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The usefulness of the new SOBIstat-F® device in children with severe acute asthma attacks in the emergency department: a randomized clinical trial

Left running head: R. IRAMAIN ET AL.

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Ricardo Iramain[a], Jose A. Castro-Rodriguez[b], Jorge Ortiz[a], Alfredo Jara[a], Laura Cardozo[a], Rocío Morínigo[a] and Katia Martinez[c] AQ1 AQ2

[a]Pediatric Emergency Department, Hospital de Clínicas, Faculty of Medical Sciences, National University of Asunción, Paraguay; AQ3

[b]Department of Pediatric Pulmonology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile;

[c]Pediatric Emergency Department. Hospital General de Barrio Obrero, Asunción, Paraguay

"Notes on Contributor" is not available

No author footnotes is available

Corresponding Author

CONTACT Iramain Ricardo iramainricardo@gmail.com Pediatric Emergency Department, Hospital de Clínicas, Faculty of Medical Sciences, National University of Asunción, Paraguay.

ABSTRACT

Introduction

Protocols for managing severe asthma exacerbations include bronchodilators (short-acting beta-2 agonists and ipratropium bromide) administered by nebulizer or pressurized metered-dose inhaler(pMDI) with a valved holding chamber, corticosteroids IV, and magnesium sulfate IV. This study aims to evaluate the effectiveness of a new device (SOBIstat-F®) for bronchodilator administration *via* pMDI compared with the conventional method. AQ4

Methods

A randomized superiority clinical trial was conducted in children with severe acute asthma at the emergency department. Patients were assigned to one of the following groups: pMDI-SOBx, in which they received bronchodilators in pMDI through the SOBIstat-F® device, or in pMDI with oxygen *via* cannula or mask (pMDI-OxStand). The primary outcome was the need for hospitalization at the end of 8 h.

Results

84 patients participated in the study, of which 43 were treated with the pMDI-SOBx device and 41 with pMDI-OxStand. There were no baseline differences between the groups. Children treated with pMDI-SOBx had a lower hospitalization rate compared to those with pMDI-OxStand (9.3% vs. 26.8%, respectively, $p = 0.036$; absolute risk difference: −17.5% [95% CI: −33.6 to −1.4] and OR: 0.26 [95% CI: 0.08-0.91]). Additionally, a significant clinical improvement (pulmonary score) was observed from 90 min ($p < 0.001$), and an increase in SpO2 was observed from 60 min ($p < 0.001$) in the pMDI-SOBx group. Side effects were similar.

Conclusions

For the first time, bronchodilator administration using the SOBIstat-F® device was more effective than the conventional method in reducing hospitalizations and improving the clinical condition of children with severe asthma exacerbations.

KEYWORDS

Severe asthma; acute exacerbation; children; bronchodilators; oxygen; pressurized meter dose inhaler; SOBIstat-F

Funding

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Introduction

AQ5AQ7To treat moderate to severe exacerbations in children with asthma, short-acting beta-2-agonist bronchodilators (SABA), ipratropium bromide (IB), systemic corticosteroids, and magnesium sulfate IV are used in a stepwise manner, along with oxygen therapy (when oxygen saturation [SpO2] < 91%). The use of SABA and IB *via* a pressurized metered-dose inhaler (MDI) with a valved holding chamber (VHC), is more effective than their administration by a nebulizer, resulting in fewer hospitalizations, clinical improvement, and fewer adverse effects (1–7). Furthermore, for severe asthma exacerbations, the administration of SABA with IB by MDI and VHC together with the use of a nasal cannula for oxygen delivery was found to be more effective than the nebulized route in reducing hospital admissions (approximately 80% decrease), clinical score, and improving SpO2, in addition to less tachycardia (8). Severe asthma attacks also indicate an increased risk of future exacerbations and deterioration of lung function (9).

Since the onset of the COVID-19 pandemic in 2020, the American Thoracic Society, the European Respiratory Society, and other entities have recommended discontinuing nebulization due to concerns about environmental contamination and instead recommending MDI+VHC. However, this requires simultaneous management of VHC and oxygen therapy during bronchodilator administration to prevent hypoxemia (9–12). Oxygen administration *via* nasal cannula is limited to 3-4 L/min, and nebulized therapies to 6-8 L/min to generate aerosols <5 µm that reach the small airways.

Goldman P. and Newhouse M (13,14). developed the SOBIstat-F® device, which offers fast, simple, and economical variable-inspired fraction of oxygen (FiO2: 24-75%) and continuous oxygen delivery, independent of aerosol therapy. This would offer an advantage over the limited nebulizer therapy (6-

8 L/min) and the frequent suspension of oxygen therapy when using bronchodilators *via* VHC, because the oxygen mask and VHC must be applied intermittently. SOBIstat-F® was explicitly developed for drug administration by health personnel in the ED and in emergency medical services (ambulances, firefighters, outpatient clinics, primary care clinics, areas with limited medical resources, and first aid in schools, stadiums, etc.).

The SOBIstat-F® system has the following advantages: 1) It starts and completes treatment in approximately 60 s and 3 min, respectively (administering up to 12 doses of bronchodilators with intervals of ~~45-60~~ 15-20 seconds between puff); with the possibility of repeating this cycle every 15-20 min as needed. 2) Oxygen therapy is adjustable to an oxygen saturation target of 92-96%, approximately. Doses of bronchodilators by MDI with SOBIstat-F® can be initiated within the first 1 or 2 min of the patient's arrival in the ED by health personnel, such as the triage nurse or first aid personnel at the patient's location.

This study aimed to determine whether bronchodilator administration using the SOBIstat-F® device reduces hospitalization and improves clinical outcomes compared with conventional pMDI oxygen delivery in children with severe acute asthma.

Methods

This randomized, open-label, superiority clinical trial included children and adolescents aged 5 to 17 years with severe acute exacerbation of asthma (defined by a value on the Pulmonary Score [PS](15) scale ≥ 7 and/or who have a SpO2 < 91%) who attended in two pediatric EDs in Asuncion, Paraguay, between 2022 and 2024 and whose parents authorized their participation in the study, and adolescents over 12 years of age who have consented to their involvement. The exclusion criteria included clinical or radiological pneumonia, congenital pulmonary disease, cardiac malformations, chronic lung disease (such as bronchopulmonary dysplasia, cystic fibrosis, or post-infectious bronchiolitis obliterans), foreign body aspiration, neurological alteration, very severe asthma exacerbation (defined as SpO2 < 80%), or imminent cardiopulmonary failure, or indication for ~~of~~ mechanical ventilation. Demographic variables were collected for all eligible children.

A structured data collection sheet containing the following aspects was administered: age, sex, presence of comorbidities, symptoms of the crisis (cough, runny nose, fever, shortness of breath), clinical data (history of atopy, asthma in one of the parents, exposure to tobacco smoke, diagnosis of asthma, background medication), clinical signs on admission, 30 min, 60 min, 90 min, 120 min, and four hour (heart rate, respiratory rate, SpO2, PS score, tremor, tachycardia, vomiting) and follow-up variables (patient destination, admission to ward or pediatric intensive care unit [PICU], exacerbation relapses and/or adverse effects of medication in the following fifteen days after discharge

The PS (15) consists of clinical criteria with a score ranging from 0 to 9, where higher scores indicate worse asthma exacerbation (0-3: low; 4-6: moderate; 7-9: severe). The PS was assessed by attending pediatric emergency physicians at each participating site, who were familiar with the scale and routinely used it in clinical practice. PS was assessed after a brief stabilization period, during which the child was calm and not crying and breathing room air. PS and SpO_2 were recorded at predefined time points according to the study protocol. Oxygen therapy was never withheld for study purposes and was adjusted solely based on clinical need to maintain SpO_2 ≥92%. The respiratory rate was determined by observing chest movement for a full minute. The degree of use of accessory muscles was based on the degree of intercostal or subcostal retraction.

The randomization was performed using a computerized random number table, with allocation occurring after eligibility assessment. Allocation concealment was ensured by assigning patients only after enrollment. Randomization was not stratified by site or baseline severity. Patients were assigned to one of two groups:

Group 1 (MDI-SOBx): Children used the SOBIstat-F® device to receive salbutamol with IB (salbutamol 100 µg/puff and IB 20 µg/puff, Salbutral-AC, Cassara Lab®, Argentina) up to 8 puffs every 20 min for a maximum of 4 h (dosage: weight in kg/3, maximum dose in children 20 kg: 4 puffs, in those over 20 kg: 8 puffs), with oxygen flow up to 5 liters, to maintain a SpO2 equal to or greater than 92%. Then, 4 puffs were administered every 60 min for 2 h. Finally, 2 puffs every 2 h. If the patients improved, defined as a decrease of 2 PS points within the first 4 h of treatment initiation, the oxygen was gradually decreased until they transitioned to conventional therapy *via* nasal cannula

and achieved a mild PS score (0-3). The oxygen was suspended with a sustained SpO2 ≥ 92% and good respiratory dynamics.

Group 2 (MDI-OxStand): Children used MDI with VHC to receive salbutamol with IB (salbutamol 100 µg/puff and IB 20 µg/puff, Salbutral-AC, Cassara Lab®, Argentina) up to 8 puffs every 20 min for up to 4 h using a single device. And to maintain a SpO2 level of 9wereor higher, a nasal cannula or a combination of a nasal cannula and a face mask with oxygen flow rates up to 5 liters were used, depending on the patient's needs (11). Then, 4 puffs were administered every 60 min for 2 h, and finally, 2 puffs every 2 h. If the patient improved, defined as a 2-point decrease in the severity score within the first 4 h of treatment, oxygen gradually decreased until a mild PS score was achieved. Oxygen was discontinued with sustained SpO2 ≥ 92% and good respiratory dynamics.

Concomitant medication: Children in both groups received IV methylprednisolone 1 mg/kg and magnesium sulfate 50 mg/kg within the first hour of treatment. Early administration of IV magnesium sulfate as a second-line treatment was part of the standard care protocol for moderate-to-severe exacerbations in both participating emergency departments, in accordance with current evidence and recommendations (16–19).

In both groups, patients remained under observation in the ED until oxygen could be discontinued. From that moment on, the patients were discharged with salbutamol by VHC every 4 h, plus prednisone at 2 mg/kg/day, to be administered at home and monitored after 24 h in the ED. Patients were followed by telephone or face-to-face contact for 15 days.

Criteria for discharge to the home: If the patient was mild PS (0 to 3), had good respiratory mechanics, and SpO2 > 94% after 4 h without requiring new rescue medication.

Hospitalization criteria: Decisions were based on predefined clinical criteria: persistent moderate PS (4 to 6) or severe PS (>7) and/or sustained oxygen requirement as reflected in routine clinical practice. Admission decisions were made based on the patient's clinical condition and were not protocol-mandated by treatment assignment. Once the patient was hospitalized, the local established protocol treatment for inpatients with severe asthma was administered.

Relapse: It was considered the presence of an asthmatic exacerbation requiring rescue medication within 15 days of the initial consultation at the exact center where the patient was enrolled. If it occurred at a different center, it was confirmed by telephone.

Outcomes: The primary outcome was the need for hospitalization (ward or PICU) at the end (8 h.) or during treatment. The secondary outcomes were improvement in PS score, SpO2, respiratory rate and heart rate (at 30 min, 60 min, 90 min, 120 min, and 4 h), relapse rate of exacerbation in the following 15 days, and medication-related adverse effects (tachycardia, vomiting, tremor, and high blood pressure) during the trial. High blood pressure was defined as above the 90th percentile for age.

Device Description: The SOBIstat-F® device consists of a standard oxygenation mask used for cardiopulmonary resuscitation (CPR) from which the one-way valve is removed and replaced with the mouthpiece of the pediatric MDI for bronchodilator administration. To ensure aerosol delivery to the patient, an extender (X) was designed to span the distance between the mask opening (typically for a 22 mm one-way valve) and the patient's mouth. The X is shaped like the mouthpiece of the MDI, measures approximately 5 cm in length, and fits snugly into the MDI's mouthpiece. The posterior wall of the MDI abuts the X, and the X then extends about 2.5 cm and joins the space between the MDI and the patient's open mouth. It can be mobilized up or down vertically, allowing the aerosol shot to be directed parallel to the tongue and toward the oropharynx during inhalation. The incoming oxygen flows around the X and therefore does not disperse the aerosol. There is ample space for both X and oxygen to enter the mouth. There is a flap protruding from the lower tip of X (see Figures 1 and 2), which is designed to gently press against the lower lip to align the spray plume toward the posterior oropharynx, parallel to the tongue. The inhalation/exhalation channel between the MDI canister and dispenser features a low-resistance electrostatic filter to prevent viral, bacterial, fungal, or sensitizing environmental contamination. With a competent mask seal on the patient's face, SOBIstat-F® is a closed system. The SOBIstat-F® devices were designed and assembled in the US and donated to the hospital by the designers. Therefore, the ED authorities requested that the devices be used to conduct an investigation. More details of the SOBIstat-F®

device and instructions for their utilization are listed in this link:

https://drive.google.com/file/d/1Czi1tNISxaFqkEzk8__n8Vz5LcQshnUZ/view?usp=sharing.

Figure 1. a. SOBIstat-F® device with filter. b. SOBIstat-F® device with MDI.

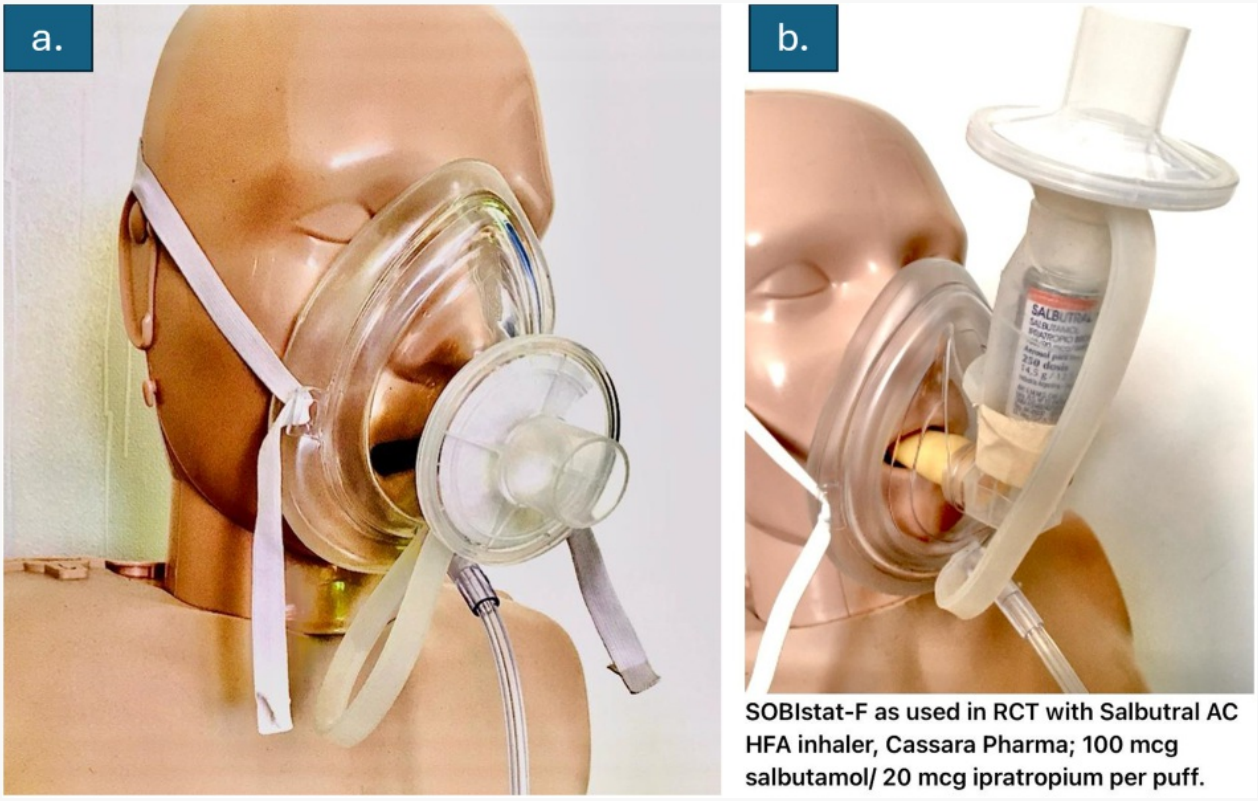
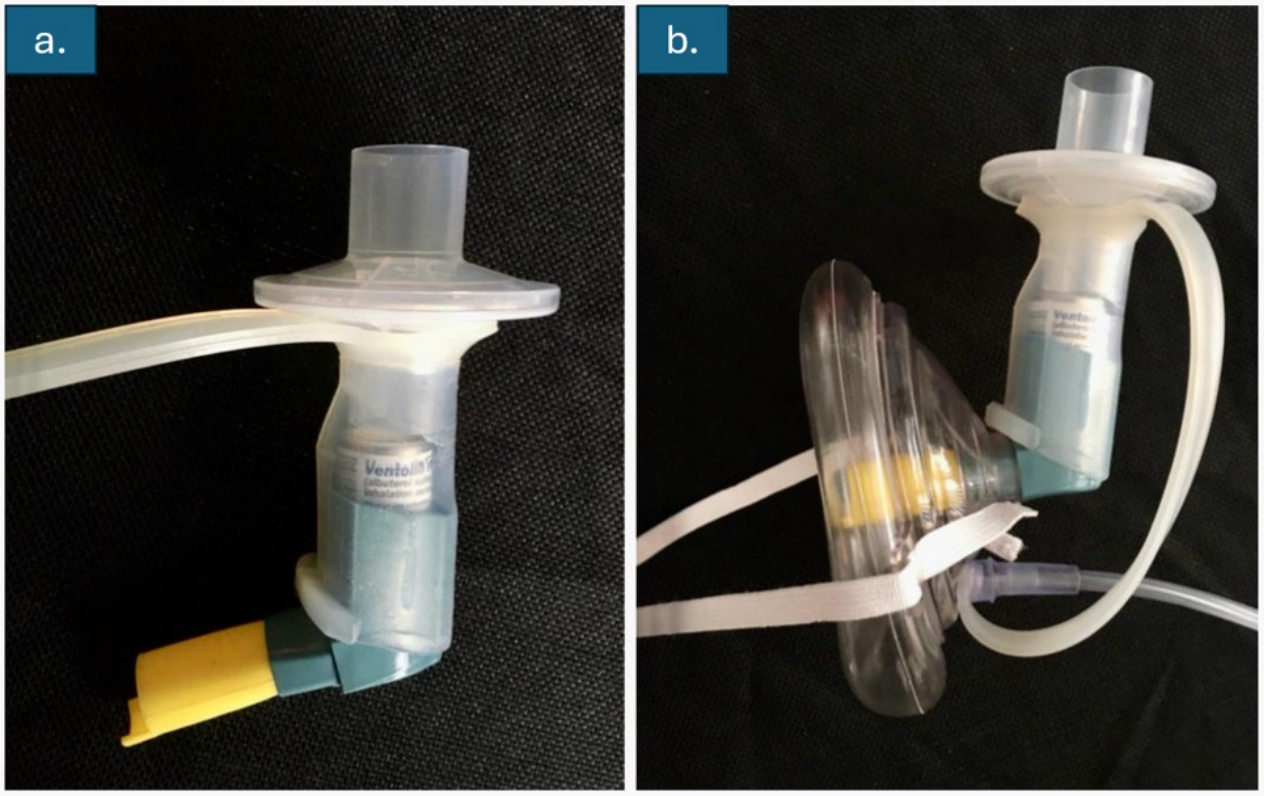


Figure 2. a. MDI is inserted into the device with a mouthpiece. b. Lateral view.



Ethical issues

The study adhered to the ethical principles of clinical research outlined in the Declaration of Helsinki. The research committee and the institutional ethics committee have approved it. The use of an experimental device is justified because all patients received the same medication indicated for treating asthma attacks; the only difference is the route of administration and the oxygen delivery device. Each parent or guardian was verbally informed, and written informed consent was requested ~~obtained~~. For adolescents aged 12 or older, informed consent will also be requested. The study was completely free. The data obtained in this research are handled confidentially, preserving the patients' identities.

Statistical analysis

To estimate the sample size, Epidat 4.2 software was used. It was calculated assuming a hospitalization rate of up to 70% in children with severe asthma exacerbations. To detect a clinically relevant absolute reduction of 30% in hospitalization rate between groups, with a two-sided alpha of 0.05 and 80% power, a minimum of 40 patients per group was required

The data were recorded in an electronic spreadsheet using Microsoft Excel 365 and analyzed with Epi-Info v. 7 (CDC, Atlanta, GA) and IBM SPSS Statistics (version 22). Categorical variables are presented as frequencies and percentages. Continuous variables with a normal distribution are reported as the average and standard deviation, while those without a normal distribution are reported as the median and interquartile range. To evaluate the differences between the MDI-SOBx and MDI-OxStand groups, the Chi-square test was used for categorical variables. For continuous variables with a normal distribution, the Student's T-test was used; otherwise, the Mann-Whitney U test was used. Kaplan–Meier curves were used for an exploratory visualization of time to clinical improvement.

Hospitalization rates (primary outcome) were compared between groups under a superiority framework, using intention-to-treat analysis. Effect sizes were reported as absolute risk differences (with 95% confidence interval [95%CI]) and odds ratios (OR).

Longitudinal analysis: repeated measurements of SpO2 and PS over time were analyzed using linear mixed-effects models to account for within-subject correlation. Treatment group, time, and their interaction were included as fixed effects, and a random intercept for each participant was specified. Time was treated as a categorical factor corresponding to predefined assessment time points. A significant treatment-by-time interaction was interpreted as evidence of different clinical trajectories between groups.

Results

A total of 91 patients were recruited, of whom 7 were excluded: 3 refused to sign the informed consent, 2 due to SpO2 < 80% requiring oxygen *via* a high-flow nasal cannula (HFNC), and 2 due to complicated pneumonia with an effusion (Figure 3). In the end, 84 patients were included in the study: 43 in group 1 (MDI-SOBIx), and 41 in group 2 (MDI-OxStand). The groups were comparable

in all demographic and clinical variables at baseline, except for cough, which was significantly more frequent in the MDI-SOBIx group (100% vs. 85.4%, $p = 0.03$). The severity of the crisis, measured by PS and SpO2, was similar between the groups (Table 1).

Figure 3. Flow chart of the recruitment and randomization process.

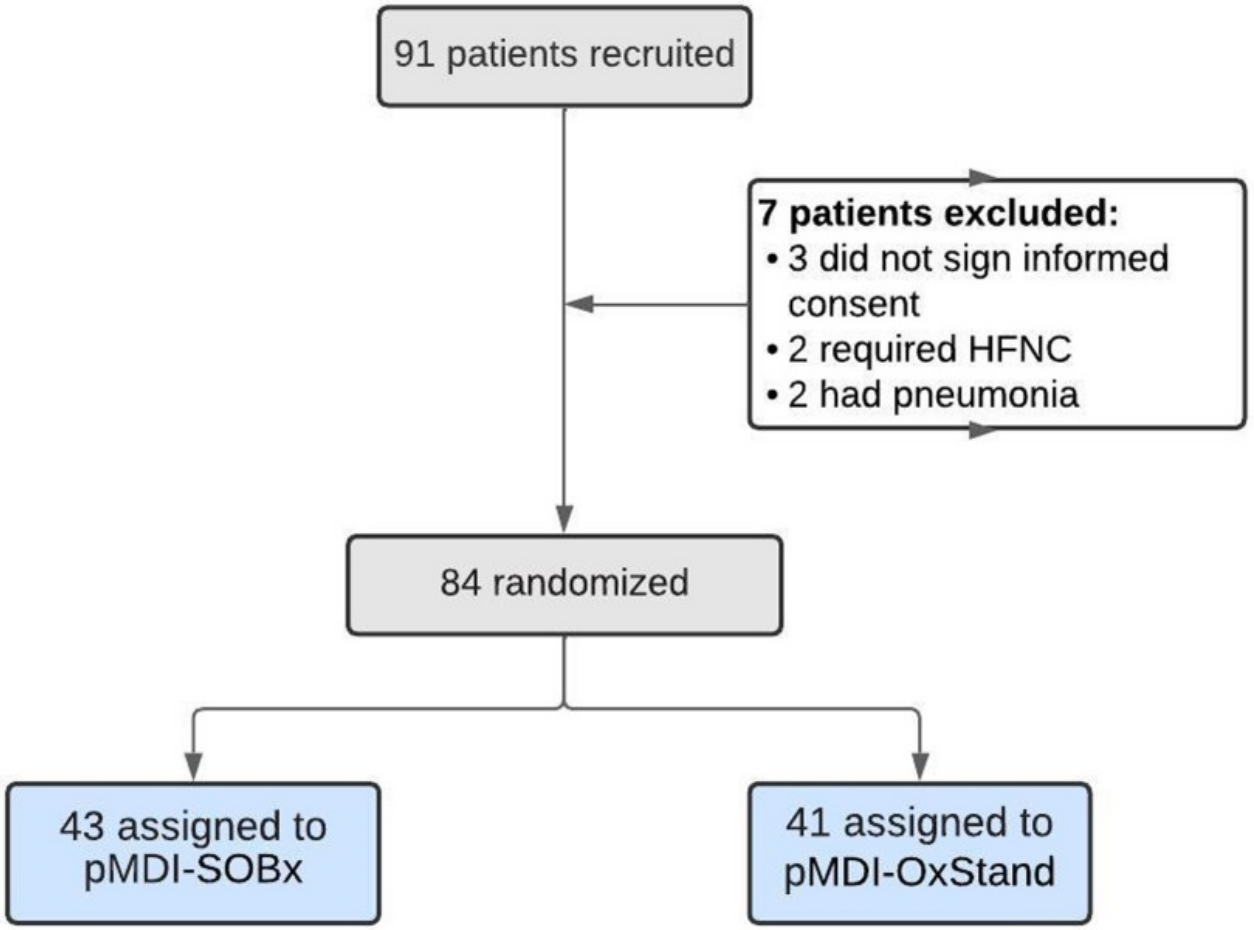


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Table 1. Demographic characteristics of patients with severe asthma exacerbation

treated with MDI-SOBx or MDI-OxStand (*n* = 84).

Characteristics	MDI-SOBx n: 43	MDI-OxStand n: 41	p value
Age (years)	7.0 [2.0]	6.0 [2.0]	0.33
Male	16 (37.2)	23 (56.1)	0.08
Cough	43 (100)	35 (85.4)	**0.029**
Rhinorrhoea	25 (58.1)	17 (41.5)	0.13
Fever	13 (30.2)	9 (22.0)	0.39
Shortness of breath	42 (97.7)	41 (100)	1.0
Atopic dermatitis	27 (65.9)	33 (80.5)	0.14
Asthma in some of the parents	18 (42.9)	13 (31.7)	0.29
Tobacco exposure	15 (35.7)	16 (39.0)	0.76
Asthma diagnosis	22 (51.2)	25 (61)	0.36
Inhaled corticosteroids use	30 (69.8)	33 (80.5)	0.26

Data are expressed as median [interquartile amplitude], or number (%).

Children from the MDI-SOBIx group had a significantly lower hospitalization rate (primary outcome) than those in the MDI-OxStand group (9.3% vs. 26.8%, respectively, $p = 0.036$, absolute risk difference of −17.5% [95% CI: −33.6 to −1.4] and OR: 0.26 [95% CI: 0.08-0.91]), Table 2. All hospitalizations occurred in the pediatric ward, and none in the PICU.

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Table 2. Comparison of study groups in patients with severe asthmatic exacerbation treated with pMDI-SOBx or pMDI-OxStand. (*n* = 84).

	pMDI-SOBx n: 43	pMDI-OxStand n: 41	p-value
Stay at ED (hrs.)	24.7 ± 1.0	25.0 ± 1.0	0.132
Primary Outcome:			
Hospitalization	4 (9.3)	11 (26.8)	**0.036***
Secondary outcomes:			
Adverse effects	1 (2.3)	2 (4.8)	0.52

Relapses during the first 15 days	2 (4.6)	5 (12.1)	0.21

Data are presented as mean ± SD or number (%) as appropriate.

*Absolute risk difference: −17.5% [95% CI: −33.6 to −1.4]; and OR: 0.26 [95% CI: 0.08-0.91.

Table 3 shows the follow-up of the clinical signs from admission to 8 h post-treatment. Children in the MDI-SOBIx group showed significant improvements in PS from 90 min (Figure 4) and SpO2 from 60 min (Figure 5) compared to those in the MDI-OxStand group. The other variables did not show significant differences between the two groups. In linear mixed-effects models accounting for within-subject correlation, both SpO2 and PS showed significant main effects of treatment and time, as well as significant treatment-by-time interactions (all $p < 0.001$), indicating distinct clinical trajectories between treatment groups.

Figure 4. Follow-up of the Pulmonary Score (PS) during the management of severe asthma attacks according to treatment groups.

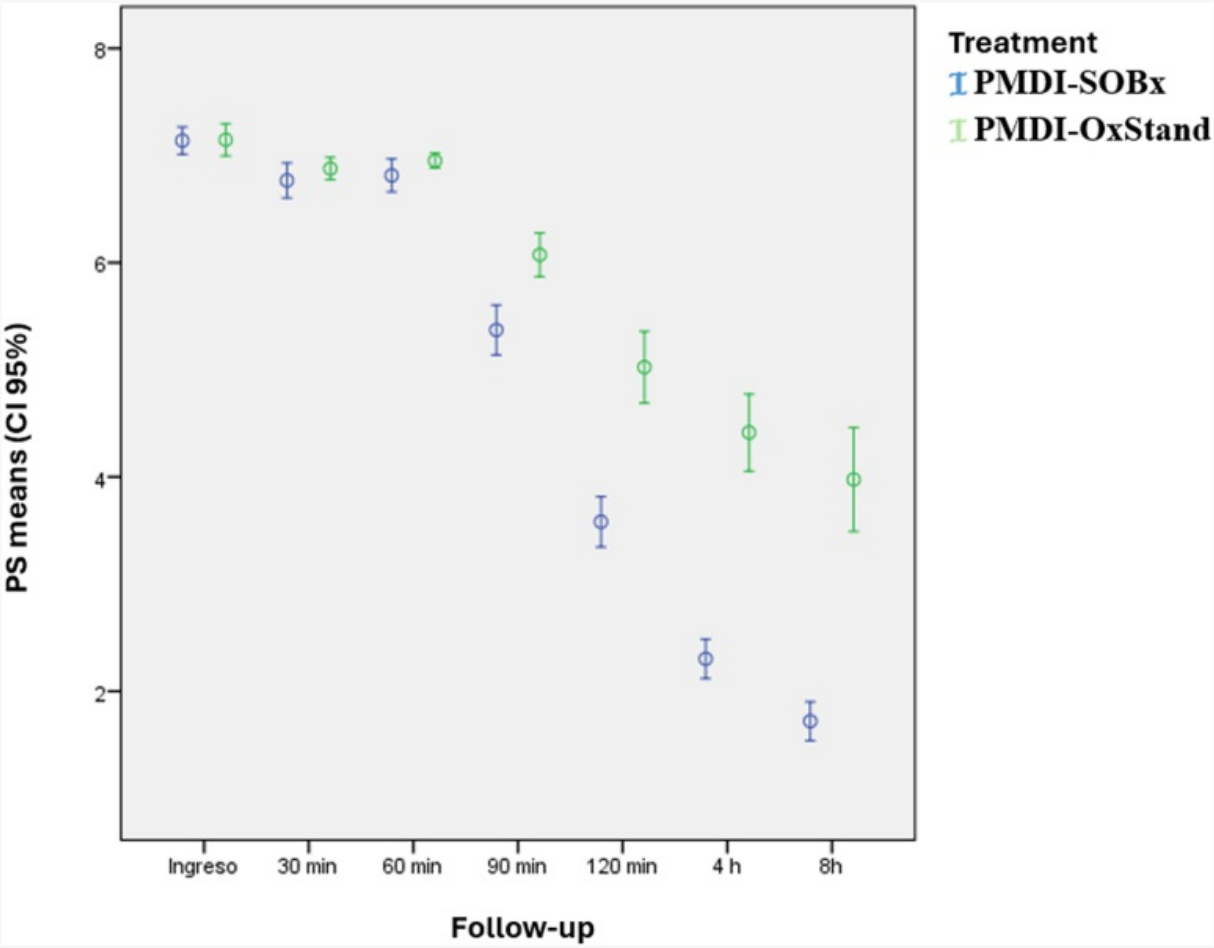

Figure 5. Evolution of oxygen saturation (SpO2) during the management of severe asthma attacks according to treatment groups.

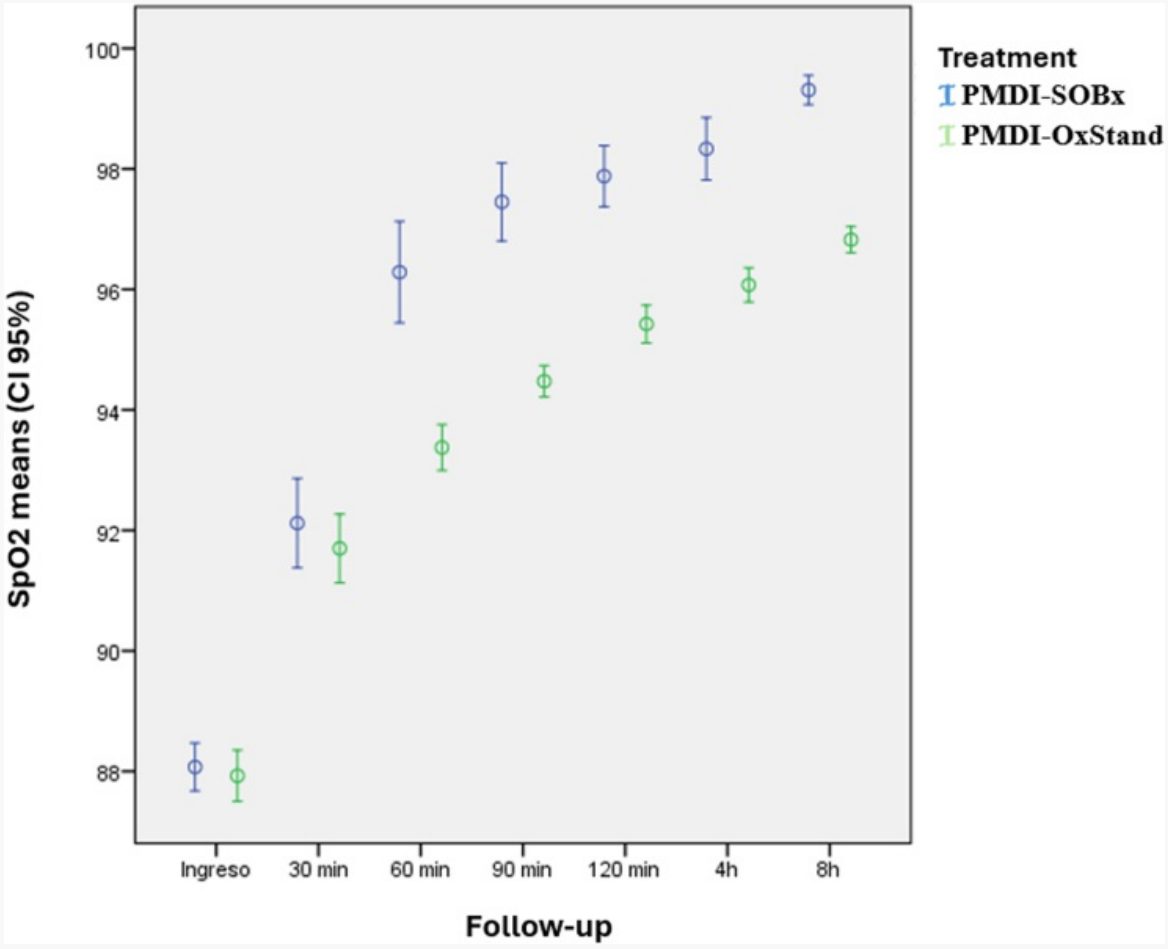

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Table 3. Follow-up of clinical signs and side effects of patients with severe asthmatic exacerbation treated with MDI-SOBx or MDI-OxStand. (*n* = 84).

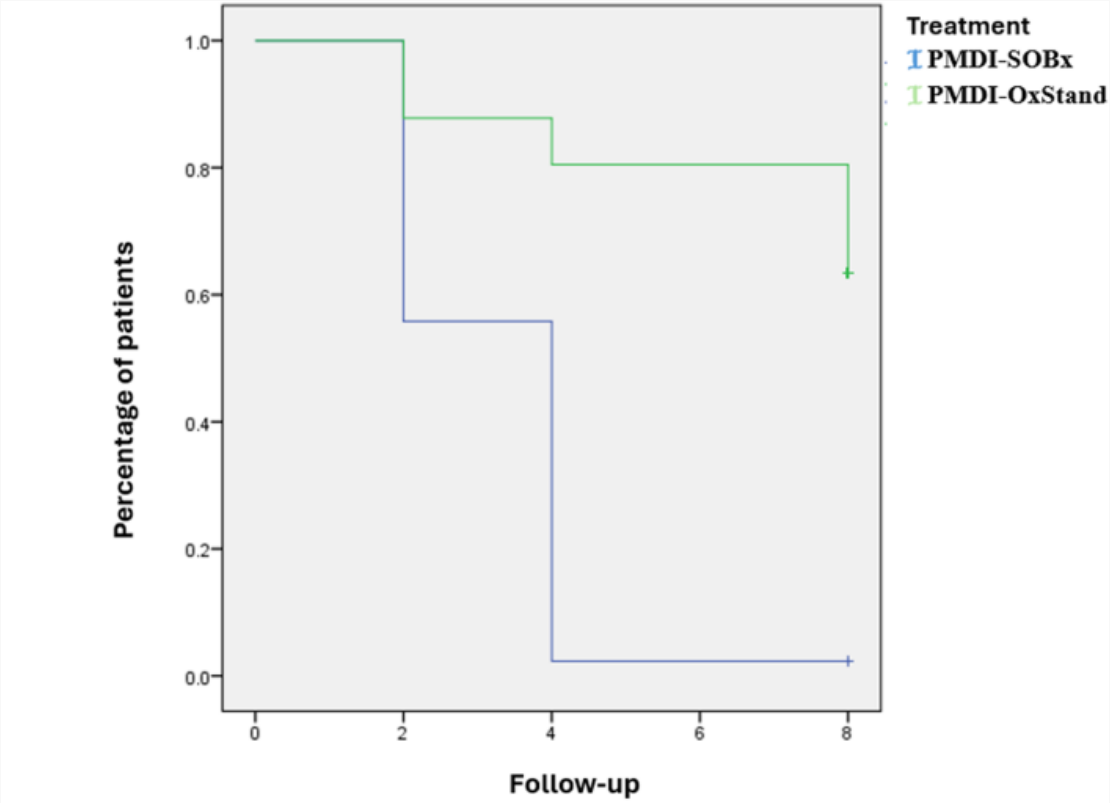
	pMDI-SOBx *n* = 43	pMDI-OxStand *n* = 41	p-value

Clinical signs:			
Pulmonary Score (PS)			
At admission	7.14 ± 0.413	7.15 ± 0.478	0.94
30 min	6.77 ± 0.443	6.88 ± 0.527	0.26
60 min	6.81 ± 0.500	6.95 ± 0.218	0.11
90 min	5.37 ± 0.757	6.07 ± 0.648	**<0.001**
120 min	3.58 ± 0.763	5.02 ± 1.060	**<0.001**
4 h	2.30 ± 0.599	4.41 ± 1.140	**<0.001**
8 h	1.72 ± 0.591	3.98 ± 1.541	**<0.001**
SpO2			
At admission	88.09 ± 1.265	87.93 ± 1.311	0.56
30 min	92.14 ± 2.356	92.49 ± 2.580	0.52
60 min	96.26 ± 2.682	94.76 ± 2.267	**0.007**
90 min	97.30 ± 2.270	95.71 ± 2.052	**0.001**
120 min	97.74 ± 1.840	96.37 ± 2.118	**0.002**
4 h	98.21 ± 1.833	96.73 ± 1.803	**<0.001**
8 h	99.09 ± 1.211	95.80 ± 1.978	**<0.001**
Heart rate			
At admission	129.72 ± 24.84	127.59 ± 17.23	0.65
30 min	134.05 ± 16.82	131.34 ± 16.13	0.45
60 min	129.58 ± 16.92	134.90 ± 15.26	0.13
90 min	131.23 ± 17.53	135.29 ± 16.22	0.27
120 min	123.58 ± 15.70	128.17 ± 16.59	0.20
4 h	125.23 ± 16.90	127.00 ± 16.83	0.63
8 h	118.07 ± 17.19	120.12 ± 17.59	0.59
Respiratory rate			
At admission	40.07 ± 10.15	36.20 ± 7.64	0.05
30 min	34.49 ± 2.92	33.59 ± 4.23	0.28
60 min	32.02 ± 8.03	33.49 ± 8.07	0.41
90 min	29.26 ± 9.75	31.78 ± 8.49	0.21
120 min	29.44 ± 7.33	30.27 ± 7.82	0.62
4 h	28.74 ± 9.01	28.83 ± 6.88	0.96
8 h	25.02 ± 6.81	28.40 ± 7.22	**0.032**
Side Effects:			
Tremors			
At admission	4 (9.3%)	0	0.08

30 min	1 (2.3%)	1 (2.3%)	1.00
60 min	4 (9.3%)	3 (7.3%)	1.00
90 min	5 (11.6%)	4 (9.8%)	1.00
120 min	6 (11.6%)	5 (9.8%)	1.00
4 h	2 (4.7%)	3 (7.3%)	0.96
8 h	0	0	–
Vomiting			
At admission	9 (20.9%)	8 (19.5%)	
30 min	1 (2.3%)	2 (2.3%)	0.97
60 min	0	0	–
90 min	1 (2.3%)	2 (4.9%)	0.97
120 min	1 (2.3%)	0	–
4 h	2 (4.7%)	1 (2.3%)	1.00
8 h	1 (2.3%)	1 (2.3%)	1.00
High blood pressure			
At admission	5 (11.6%)	1 (2.3%)	0.23
30 min	4 (9.3%)	3 (7.3%)	1.00
60 min	2 (4.7%)	3 (7.3%)	0.96
90 min	0	2 (4.9%)	0.45
120 min	3 (7.0%)	1 (2.3%)	0.64
4 h	1 (2.3%)	2 (4.9%)	0.97
8 h	0	0	–
Data are presented as mean ± SD or number (%) as appropriate.			

No significant difference was observed between groups ($p = 0.132$). Also, no differences between groups in relapse during the first 15 days after intervention and in side effects were observed (Table 3). The survival analysis revealed that children in the MDI-SOBIx group were significantly less likely to experience PS > 4 (moderate-to-severe asthma exacerbations) than those in the MDI-OxStand group (Figure 6).

Figure 6. Survival analysis of pulmonary score < 4 (p 0.0001).



Time (hours)	0	1	2	4	8
PMDI-SOBx	43	43	4	1	0
PMDI-OxStand	41	41	30	23	21

Discussion

The present study evaluated, for the first time, the effectiveness of the new SOBIstat-F® device compared to the conventional device for administering bronchodilator in children with severe acute exacerbations of asthma. The results indicate that the use of bronchodilators (salbutamol with IB) with the SOBIstat-F® device was superior to the use of the same bronchodilators with a conventional device (MDI with oxygen by cannula or mask) in terms of significantly lower need for hospitalizations, and improvement in PS from 90 min and SpO2 from 60 min. This suggests that the

SOBIstat-F® device would enable more efficient, uniform drug delivery to the airways, thereby improving oxygen delivery and facilitating a quicker recovery of symptoms. The side effects were similar between groups.

It is known that the delivery of bronchodilators in acute asthma attacks is more efficient ~~through aerosol~~ from ~~through~~ MDI aerosol~~s~~ compared to nebulization aerosol, obtaining better clinical outcomes (8,17,18), which is why it is interesting to design new devices that can favor the administration of medication, without implying variations in oxygen delivery, it is in this sense that the SOBIstat-F® emerges as a useful, comfortable and efficient option.

An explanation of why, in our study, patients receiving bronchodilators with the SOBIstat-F® device had better results than those with the conventional device (MDI-VHC with oxygen by cannula or mask) is the speed of administering the equivalent therapeutic dose of bronchodilators, which is completed in significantly less time than the MDI-VHC with O2 from nasal cannula (13,14). Previous studies have demonstrated that with SOBIstat-F®, the time from initiation of the primary albuterol (salbutamol) series to completion is 3 min or less (13,14). The worse the case of bronchospasm, the more this ~~these~~ matters. While the aerosol mass per puff from SOBIstat-F® was ~1/3 that of the inhaler, the pharmacokinetic (PK) results were in similar ranges. A previous study found a similar PK: the Tmax plasma albuterol (salbutamol) drawn 25 min post-dose using SOBIstat-F® was 3.6 ng/ml, compared to 3.0 ng/ml with MDI alone (13). Just as with the VHC, the SOBIstat-F® mouthpiece extender eliminates much of the larger peripheral non-respirable albuterol particles from the inhaler plume. As such, this also reduces beta-adrenergic side effects, such as tachycardia/tremor, which are primarily caused by the oral absorption of larger, non-respirable particles (13,14). This could explain why we did not find more tachycardia and tremors with SOBIstat-F® than with the conventional device. When comparing certain attributes with the SOBIstat-F®, its simplicity, ergonomic design, low cost, and ease of use are also advantages compared to the control MDI-VHC with a nasal canula for O2. The ease of handling and perceived efficiency of the device may have contributed to better patient adherence to treatment, a key factor in the successful management of

asthma attacks in children. This highlights the importance of considering not only clinical efficacy, but also user experience when choosing medical devices for this population.

Other medications and devices that are adjuvant alternatives for severe exacerbations are described in the literature in the second line of treatment and during hospitalization, such as IV magnesium sulfate (16), IV aminophylline and IV salbutamol (20,21), heliox-driven nebulization (22), high-flow nasal cannula (23), or noninvasive ventilation (24).

In our study, 75% of patients were treated with inhaled corticosteroids, although curiously, 44% of the children who presented to the ED did not have a previous diagnosis of asthma. These findings are consistent with a recent study conducted in the US, in a population of 362 children with asthma attacks treated in the ED, where up to 36% of them did not have an asthma diagnosis (25). This may be because, in many cases, physicians expect to have altered lung function tests to make the diagnosis of asthma or prefer not to mention that word because of the social stigma it can bring, or that parents do not want to accept this chronic condition of asthma.

Among the study's strengths is that it is the first multicenter clinical trial to demonstrate the effectiveness of this new device (SOBIstat-F®) in children. However, the study has some limitations. First, blinding was not feasible because the intervention device is inherently different from standard treatment, making treatment allocation apparent to both clinicians and patients. This open-label design may have introduced performance and assessment bias. Although the PS assessment followed predefined criteria and reflected routine clinical practice, some subjectivity is unavoidable, and hospitalization decisions partly relied on an unblinded clinical score. Second, a formal subgroup analysis by center was not feasible due to the limited sample size, and this should be taken into account when interpreting the results. Third, IV magnesium sulfate was administered early and broadly to patients in both groups as part of standard care at the participating sites. While this approach is supported by current evidence (19), it may limit the generalizability of the findings to settings where magnesium sulfate is used more selectively. Fourth, since SOBIstat-F® is a reusable device that costs around US$78 in the US, cost-analysis studies are needed to assess its impact. Also, cost-effective studies that incorporate longer follow-up periods than traditional methods are

necessary. Fifth, it is also important to evaluate the feasibility of bronchodilator administration *via* MDI with SOBIstat-F® treatment in a broader clinical setting, including inpatients, and to conduct studies comparing SOBIstat-F® with newer devices, such as breath-triggered nebulizers.

Conclusion

In conclusion, bronchodilator *via* MDI administration with oxygen using the SOBIstat-F® device was more effective than conventional devices (bronchodilator *via* MDI-VHC and oxygen *via* nasal cannula or mask) in reducing hospitalizations and improving clinical outcomes (score and SpO2) in children with severe acute asthma exacerbations at the ED. However, further studies are required to confirm these findings in a broader context and to assess the benefit of incorporating bronchodilators *via* MDI with the SOBIstat-F® device into daily clinical practice.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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