admitted with Asthmatic Attack

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Background: Inhaled bronchodilator treatment given via the pressurized metered-dose inhaler (pMDI) with spacer has been recommended for an acute asthma treatment. Unfortunately, most of commercially available spacers are at high cost while a do-it-yourself (DIY) spacer has lower cost as it is made from plastic bottle and siphon pump which are inexpensive and easily-found materials.

Objective: This study aims to compare treatment response in nebulizer and DIY spacer used for asthmatic children.

Material and Method: A prospective, randomized control study was conducted in children aged 1-15 years old hospitalized for mild to moderate asthmatic attack at Thammasat University Hospital between June 2014 and March 2015. The patients were divided into 2 groups, receiving β_2 -agonist via nebulization and via pMDI with DIY spacer. Their vital signs and oxygen saturation were monitored and asthma scores were also recorded at admission, 24 hours, 48 hours, and before discharge. The satisfaction of equipment use was evaluated employing questionnaires.

Results: 40 childrens were enrolled with male at 72.5% and mean age at 3.1 ± 1.6 years old. There was no significant difference in efficacy of β_2 -agonist among 2 groups when comparing in consideration of vital signs, oximetry, asthma scores and hospital stay. However, there were significantly different on side effect in which the DIY spacer had less tachycardia and agitation. Satisfaction of parents and healthcare workers were higher in DIY spacer.

Conclusion: MDI with DIY spacer was able to be used effectively when compared with nebulization to treat mild to moderate acute exacerbations of asthma in children admitted in hospital.

Keywords: DIY spacer, Valved-holding chamber with mask, Pressurized metered-dose inhaler, Asthmatic attack

J Med Assoc Thai 2016; 99 (Suppl. 4): S265-S274 Full text. e-Journal: http://www.jmatonline.com

Asthma is a common and potentially serious disease and its prevalence has increased worldwide. In Thailand, the overall prevalence of childhood asthma has been reported varying at 6.8-14.1%⁽¹⁻³⁾ indicating 3- to 4-fold increase since the 1990s⁽²⁾. It has been demonstrated higher prevalence in older children than the younger group, 13.6% and 11.7% respectively⁽³⁾. Asthma, a disease of hyperactive airway causes symptoms such as cough, shortness of breath, chest tightness and wheezing varying in severity. Following

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Asthma Treatment Guideline 2008, inhaled rapid acting β₂-agonist of 2.5-5 mg administered via nebulizer or Pressurized Metered-Dose Inhaler (pMDI) is recommended to patient with acute asthmatic attack⁽⁴⁾. Although use of bronchodilator administered via nebulizer for acute asthmatic attack treatment is worldwide, there are still several limitations. Hospitalization is necessary coupled with higher cost and resources. Many young patients are scared and agitated by set of nebulizer equipment causing their less cooperation. Therefore, the pMDI has been recommended for home treatment in exacerbation group due to a greater convenience, more effective lung deposition, and lower cost⁽⁴⁾. However, previously known, this device is not fully beneficial in children with asthmatic attack as it requires correctly coordinated inhalation.

Consequently, assisting device of pMDI has been developed and now widely used. A reservoir called "spacer" is a cone-shaped chamber with an opening at each end. The opening connecting with pMDI, and the other is wider for applying on the patient's mouth and nose. Its advantage is that there is no need to have coordinated inhalation since particle of administered bronchodilator is collected in the spacer and delivered into the patients by every breath of them. However, there is a practical problem of using the spacer; the patient's exhaled air mixes with aerosol particle inside the spacer resulting in the decreased drug aerosol for next inhalation. A one-way valve then has been added into the spacer to control and provide drug aerosol triggered by patient's breathing in simultaneously.

Previous studies provide information that administration of bronchodilator via MDI with spacer is sufficient as nebulizer to treat mild to moderate acute asthma^(2,5-9). Furthermore, MDI with spacer associated with less side effects states decreased cost, more convenience, and higher satisfaction of parent and child^(5,8,10-12). In consequence, most established policies recommend the use of MDI with spacer for acute asthma treatment^(4,12).

As most of commercially available spacers are at high cost about 42-45 USD each, therefore easily self-made spacer has been created. We have collaborated with National Metal and Materials Technology Center (MTEC) to design a simple and effective valved-holding spacer called Do It Yourself (DIY) spacer (Fig. 1). The one-way valve used in DIY spacer is composed of two leaflets. The mechanism of this valve is when fluid flows from inlet through outlet, one leaflet of this valve is opened, while another is closed; on the other hand, when fluid reversely flows from another outlet through inlet, one leaflet of this valve is reversely closed, while another is reversely



Fig. 1 DIY spacer with siphon pump.

opened. Therefore, using this valve, the drug aerosol can flow into the chamber and then into the patient's airway during inhalation, while the exhaled air ran out through the opening at the upper side of chamber without reflux during exhalation.

The present, we propose to find out whether the administration of bronchodilator agent by using pMDI with DIY spacer is effective method compared with the standard nebulizer.

Material and Method

At Thammasat University Hospital, patients at the age of 1-15 years old who were diagnosed with asthmatic attack at Emergency Department and did not improve after initial bronchodilator therapy were admitted into Pediatric Wards. 40 patients were enrolled into the study. A history taking and physical examination were completed thoroughly. If their conditions were suitable for inclusion criteria which were diagnosed as acute asthmatic attack, mild to moderate severity (score <7 on Siriraj asthma score) (1) and oxygen saturation more than 92%. Informed consent was obtained from patient's parent prior to enrollment and then they were enrolled into the study. The criteria for exclusion were presence of other conditions such as heart disease, chronic pulmonary diseases, patient with tracheostomy and severe exacerbation (score >7 on Siriraj asthma score) (1) requiring intensive care or mechanical ventilation and oxygen saturation less than 92%. After important detail of the study was all informed and the consents were provided by the patients' parents, they were simply randomized into 2 groups. A control group was treated with salbutamol administered via standard nebulizer set and DIY spacer was used as inhaler for another group instead. Salbutamol was administered every 2-6 hours depending on symptoms of both groups. During bronchodilator therapy, patient's clinical condition was closely observed. In addition, their vital sign and oxygen saturation were monitored and asthma scores were also recorded. Besides, a questionnaire for parents and trained healthcare workers taking care of the patients was used as a tool to acquire opinions toward equipment used to apply bronchodilator, consisting of two parts: part one regarding parent's perspective and second part for healthcare worker's perspective. They were asked about convenience, cooperation of patient, time of use, reasonable budget, and overall satisfaction of both devices. All questionnaires were collected before the patients were discharged from hospital.

All calculations were performed employing

the statistical package for the social sciences (SPSS) version 10, statistical package for windows. Demographic data were expressed applying descriptive statistics. Furthermore, the Chi-square test or Fisher's exact test was used for categorical variables. For all analyses, a 2-sided probability value below 0.05 was considered to indicate statistical significance.

The study protocol and informed consent were reviewed and approved by the Ethics Committee of Thammasat University before study initiation, and then written informed consent was obtained from patient's parent.

Results

During period of June 2014 until March 2015, 40 patients were hospitalized because of mild to moderate asthmatic attack. As their conditions met the inclusion criteria, they were enrolled into the study. As shown in Table 1, most of the patients enrolled in the study were male at 72.5%, aged ranging from 1 to 7 years old with mean \pm SD at 3.1 ± 1.6 years old. Additionally, 20 subjects were previously diagnosed with asthma before this admission and 8 of them were known case of asthma more than 1 year. Only 9 patients had at least one first-degree relative with known diagnosis of asthma. Half of the patients in this trial were first diagnosis of asthma, presenting recurrent wheezing which was a good response to bronchodilator without first-degree relative family.

After 40 patients were admitted and treated with bronchodilators, they all improved in clinical setting and recorded asthma score was demonstrated in Table 2. The initial asthma score of both groups was not significantly different at the time of admission. During bronchodilator therapy, the asthma score was decreasing at every recorded point of time and it was not significantly different between both methods of treatment. Table 3 demonstrated statistically significant decrease in asthma score at the points of 24-hour, 48-hour, and patient's discharge when comparing with the score at the time of admission. These results were found similarly in both groups. Moreover, the numbers of hospital stay were comparable.

Comparing total dose of bronchodilators used on the admission between 2 groups was shown in Table 4. Salbutamol was administered in the DIY spacer group less than the nebulizer group significantly. However, the use of ipratropium bromide was not different. Subsequently, complications of bronchodilator were analyzed. Percentage of increasing pulse rate of the nebulizer group was higher than the DIY spacer group at 20.4% and 10.1% respectively as shown in Table 5. Moreover, the patients complained about palpitation or the parents observed their child's agitation during bronchodilator administration more in the nebulizer group.

As shown in Table 6, satisfaction of parents and healthcare workers were demonstrated statistically

Table 1. Demographic data comparing between two groups

	Total	DIY	NB	<i>p</i> -value
Male	29/40 (72%)	13/20 (65%)	16/20 (80%)	0.288
Age (Mean \pm SD, years)	3.1 <u>±</u> 1.6	3.5 ± 1.8	2.8 ± 1.3	0.202
Body weight (kg)	16.2 <u>+</u> 5.2	16.7 <u>+</u> 5.7	15.7 ± 4.8	0.568
Previously diagnosed asthma (N)	20/40 (50%)	9/20 (45%)	11/20 (55%)	0.534
Diagnosed asthma >1 year	8	4	4	1.000
Family history of asthma	9/40 (22%)	4/20 (20%)	5/20 (25%)	0.706

Table 2. Results of treatment for asthmatic attack during hospitalization

	Total	DIY	NB	<i>p</i> -value
Asthma score				
Admission	3.9 ± 1.5	3.6 <u>+</u> 1.3	4.3 ± 1.7	0.177
24-hour	2.0 ± 1.3	1.9 <u>+</u> 1.1	2.1 ± 1.5	0.721
48-hour	0.8 ± 0.9	0.8 ± 0.7	0.9 ± 1.0	0.719
Discharge	0.2 ± 0.5	0.1 ± 0.3	0.3 ± 0.7	0.228
Hospital stay (days)	3.3+1.1	3.3±1.1	3.4 ± 1.1	0.892

different between DIY spacer and nebulizer. In parent's perspective, they were more satisfied with DIY spacer in aspect of patient's cooperation, time of use, and reasonable budget. Likewise, the healthcare workers favored the DIY spacer because of its convenience, patient's cooperation, time of use, reasonable budget, and easy equipment care.

Discussion

Bronchodilator appears to be the most important role in asthmatic attack treatment and administration of agents is also a crucial factor in treatment response. Nebulizer is a standard modality to deliver the bronchodilator into the patient's airway.

Table 3. The asthma score reducing between 2 points of time during hospitalization comparing between 2 different methods of bronchodilator therapy

	DIY reduced score (p-value)	NB reduced score (p-value)	p-value of comparing reduced scores between both groups
At admission - at 24 hours	1.7±0.7 (<i>p</i> <0.01)	2.2±1.6 (<i>p</i> <0.01)	0.224
At admission - at 48 hours	2.9±1.1 (<i>p</i> <0.01)	3.4±1.6 (<i>p</i> <0.01)	0.219
At admission - at discharge	3.5±1.2 (<i>p</i> <0.01)	4.0±1.5 (<i>p</i> <0.01)	0.308

Table 4. Total dose of bronchodilators

	Total	DIY	NB	<i>p</i> -value
Ventolin (mg)	35.6±38.6	7.4±1.6	63.9±37.1	<0.001
Berodual (ml)	19.3±21.1	15.4±16.5	23.2±24.7	0.248

Table 5. Complications of bronchodilator administration

	Total	DIY	NB	<i>p</i> -value
Increased PR (%) Palpitation/agitation	15.2 <u>±</u> 11.0	10.1 <u>+</u> 8.4	20.4±11.0	0.002
	12	1 (5%)	11 (55%)	<0.001

Table 6. Satisfactory

	DIY	NB	<i>p</i> -value
Parent's perspective			
Convenience	4.7 <u>+</u> 0.5	4.4 <u>+</u> 0.7	0.064
Patient's cooperation	4.8 <u>+</u> 0.6	3.6±1.5	< 0.001
Consumed time	4.4 ± 0.6	3.6 ± 0.5	< 0.001
Reasonable budget	3.9 ± 0.7	3.4 ± 0.6	0.022
DIY	4.6 <u>+</u> 0.8	1.8 <u>+</u> 0.8	< 0.001
Overall satisfactory	4.8 ± 0.4	4.3 ± 0.7	0.016
Healthcare worker's perspective			
Convenience	4.9+0.4	4.2+0.7	< 0.001
Patient's cooperation	$\frac{-}{4.7+0.6}$	3.3+1.0	< 0.001
Consumed time	4.6+0.5	3.4+0.5	< 0.001
Reasonable budget	4.1+0.6	2.8+0.8	< 0.001
Equipment care	-4.4+0.6	3.5+0.6	< 0.001

However, hospitalization is necessary, followed by high expense and associated with poor patient's compliance. Currently, MDI seems to be a good alternative method for bronchodilator administration. Its use demonstrates more benefit than nebulizer in aspect of easy use at home. The spacer was designed to use with MDI to minimize effect of poor lung-hand coordination especially in young children⁽¹⁻³⁾. The further development of spacer was the addition of one-way valve into the chamber in order to control the direction of airflow and keep the high level of drug aerosol within the inhaled air. Many studies stated that this method of administration provided the comparable therapeutic result with the nebulizer⁽⁴⁾. The asthma care team in our hospital has implemented clinical guideline for asthma patients for many years and realized that MDI with spacer was an important key to successfully control symptoms at home and lower frequency of hospitalization. Due to high cost of commercially available spacer, we made a first generation of do-ityourself spacer in 2010 and suggested its good result in clinical use by Poachanukoon et al. Since then, we attempted to improve our equipment for more convenience and better results. In 2012, we applied a water pump within the chamber as a valved-holding spacer called DIY spacer costing only 2 USD, comparing with commercial one costing 42 USD. Then this study was conducted to confirm its possible benefit in clinical setting.

In the study, both groups including similar demographic data and severity of asthmatic attack responded well to the bronchodilators. Their asthma score improved significantly after treatment. The result of salbutamol administered with DIY spacer was comparable to standard treatment with nebulizer in aspect of clinical signs, asthma score improvement, and length of hospital stay. Moreover, the total dose of salbutamol utilized via MDI with DIY spacer became significantly less than the control group resulting in lower complications and better compliance. More importantly, it was designed to work as home therapy with convenience and it was favorable in parent's and healthcare provider's opinions.

Since this is an initial study of new adapted equipment conducted on small sample size, the results might indicate more benefits in further study consisting of larger subject group. Although use of steroid, either intravenous or oral route is one of the important modalities in asthmatic attack treatment, it is not included in this analysis. However, it might be a crucial confounding factor of the study and should be

concerned in the next research design. Furthermore, analysis of overall treatment cost including equipment set, total dose of all medications, hospitalization, and healthcare provider would be a good opportunity for another further investigation.

Conclusion

The administration of bronchodilator by using MDI with our new simplified valved-holding spacer or DIY spacer was effective when compared with nebulization to treat mild to moderate acute exacerbations of asthma in children admitted in hospital. Furthermore, pMDI with DIY spacer associated with less side effects, more convenience, and higher satisfaction of parent and healthcare worker.

What is already known on this topic?

Administration of bronchodilator via MDI with spacer is sufficient as nebulizer to treat mild to moderate acute asthma. Furthermore, MDI with spacer associated with less side effects states decreased cost, more convenience, and higher satisfaction of parent and child.

What this study adds?

As most of commercially available spacers are at high cost, therefore easily self-made spacer has been created. It has been called Do It Yourself (DIY) spacer. We propose to find out whether the administration of bronchodilator agent by using pMDI with DIY spacer is effective method compared with the standard nebulizer.

Acknowledgements

We would like to thank all pediatric residents and clinical staff members at Thammasat University Hospital who cared for these patients. We are deeply grateful to all children and caregivers for all participation.

The present was supported by a grant obtained from the Faculty of Medicine, Thammasat University.

Potential conflicts of interest

None.

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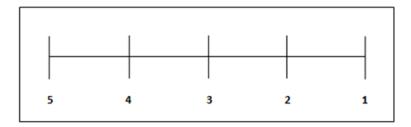
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ภาคผนวก

<u>แบบบันทึกข้อมูลทั่วไปของผู้ป่วยเด็กโรคหืดและผู้ดูแล</u> วันที่สัมภาษณ์/
<u>ข้อมูลทั่วไป</u>
ผู้ป่วย: ชื่อ - สกุลเบอร์ติดต่อ
อายุ
เพศ 🗆 ซาย 🗆 หญิง น้ำหนักกิโลกรัม ส่วนสูงเซนติเมตร
สิทธิการรักษา□ บัตรทอง 🗆 ข้าราชการ/รัฐวิสาหกิจ 🗆 ชำระผินเอง 🗆 อื่นๆ
<u>ข้อมูลโรคประจำตัว</u>
โรคประจำตัว
แพทย์วินิจฉัยว่าเป็นโรคหอบหืดตั้งแต่อายุ
ยาที่ใช้ประจำ:
ใช้ยารักษาควบคุมอาการโรคหอบหืดเป็นประจำ
□ ไม่ได้ใช้ □ ใช้ยา □ ใช้ยาไม่สม่ำเสมอ □ ใช้ยาสม่ำเสม
มียาขยายหลอดลม(ยาฉุกเฉิน) ที่บ้าน 🗆 ไม่มี 🗆 มี
ใช้ยาขยายหลอดลม(ยาฉุกเฉิน) เมื่ออาการกำเริบ 🗆 ไม่ได้ใช้ 🗆 ใช้
บุคคลในครอบครัวที่เป็นโรคหอบหืด
พ่อ ⊏ไม่มี ⊏มี
แม่ 🗆 ไม่มี 🗆 มี
พื/น้อง 🗆 ไม่มี 🗆 มี
ประวัติการเข้ารับการรักษาตัวในโรงพยาบาลด้วยเรื่องหอบกำเริบจำนวนครั้ง/ปี
ครั้งสุดท้ายที่นอนโรงพยาบาลระยะเวลาในการนอนรักษาวัน
ครั้งสุดท้ายที่มาพ่นยาที่แผนกฉุกเฉิน
ครั้งสุดท้ายที่หอบกำเริบ (ใช้ยาพ่นเวลามีอาการ)
การควบคุมโรคหืด
 □ ควบคุมได้ □ ควบคุมได้ □ ควบคุมไม่ได้
ประวัติโรคภูมิแพ้
การทดสอบภูมิแพ้
🗆 ไม่เคยทดสอบ 🗆 ไม่แพ้ 🗆 แพ้
🗆 แมลงสาบ 🗆 ขนสุนัข 🗆 ขนแมว 🗆 เกสรหญ้า 🗆 เชื้อรา 🗆 ไรฝุ่น
ใรคภูมิแพ้ที่พบร่วม
🗆 โรคจมูกอักเสบจากภูมิแพ้/แพ้อากาศ 🗆 ภูมิแพ้ผิวหนัง 🗆 ภูมิแพ้ทางตา 🛭 แพ้อาหาร 🗆 แพ้รุนแรง

□ DIY spacer □ Nebulizer
□ DIY spacer □ Nebulizer
drocortisone Oral Prednisolone
□ 1NB [BW >10 kg]
□ DIY spacer □ Nebulizer
drocortisone Oral Prednisolone
izer
Tremor

Appendix 1. Cont.



<u>ความพึงพอใจของอุปกรณ์พ่นยาของผู้ดูแลเด็กโรคหืด</u>

โปรดเลือกคะแนนความพึงพอใจในการใช้อุปกรณ์พ่นยาขยายหลอดลม

ความพึงพอใจของผู้ดูแล	5	4	3	2	1
1.ความสะดวกในการใช้งาน					
2.ความร่วมมือของผู้ป่วย					
3.ระยะเวลาในการพ่นยา					
4.งบประมาณ					
5.ทำเองได้ที่บ้าน					

ความพึงพอใจของอุปกรณ์พ่นยาของผู้ให้บริการ

โปรดเลือกคะแนนความพึงพอใจในการใช้อุปกรณ์พ่นยาขยายหลอดสม

ความพึงพอใจของผู้ให้บริการ	5	4	3	2	1
1.ความสะดวกในการใช้งาน					
2.ความร่วมมือของผู้ป่วย					
3.ระยะเวลาในการพ่นยา					
4.การดูแลรักษาอุปกรณ์					
5.ผู้ป่วยทำได้เอง					
6.งบประมาณ					

*Nebulizer	ราคา	120	บาทตอหนวย	Ventolin NB 3181	20	บาทตอหนวย	
*DIY Spacer	ราคา	45 บา	ทต่อหน่วยVento	blin MDI ราคา 166	บาทต่อ	หน่วย	
ความคิดเห็นอื่	u						

เปรียบเทียบการใช้ยาพนขยายหลอดลมทาง DIY Spacer และ Nebulizer ในผู้ป่วยเด็กหืดกำเริบที่รักษาตัวในโรงพยาบาล

ลลิต ลีลาทิพย๎กุล, ภัทรา ตันติเจริญวิวัฒน, จุดินันท ์อิทธิอาวัชกุล, อรพรรณ โพชนุกูล

Rapid-acting inhaled \$\beta 2\$ agonist เป็นยามาตรฐานในการรักษาโรคหืดในระยะเฉียบพลัน ผู้ป่วยเด็กหืดกำเริบมักได้รับการพ[่]นยาผานทาง
Nebulizer แต่ยังมีข้อจำกัดปริมาณมาก ปัจจุบันจึงมีการคิดค้นการพ[่]นยา pMDI ผานทางกระบอกพ[่]นยา Spacer เพื่อให้พ[่]นยาได้งายขึ้นแต[่] Spacer
ชนิดที่มีลิ้นและหนากากที่แนบหนานั้นมีราคาค่อนขางสูงจึงได้มีการผลิต Spacer ขึ้นมาเองเรียกว่า DIY Spacer ซึ่งสามารถทำได้จากวัตถุที่หาได้งาย
และราคาถูก แต่ยังไม่มีการศึกษาเปรียบเทียบถึงประสิทธิภาพของ DIY Spacer และ Nebulizer ในการรักษาผู้ป่วยเด็กหืดกำเริบที่เขารับการรักษาตัว
ในโรงพยาบาล

วัตถุประสงค์: เพื่อศึกษาถึงประสิทธิภาพ ผลข้างเคียง และความพึงพอใจของผู้ดูแลผู้ป่วยเด็กหืดกำเริบในการบริหารยาขยายหลอดลม โดยเปรียบเทียบ ระหว่างกลุ่มผู้ใช^{*} pMDI ผานทาง DIY Spacer กับกลุ่มผู้ใช^{*} Nebulizer

วัสดุและวิธีการ: การศึกษาเชิงทดลองทางคลินิกแบบไปข้างหน้าในผู้ป่วยโรคหืดกำเริบอายุตั้งแต่ 1-15 ปี ที่มีอาการหอบเฉียบพลัน ความรุนแรง ระดับน้อยถึงปานกลางที่เข้ารับการรักษาที่หอผู้ป่วยกุมารเวชกรรม โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ ระหวางเดือนมิถุนายน พ.ศ. 2557 ถึงเดือนมีนาคม พ.ศ. 2558 โดยแบ่งแบบสุ่มเป็น 2 กลุ่ม กลุ่มละ 20 คน กลุ่มควบคุมใช้การพ่นยาขยายหลอดลมชนิดละอองฝอยผ่านทาง Nebulizer และกลุ่มทดลองใช้การพ่นยาขยายหลอดลม pMDI ผ่านทาง DIY spacer ประเมินอาการทางคลินิกที่แรกรับ หลังได้รับยาที่ 24, 48 ชั่วโมง และก่อน จำหนายจากโรงพยาบาล ร่วมกับให้ผู้ดูแลผู้ป่วยเด็กหืดกำเริบตอบแบบสอบถามด้านความพึงพอใจในอุปกรณ์การพ่นยาทั้ง 2 ชนิด

ผลการศึกษา: ผู้ป่วยเด็กโรคหืดที่มีอาการหืดกำเริบความรุนแรงระดับน้อยถึงปานกลางจำนวน 40 คนที่มารับการรักษาที่หอผู้ป่วยกุมารเวชกรรม โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ เพศชาย 29 คน (72.5%) เพศหญิง 11 คน (27.5%) อายุเฉลี่ย 3.1±1.6 ปี พบวาประสิทธิภาพการให้ยา ขยายหลอดลมและระยะเวลาการนอนโรงพยาบาลของทั้ง 2 กลุ่ม ไม่แตกต่างกัน แต่พบผลข้างเคียงที่น้อยกวาในกลุ่มทดลองที่ใช้การพ่นยาขยายหลอดลม ผ่านทาง DIY spacer และพบวาผู้ดูแลผู้ป่วยเด็กหืดกำเริบมีความพึงพอใจในการใช้อุปกรณ์ DIY spacer มากกวา

สรุป: การพ่นยาขยายหลอดลมผานทาง DIY spacer มีประสิทธิภาพเทียบเทาการใช้อุปกรณ์พนยาละอองฝอยผานทาง Nebulizer ในกลุ่มผู้ป่วยเด็ก หืดกำเริบที่เข้ารับการรักษาตัวในโรงพยาบาล ทั้งในด้านผลการรักษาและระยะเวลาการนอนโรงพยาบาล