



aeolos Anti-Static
Valved Holding
Chamber
Αεροθάλαμος Εισπνοών aeolos

CLINICAL STUDY
ΚΛΙΝΙΚΗ ΜΕΛΕΤΗ



**Allergologia et
immunopathologia**
Sociedad Española de Inmunología Clínica,
Alergología y Asma Pediátrica
www.all-imm.com



SHORT COMMUNICATION

OPEN ACCESS

Assessment and management of asthma exacerbations in an emergency department unit

Konstantinos Douros^{a*}, Dafni Moriki^a, Olympia Sardeli^a, Barbara Boutopoulou^{a,b}, Angeliki Galani^a, Vasiliki Papaevangelou^a, Kostas N. Priftis^{a,b*}

^a3rd Department of Pediatrics, "Attikon" University Hospital, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

^bPediatrics Center of Athens, Marousi, Athens, Greece

Received 4 July 2022; Accepted 21 August 2022

KEYWORDS

asthma;
children;
salbutamol;
PRAM;
metered-dose inhaler;
spacer

Abstract

Background: The Pediatric Respiratory Assessment Measure (PRAM) score is a useful tool for the assessment of asthma exacerbations in children. This study aimed to estimate the risk of hospitalization in children, assessed with the PRAM score as having mild-moderate asthma exacerbation, who were treated with salbutamol delivered via a metered-dose inhaler and spacer (MDI/S).

Methods: The study population consisted of children aged 3-16 years with mild-moderate asthma exacerbations. All children received 1mg/kg prednisolone p.o. (max 40 mg) and 4-6 puffs of salbutamol via MDI/S.

Results: Fifty patients participated in the study. Admission was associated positively with the initial PRAM score (OR: 18.91, CI: 2.42-123.12, P = 0.005) and negatively with the improvement in PRAM score (OR: 0.52, CI: 0.01-0.78, P = 0.032).

Conclusion: PRAM is a reliable tool that can be used effectively to estimate the asthma exacerbation severity. © 2023 Codon Publications. Published by Codon Publications.

Introduction

Clinical assessment of asthma exacerbations is based mainly on signs and symptoms. The Pediatric Respiratory Assessment Measure (PRAM) is a clinical score that was developed to guide the management of exacerbations in children aged 2-17 years; it consists of the estimation of five components, namely wheezing, air entry, contraction of scalene muscles, suprasternal retraction, and oxygen saturation, into a validated scale.¹ The treatment of acute exacerbations consists of a combination of salbutamol and systemic corticosteroids (although approaches that include drugs such as inhaled corticosteroids, ipratropium bromide, and xanthines have also been suggested).² It has to be noted that significant variation has been recognized between guideline recommendations and their implementation in clinical practice, affecting the actual management of exacerbations.²

Although salbutamol used to be delivered via nebulization, it is now widely accepted that delivery via a metered-dose inhaler and spacer (MDI/S) leads to similar improvements in lung function, fewer side effects, and less noise, time, and cost.³ Despite these advantages, the practice of delivering

salbutamol via nebulizers remained the prevailing method in majority of the emergency departments (ED) in Greece and many other parts of the world.⁴ However, the SARS-CoV2 pandemic and the avoidance of nebulization due to the risk of airborne transmission of the virus essentially rendered MDI/S the only available method for providing salbutamol in the ED.

This study aimed to estimate the risk of hospitalization for children, assessed with PRAM score as having mild-moderate asthma exacerbation, who were treated with salbutamol delivered via MDI/S, in a real-world ED setting.

Methods

The study population consisted of children, 3-16 years old, who visited the ED of Attikon Hospital from October 2020 to February 2022, with mild-moderate asthma exacerbations defined as an acute or subacute worsening in respiratory symptoms⁵⁻⁷ (mild: PRAM 0-3; moderate: PRAM 4-7). Patients must have received a prior diagnosis of asthma by a physician or have had at least three episodes of wheezing responsive to salbutamol. Exclusion criteria were

*Corresponding author: Konstantinos Douros, Pediatric Allergy and Respiratory Unit, 3rd Department of Pediatrics, "Attikon" University Hospital, Rimini 1, 12462 Athens, Greece. Email address: costasdouros@gmail.com

<https://doi.org/10.15586/aei.v51i0.720>

Copyright: Douros K, et al.

License: This open access article is licensed under Creative Commons Attribution 4.0 International (CC BY 4.0). <http://creativecommons.org/>

(i) pulse oximetry saturation (SaO_2) <92%; (ii) having received salbutamol in the previous 6 h, or systemic corticosteroids within the previous 24 h; (iii) chronic respiratory disorders other than asthma; (iv) cardiac, immunologic, or metabolic disorders. All patients who visited the ED with respiratory complaints were evaluated for inclusion and exclusion criteria and approached for consent if the aforementioned criteria were met. Those with repeat visits were included only once. The final study group was a convenience sample of 50 children.

All children received 1mg/kg prednisolone p.o. (max 40 mg) and 4–6 puffs of salbutamol via MDI and a novel, valve-holding chamber (the 175-ml Aeolos®; Kougioumtzis M & Co, Thessaloniki, Greece) equipped with both a mouthpiece and a liquid silicone facemask that requires low pressure (1.5 kg) to achieve an airtight seal. Each puff was followed with 2–3 slow and steady deep inhalations. Treatment with salbutamol was repeated, at 20- to 25-min intervals, up to three times and according to each child's clinical improvement. The clinical assessment of children was performed with the PRAM score, before the commencement of treatment, and then 20 min after each salbutamol administration.

The study was approved by the Attikon Hospital Ethics Committee.

Statistical analysis was performed with a logistic regression model using admission as the response variable. Age, PRAM score at presentation, and the difference between the initial and the last measured PRAM score were used as predictive variables. The number of salbutamol treatments was used as a proxy for the time to complete remission of the exacerbation (PRAM score = 0), and it was analyzed with a Cox proportional hazard model. Variables were expressed as medians with 25th and 75th percentiles (p25–p75) and results as odds ratios (OR) or hazard ratios (HR) with 95% confidence intervals (CI).

Table 1 Patients' clinical characteristics.

Age (years), median (p25–p75)	9.6 (6.4–12.9)
Gender (m/f)	27/23
Family history of asthma, n(%)	22 (44%)
Duration of symptoms (hours), median (p25–p75)	11 (5–22)
SaO_2 at presentation, median (p25–p75)	95 (93, 96)
Number of previous episodes	6 (3, 10)
Previous admissions	2 (1, 5)
Prophylactic treatment	
Inhaled steroids, n(%)	15 (30%)
Montelukast, n(%)	8 (16%)
PRAM (median, p25–p75) at presentation	3, 2–5
Last measured PRAM (median, p25–p75)	1, 0–1
PRAM: Pediatric respiratory assessment measure score; SaO_2 : Pulse oximetry saturation	

Results

Fifty-three patients were asked to participate in the study, and all but three agreed. Patients' clinical characteristics are shown in Table 1. Eight (16%) children needed the facemask for effective delivery of salbutamol. Twenty-nine cases (58%) were classified as mild and 21 (42%) as moderate exacerbations. Seven (14%) patients were admitted, all of whom had a moderate exacerbation. Admission was associated positively with the initial PRAM score (OR: 18.91, CI: 2.42–123.12, $P = 0.005$) and negatively with the improvement in PRAM score (OR: 0.52, CI: 0.01–0.78, $P = 0.032$). Twenty-seven (93.1%) mild and four (19.0%) moderate cases attained complete remission (PRAM = 0) with the treatment in the ED. The initial PRAM score was negatively associated with achieving complete remission in the ED (HR: 0.39, CI: 0.27–0.56, $P < 0.005$). Three (6%) children experienced a nonclinically significant tremor.

Discussion

Our study showed that salbutamol can be used effectively via MDI/S in the treatment of mild and moderate asthmatic exacerbation in ED. PRAM score can largely predict complete remission after treatment in the ED or the need for hospitalization, as was shown previously.⁶ The negative relationship between the improvement in PRAM score and hospitalization is consistent with the observed ability of the PRAM score to detect clinically important changes over time.¹

Aeolos® was an easy-to-use and reliable device for the administration of salbutamol. Using a mouthpiece has some theoretical advantages over facemasks, such as the lack of deposition on the face and avoidance of the nose which may act as an effective filter,⁷ although there is no actual evidence that a significant difference in the deposition of aerosols in the lungs exists between these two different modalities.⁸ Nevertheless, many young children are not able to perform a tight seal around the mouthpiece, and the use of a facemask is the only available option. One of the convenient characteristics of Aeolos® is that it comes with facemasks of different sizes that could fit easily on the face of every child. Salbutamol has been traditionally delivered

via nebulizers during asthma exacerbations. However, the benefits of the drug being delivered via MDI/S have been long and widely recognized. More specifically, it has been shown that the administration of salbutamol via MDI/S is correlated with significant improvements in hospitalization rates,^{9–11} length of stay,¹² clinical severity scores, and extra-pulmonary sympathetic effects such as anxiety, tremor, and tachycardia.^{11,13,14} Additionally, the MDI/S need less administration time and utilization of resources, and provide higher treatment satisfaction and reduce the exposure of staff to respiratory infectious agents.^{15,16} However, despite the ample evidence favoring MDI/S over nebulizers, the latter remain as the preferred approach for the treatment of pediatric asthma exacerbations in many ED.¹⁴ This apparent disconnect between evidence-based guideline recommendations and clinical practice is likely to lead to poorer therapeutic results, and increased use of resources.¹⁷ The reasons that clinicians in the ED still prefer the use of nebulizers instead of MDI/S for the administration of salbutamol are not clear but probably reflect a "clinical inertia," namely an unwillingness to change the treatment with which they are familiar.¹⁴ However, what the scientific evidence has failed to change was finally imposed from the SARS-Cov2 pandemic and the actual ban of nebulizer use in the ED.

The main limitation of our study was the absence of a comparison group treated with nebulized salbutamol. However, this was not possible given the restrictions of the pandemic. Another limitation is that our results were obtained from a convenience sample and not a random and representative population sample and thus cannot be generalized. Also, because the study was conducted in an ED setting, we were unable to perform any lung function tests and use a formal definition of asthma.

Conclusively, PRAM is a reliable tool that can be used effectively in the ED to estimate asthma exacerbation severity.

Funding

This study did not receive any specific funding.

Conflicts of Interest

The authors have no conflicts of interest to declare.

References

- Ducharme FM, Chalut D, Plotnick L, Savdie C, Kudirka D, Zhang X, et al. The Pediatric Respiratory Assessment Measure: A valid clinical score for assessing acute asthma severity from toddlers to teenagers. *J Pediatr*. 2008;152(4):476–80:80.e1. <https://doi.org/10.1016/j.jpeds.2007.08.034>
- Manti S, Licari A, Leonardi S, Marseglia GL. Management of asthma exacerbations in the paediatric population: A systematic review. *Eur Respir Rev*. 2021;30(161):200367. <https://doi.org/10.1183/16000617.0367-2020>
- Payares-Salamanca L, Contreras-Arrieta S, Florez-García V, Barrios-Sanjuanelo A, Stand-Niño I, Rodríguez-Martínez CE. Metered-dose inhalers versus nebulization for the delivery of albuterol for acute exacerbations of wheezing or asthma in children: A systematic review with meta-analysis. *Pediatr Pulmonol*. 2020;55(12):3268–78. <https://doi.org/10.1002/ppul.25077>
- Breuer O, Shoseyov D, Kerem E, Brooks R. Implementation of a policy change: Replacement of nebulizers by spacers for the treatment of asthma in children. *Isr Med Assoc J*. 2015;17(7):421–4.
- Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, et al. Global Initiative for Asthma Strategy 2021: Executive summary and rationale for key changes. *Eur Respir J*. 2022;59(1):2102730. <https://doi.org/10.1183/13993003.02730-2021>
- Alnaji F, Zemek R, Barrowman N, Plint A. PRAM score as predictor of pediatric asthma hospitalization. *Acad Emerg Med*. 2014;21(8):872–8. <https://doi.org/10.1111/acem.12422>
- De Benedictis FM, Selvaggio D. Use of inhaler devices in pediatric asthma. *Paediatr Drugs*. 2003;5(9):629–38. <https://doi.org/10.2165/00148581-200305090-00005>
- Ditcham W, Murdzoska J, Zhang G, Roller C, von Hollen D, Nikander K, et al. Lung deposition of 99mTc-radiolabeled albuterol delivered through a pressurized metered dose inhaler and spacer with facemask or mouthpiece in children with asthma. *J Aerosol Med Pulm Drug Deliv*. 2014;27 Suppl 1:S63–75. <https://doi.org/10.1089/jamp.2014.1139>
- Doan Q, Shefrin A, Johnson D. Cost-effectiveness of metered-dose inhalers for asthma exacerbations in the pediatric emergency department. *Pediatrics*. 2011;127(5):e1105–11. <https://doi.org/10.1542/peds.2010-2963>
- Leversha AM, Campanella SG, Aickin RP, Asher MI. Costs and effectiveness of spacer versus nebulizer in young children with moderate and severe acute asthma. *J Pediatr*. 2000;136(4):497–502. [https://doi.org/10.1016/S0022-3476\(00\)90013-1](https://doi.org/10.1016/S0022-3476(00)90013-1)
- Castro-Rodríguez JA, Rodrigo GJ. beta-agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: A systematic review with meta-analysis. *J Pediatr*. 2004;145(2):172–7. <https://doi.org/10.1016/j.jpeds.2004.04.007>
- Staggs L, Peek M, Southard G, Gracely E, Baxendale S, Cross KP, et al. Evaluating the length of stay and value of time in a pediatric emergency department with two models by comparing two different albuterol delivery systems. *J Med Econ*. 2012;15(4):704–11. <https://doi.org/10.3111/13696998.2012.674587>
- Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev*. 2013;2013(9):Cd000052. <https://doi.org/10.1002/14651858.CD000052.pub3>
- Rodríguez-Martínez CE, Sossa-Briceño MP, Castro-Rodríguez JA. Metered-dose inhalers vs nebulization for the delivery of albuterol in pediatric asthma exacerbations: A cost-effectiveness analysis in a middle-income country. *Pediatr Pulmonol*. 2020;55(4):866–73. <https://doi.org/10.1002/ppul.24650>
- Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: A systematic review. *PLoS One*. 2012;7(4):e35797. <https://doi.org/10.1371/journal.pone.0035797>
- Cotterell EM, Gazarian M, Henry RL, O'Meara MW, Wales SR. Child and parent satisfaction with the use of spacer devices in acute asthma. *J Paediatr Child Health*. 2002;38(6):604–7. <https://doi.org/10.1046/j.1440-1754.2002.00063.x>
- Licari A, Manti S, Chiappini E, Ciprandi G, Marseglia GL. Severe asthma in children: Current goals and unmet needs. *Pediatr Allergy Immunol*. 2020;31 Suppl 24:40–2. <https://doi.org/10.1111/pai.13168>