High-Flow Nasal Cannula in Pediatric Critical Asthma

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BACKGROUND: High-flow nasal cannula (HFNC) has been used in the treatment of pediatric asthma, although high-quality data comparing HFNC to aerosol mask nebulizer are lacking. We hypothesized that HFNC would perform similarly to the aerosol mask for meaningful clinical outcomes in children with critical asthma. METHODS: We retrospectively reviewed the medical records of children with critical asthma (age 2–17 y) with a modified pulmonary index score (MPIS) ≥ 8 admitted to our pediatric ICU as part of a quality improvement project. Patients were managed with our MPIS-based, respiratory therapist-driven protocol. Subjects were divided into 2 cohorts by initial respiratory support: HFNC or aerosol mask. Data included demographics, initial respiratory support, and MPIS over time. Primary outcome was hospital length of stay (LOS). Secondary outcome was difference in MPIS over time. RESULTS: We included 171 subjects, with 104 in the HFNC group and 67 in the aerosol mask group. Median (interquartile range [IQR]) age was lower in the HFNC group (5 [IQR 4–9] vs 7 [IQR 5–10] y, $P = .006$)], while other demographic characteristics were similar. Initial MPIS was similar between HFNC and aerosol mask groups (11 [IQR 9–12] vs 10 [IQR 9–12], $P = .15$). There were no significant differences for hospital LOS (2.9 [IQR 2.1–3.9] vs 3.0 [IQR 2.3–4.4] d, $P = .47$), pediatric ICU LOS (1.9 [IQR 1.4–2.8] vs 1.8 [IQR 1.5–3.0] d, $P = .92$), or time to MPIS < 6 (1.0 [IQR 0.6–1.6] vs 1.3 [IQR 0.8–1.9) d, $P = .09$) between the HFNC and aerosol mask groups, respectively. Median time on continuous albuterol was shorter in the HFNC group compared to the aerosol mask group (1.0 [IQR 0.7–1.8] vs 1.5 [IQR 0.9–2.3] d, $P = .048$). Of note, 16 (24%) subjects in the aerosol mask group were eventually treated with HFNC. Use of a helium-oxygen mixture and noninvasive ventilation was similar between groups. CONCLUSIONS: HFNC performed similarly to aerosol mask in pediatric patients with critical asthma. *Key words: asthma; status asthmaticus; high-flow nasal cannula; pediatrics; pediatric critical care; intensive care.* [Respir Care 2021;66(8):1240–1246. © 2021 Daedalus Enterprises]

Introduction

Critical asthma is a common reason for admission to the pediatric ICU (PICU).[1] Patients with critical asthma often require supplemental oxygen and continuous bronchodilator therapy, which have historically been delivered via aerosol mask.[2] Although high-quality data are lacking, high-flow nasal cannula (HFNC) use has greatly increased in recent years for a variety of respiratory illnesses, including pediatric asthma.[3] HFNC has been shown to have physiologic benefits in other patient populations and may be beneficial to patients

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with asthma, including washout of anatomic dead space, minimal levels of PEEP, more consistent oxygen delivery, and conditioning of inspired gases.[4]

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One concern regarding HFNC use in patients with acute asthma is that it could affect aerosolized drug delivery; in vitro studies have reported that aerosol deposition is affected by cannula size, type of nebulizer, and HFNC flow.[5] These studies indicate that higher HFNC flows result in decreased aerosol deposition in vitro. In contrast, a recent bench model of continuous aerosol delivery found higher aerosol deposition with HFNC compared to aerosol mask.[6] Although bench studies indicate aerosol is delivered to the airway during HFNC, in vivo studies in children are limited. Studies in adult subjects have shown physiologic responses to bronchodilators delivered via HFNC, although no differences in outcomes were noted when compared to conventional oxygen therapy.[7,8] Most recently, HFNC was found to be an effective aerosol delivery method for bronchodilators under low-flow conditions (ie, $\leq$ 4 L/min) in a small cohort of children, but HFNC did not increase patient comfort and increased therapist time at the bedside.[9] Half of the subjects in that study were admitted for asthma, and flow was decreased during treatments to maximize aerosol deposition. Studies evaluating patient-oriented outcomes for HFNC use in pediatric asthma have yielded conflicting results.[10-14]

At our institution, in-patient pediatric asthma is managed via a respiratory therapist-driven protocol that has been associated with decreased length of stay (LOS) in the hospital for patients admitted to our PICU.[15] In our PICU, HFNC use in acute asthma has increased due to clinician preference and the perception of improved patient comfort because HFNC allows patients to eat, drink, and be more active while also providing an alternative for patients intolerant of an aerosol face mask. We hypothesized that there would be no difference in hospital LOS for those treated with HFNC compared to aerosol mask.

QUICK LOOK

Current knowledge

High-flow nasal cannula (HFNC) is commonly used for respiratory distress in pediatric patients, including those with asthma. The utility of HFNC in pediatric asthma is unclear as conflicting data have been published to date.

What this paper contributes to our knowledge

In this retrospective cohort study, HFNC performed similarly to aerosol face mask. Time on continuous albuterol was shorter for HFNC; however, there was no difference for time spent in the hospital or in the pediatric ICU. The modified pulmonary index scores were similar in both groups, and these scores improved at a similar rate.

Methods

Following institutional review board approval, we retrospectively reviewed the medical records of children with critical asthma age 2–17 y with a modified pulmonary index score (MPIS) $\geq$ 8 admitted to our PICU between June 2014 and March 2020. Patients are managed with our MPIS-based, respiratory therapist-driven protocol, wherein bronchodilator therapy intensity can be decreased or increased by respiratory therapists on the basis of the MPIS, and all subjects were initially placed on continuous albuterol at a dose of 20 mg/h.[15,16] Once albuterol therapy was decreased to intermittent dosing, the medication was administered every 2 h via nebulizer or pressurized metered-dose inhaler at a dosage of 8 puffs or 5 mg for subjects $>$ 15 kg, or 4 puffs or 2.5 mg for subjects $<$ 15 kg. Once the MPIS score was $<$ 6, albuterol was decreased to every 3 h (at same dosage as prior), then to every 4 h (4 puffs or 2.5 mg for subjects $>$ 15 kg, or 2 puffs or 2.5 mg for subjects $<$ 15 kg). We chose an inclusion MPIS cutoff of 8 because prior data from our group indicated an increase in hospital LOS when MPIS was $\geq$ 8 compared to $<$ 8.[17] For the aerosol mask, we used the HOPE Nebulizer (B&B Medical Technologies, Carlsbad, California) powered by an air/oxygen blender to deliver albuterol and O_2 to the subjects with F_{IO_2} analyzed continuously.[18] For HFNC, we selected Optiflow or Optiflow Jr circuits (Fisher and Paykel, Auckland, New Zealand) and nasal prongs based on subject age and nostril size. The Aerogen Pro-X (Aerogen, Galway, Ireland) vibrating mesh nebulizer was inserted on the dry side of the HFNC heated humidifier, and albuterol was delivered continuously via syringe pump at a concentration of 5 mg/mL. HFNC and noninvasive ventilation (NIV) use are independent of the asthma pathway and were employed at the discretion of the clinical team. All patients with critical asthma admitted to the PICU receive systemic corticosteroids every 6 h. Intravenous magnesium and heliox (ie, helium-oxygen mixture) are considered if the MPIS is $\geq$ 12. HFNC flow and F_{IO_2} were initially titrated on the basis of the subject's inspiratory flow demand and to keep $S_{pO_2} > 92\%$ per our pediatric HFNC use policy. Further adjustments to the HFNC were guided by the clinical team and not by protocol.

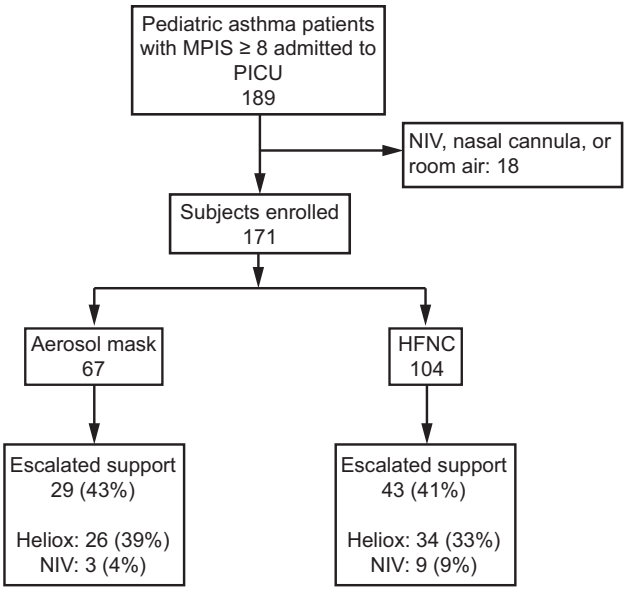

Fig. 1. Flow chart. MPIS = modified pulmonary index score; PICU = pediatric ICU; NIV = noninvasive ventilation; HFNC = high-flow nasal cannula; heliox = helium-oxygen mixture.

We retrospectively collected data on subject age, weight, gender, home medications, medical history, route of admission, initial PICU respiratory support, initial PICU vital signs, MPIS over time, and use of NIV or heliox. Subjects were divided into 2 cohorts based on initial respiratory support: HFNC or aerosol mask. We excluded patients who received NIV, supplemental oxygen via standard nasal cannula, or no respiratory support. PICU LOS, hospital LOS, time on continuous albuterol, and MPIS over time were compared between groups. The primary outcome was hospital LOS. Secondary outcomes were difference in MPIS over time, PICU LOS, and time on continuous albuterol. To evaluate the effect of flow, we compared subjects who received a HFNC flow ≥ 0.5 L/kg/min to those with flows < 0.5 L/kg/min. Data were analyzed with SPSS 25 (IBM, Armonk, New York) and Stata (StataCorp, College Station, Texas). We utilized the chi-square test to compare categorical data and the Mann-Whitney rank-sum test to compare continuous data. Treatment effects models with propensity score matching were used to estimate the average treatment effect of HFNC on hospital LOS ≥ 3 d and achieving an MPIS < 6 at 6, 12, and 24 h after initiation. Statistical significance was set at alpha < 0.05.

Results

We identified a total of 189 patients with an MPIS ≥ 8 upon admission to the PICU. Of these, 18 were excluded based on their initial respiratory support (NIV, standard nasal cannula, or room air), leaving 171 total subjects, consisting of 67 in the aerosol mask group and 104 in the HFNC group (Fig. 1).

There were no differences between groups for gender, weight, home medications, medical history, cause of exacerbation, route of admission, or initial PICU vital signs. Median (interquartile range [IQR]) age for HFNC subjects was 5 (IQR 4–9) y versus 7 (IQR 5–10) y for the aerosol mask group ($P = .006$). Data on flow were available for 103 of 104 subjects in the HFNC group; median (IQR) initial HFNC flow was 10 (IQR 10–15) L/min or 0.5 (IQR 0.3–0.7) L/kg/min. The median (IQR) maximum flow during HFNC was 15 (IQR 10–20) L/min or 0.6 (IQR 0.4–0.9) L/kg/min. Median (IQR) initial MPIS was similar between HFNC and aerosol mask groups (11 [IQR 9–12] vs 10 [IQR 9–12], $P = .15$) (Table 1).

In unadjusted analysis, there were no differences between groups for median (IQR) hospital LOS (2.9 [IQR 2.1–3.9] vs 3.0 [IQR 2.3–4.4] d, $P = .47$), PICU LOS (1.9 [IQR 1.4–2.8] vs 1.8 [IQR 1.5–3.0] d, $P = .92$) or time to MPIS < 6 (1.0 [IQR 0.6–1.6] vs 1.3 [IQR 0.8–1.9] d, $P = .09$). Median (IQR) time on continuous albuterol was shorter in the HFNC group (1.0 [IQR 0.7–1.8] vs 1.5 [IQR 0.9–2.3] d, $P = .048$). Of note, 16 (24%) subjects in the aerosol mask group were eventually treated with HFNC. There were no differences between groups in the need for escalation to heliox or NIV (43% vs 41%, $P = .93$). Results are summarized in Table 2 and Figure 2.

Treatment effect models revealed no differences for hospital LOS ≥ 3 d versus < 3 d (risk difference 5.1 [95% CI –10.7 to 20.8], $P = .53$), MPIS < 6 at 6 h after PICU admission (risk difference 2.2 [95% CI –8.4 to 12.9], $P = .68$), MPIS < 6 at 12 h after PICU admission (risk difference –9.0 [95% CI –22.9 to 5.0], $P = .21$), or MPIS < 6 at 24 h after PICU admission (risk difference –0.6 [95% CI –18.5 to 17.4], $P = .95$).

In the HFNC group, there were no differences between those who received flows < 0.50 L/kg/min compared to ≥ 0.50 L/kg/min for median (IQR) hospital LOS (2.7 [IQR 1.9–3.9] vs 3.1 [IQR 2.6–3.9] d, $P = .17$), PICU LOS (1.9 [IQR 1.4–3.0] vs 2.0 [IQR 1.6–2.7] d, $P = .70$), or time to MPIS < 6 (1.0 [IQR 0.6–1.7] vs 1.0 [IQR 0.7–1.6] d, $P = .55$). S_{pO_2} was higher in the ≥ 0.50 L/kg/min group, but no other differences were observed. Results are summarized in the supplementary materials (available at http://www.rcjournal.com).

Discussion

In our study, HFNC performed similarly to aerosol mask in terms of hospital LOS, PICU LOS, and MPIS over time. Subjects in the HFNC group were younger, which could have been due to clinician preference (ie, based on an assumption that younger children would be less tolerant of a face mask and more tolerant of HFNC) or to true patient

Table 1. Subject Demographics

	Aerosol Mask ($n = 67$)	HFNC ($n = 104$)	P
Age, y	7 (5–10)	5 (4–9)	.006
Female	29 (43)	53 (51)	.33
Weight, kg	29.8 ± 15.5	26.6 ± 15.6	.19
Home medications			
Short-acting β_2 agonist	55 (82)	89 (86)	.54
Inhaled corticosteroid	34 (51)	41 (39)	.15
Long-acting β_2 agonist + inhaled corticosteroid	9 (13)	16 (15)	.72
None	12 (18)	12 (12)	.24
History			
Intubation	3 (4)	3 (3)	.58
ICU admission	22 (33)	32 (31)	.78
Noninvasive ventilation	2 (3)	1 (1)	.33
None	44 (66)	71 (68)	.72
Cause of exacerbation			.41
Viral	46 (69)	63 (61)	
Unknown/unreported	1 (1)	5 (5)	
Environmental	2 (3)	9 (9)	
Nonadherence	4 (6)	6 (6)	
Exposure	1 (1)	5 (5)	
Route of admission			.71
Emergency department	30 (45)	39 (38)	
Hospital wards	8 (12)	11 (11)	
Outside hospital	27 (40)	47 (45)	
Stepdown	1 (1)	5 (5)	
Admission data			
Heart rate, beats/min	155 ± 14	158 ± 16	.24
Breathing frequency, breaths/min	37 ± 0.5	37 ± 0.4	.36
F_{IO_2}	0.50 ± 0.29	0.45 ± 0.28	.38
S_{pO_2}, %	96 ± 3	95 ± 3	.68
Admission MPIS	10 (9–12)	11 (9–12)	.15
MPIS 8–9	29 (43)	31 (30)	.16
MPIS 10–11	17 (25)	38 (37)	
MPIS ≥ 12	21 (31)	35 (34)	

Data are presented as n (%), mean ± SD, or median (interquartile range).
MPIS = modified pulmonary index score

intolerance of aerosol mask during intermittent aerosol therapy. Subjects initially placed on HFNC spent less time on continuous albuterol but ultimately spent the same amount of time in the hospital as those initially placed on aerosol mask. This may have been related to the need to wean subjects from HFNC after meeting de-escalation criteria. For subjects treated in the HFNC group, those who were treated with higher flows had a similar hospital LOS, PICU LOS, and MPIS over time as those who were treated with lower HFNC flows. Subjects in both groups were equally likely to need escalation to either NIV or heliox. A significant portion of subjects initially treated with aerosol mask were eventually transitioned to HFNC at the clinical team's discretion; this could have been caused by patient intolerance, failure of treatment, or clinician preference. Due to our methodology, we were unable to objectively measure the reason subjects were transitioned to HFNC from aerosol face mask, although we have observed anecdotally that many of our respiratory therapists have a strong preference for HFNC or have a low threshold for changing patients who are intolerant of mask therapy to HFNC.

A retrospective observational study that compared HFNC to conventional oxygen therapy in the PICU reported that HFNC improved heart rate, breathing frequency, S_{pO_2}/F_{IO_2} ratio, pH, and P_{CO_2}, in the first 24 h.[11] Although their groups had similar breathing frequency, heart rate, and S_{pO_2} on admission, those who received HFNC seemed to be less severe at admission (ie, lower respiratory scores and P_{CO_2} values) and fewer had acidosis, which may have influenced their results. We did not measure pH or CO_2 values in our

Table 2. Subject Outcomes

	Aerosol Mask ($n = 67$)	HFNC ($n = 104$)	P
Hospital LOS, d	3.0 (2.3–4.4)	2.9 (2.1–3.9)	.47
Pediatric ICU LOS, d	1.8 (1.5–3.0)	1.9 (1.4–2.8)	.92
Time to MPIS < 6, d	1.3 (0.8–1.9)	1.0 (0.6–1.6)	.09
Time on continuous albuterol, d	1.5 (0.9–2.3)	1.0 (0.7–1.8)	.048
Intubated	0 (0)	2 (2)	.25
Pediatric ICU readmission	0 (0)	1 (1)	.37
Helium-oxygen mixture	26 (39)	34 (33)	.40
Noninvasive ventilation	3 (4)	9 (9)	.56
Crossed to HFNC	16 (24)	NA	

Data are presented as *n* (%) or median (interquartile range).
LOS = length of stay
MPIS = modified pulmonary index score
HFNC = high-flow nasal cannula
NA = not applicable

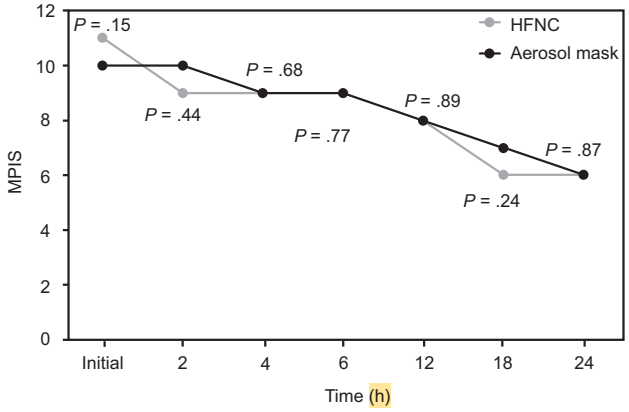

Fig. 2. Progression of modified pulmonary index score (MPIS) over time. HFNC = high-flow nasal cannula.

study as we rarely evaluate blood gases in patients with critical asthma.

González Martínez et al[13] performed a retrospective observational study in children with asthma treated with HFNC or conventional oxygen therapy admitted to an inpatient unit. In that study, HFNC was associated with significant decreases in breathing frequency, heart rate, and pulmonary score in the first hours of treatment, although LOS was similar between groups. They reported higher HFNC flows to be associated with decreased need for PICU admission. Pilar et al[14] compared HFNC and NIV as the initial respiratory support in children with critical asthma and noted a similar PICU LOS but a 3-fold longer duration of ventilatory support for subjects who failed HFNC and needed escalation to NIV. They concluded that HFNC could delay initiation of NIV, resulting in longer respiratory support and longer PICU LOS. Although our study was larger, we had similar rates of increased respiratory support in our HFNC groups, but only 9% of HFNC subjects in our study required escalation to NIV, compared to the 40% reported by Pilar et al.[14] This could be related to differences in illness severity or institutional thresholds for NIV initiation.

Gauto Benítez et al[12] conducted an open, randomized controlled clinical trial on pediatric subjects treated in the emergency department to compare HFNC to conventional oxygen therapy and found subjects on HFNC had a similar decrease in pulmonary index score compared to conventional oxygen therapy. They concluded that the addition of HFNC to the initial treatment of acute asthma in children did not result in clinical benefit or reduction in emergency department LOS. Ballestero et al[10] performed a pilot randomized trial in the pediatric emergency department comparing HFNC to conventional oxygen therapy (ie, nasal cannula, air-entrainment mask, or non-rebreather mask) and reported HFNC to be superior for reducing distress, as measured by the pulmonary score, within the first 2 h of treatment, but LOS and escalation to NIV were similar between groups. While it is difficult to compare studies using different scoring systems or those conducted in the emergency department instead of in the PICU, both studies considered HFNC and aerosol mask to be equivalent, in congruence with our findings.

Our findings are also similar to those of adult studies of HFNC use in asthma. Raeisi et al[8] performed a randomized pilot study on subjects ≥ 18 y old with moderate-to-severe asthma exacerbations to compare HFNC and conventional oxygen therapy. The dyspnea scale decreased significantly in that study, and P_{aO_2} and S_{pO_2} increased significantly in both groups within the first 2 h of treatment; the investigators concluded that HFNC could be a therapeutic option for adult patients with asthma. Geng et al[7] conducted a single-center randomized controlled trial on adult subjects with severe asthma complicated with respiratory failure to compare HFNC and conventional oxygen therapy in improving oxygenation. They reported no significant differences in LOS, intubation rate, or duration of oxygen therapy between groups, although they noted that HFNC was associated with higher P_{O_2} and reduced heart rate and breathing frequency at 24 and 48 h post-admission. While these small, single-center randomized controlled trials are not directly applicable to the PICU, they support the equivalence between HFNC and aerosol mask use.

While aerosol delivery through a HFNC is highly debated and its effectiveness at higher flows is questioned, flow did not appear to impact outcomes in our study. Al-Subu et al[9] evaluated aerosol delivery via HFNC at low gas flows, the effect on patient comfort and respiratory therapist bedside time in their PICU in 28 subjects. The

investigators reported that aerosol delivery was feasible with HFNC, but the use of HFNC increased respiratory therapist bedside time and did not affect patient comfort, and PICU LOS was similar between those treated with HFNC versus the traditional interfaces. Importantly, HFNC flow was decreased during treatments due to concerns about aerosol deposition at higher flows. Half of the subjects in that study had asthma (although the median age in the HFNC group was 21 months, much younger than subjects in our study), subjects were receiving intermittent bronchodilator therapy, and the study was not designed to detect difference in clinical outcomes. In comparison, our study had a larger number of subjects, and we did not decrease HFNC flows to increase aerosol deposition. Li et al[5] concluded that bronchodilator doses were similar when delivered at 1 L/kg/min via HFNC to traditional delivery devices. In our PICU, HFNC flows are typically set between 0.5 and 2 L/kg/min based on the patient's inspiratory flow demand, and HFNC flows are not reduced for aerosol delivery purposes. While aerosol delivery may be affected at higher flows, our study found similar patient outcomes with higher and lower HFNC flows, as well as between HFNC and aerosol mask.

Our results indicate that HFNC and aerosol mask were equivalent in the treatment of pediatric critical asthma. These results are in line with studies done in both pediatric and adult populations. Our findings provide us with reassurance that the change of practice in our PICU toward utilizing HFNC more frequently did not result in increased LOS. While we were unable to determine the exact reasons for increased HFNC use, our anecdotal experience indicates that HFNC improves patient comfort and tolerance to therapy and allows patients to be more active, and providers are more likely to allow patients treated with HFNC to eat, drink, and be more mobile within the unit. The increased use of HFNC may also have been influenced by clinician bias. With use of HFNC becoming increasingly more frequent in PICUs, our results indicate that its application in pediatric critical asthma is associated with similar hospital and PICU LOS compared to aerosol mask.

Limitations

Our study was limited by its retrospective design and the data available in the electronic medical record. Bed availability on the general pediatric in-patient units could have influenced PICU LOS in our study, and we do not have a mechanism to resolve this potential confounder. Nevertheless, the fact that both groups had similar hospital LOS and time to MPIS < 6 suggests that bed availability was not an impactful limiting factor for transfer out of the PICU. The decision to use HFNC or aerosol mask was left to the discretion of the respiratory therapist and clinical team, and there was a notable number of crossover patients in our cohort. We were unable to determine the indication for HFNC. HFNC flows and weaning were not standardized or managed by our asthma protocol, and variations in these spaces could have impacted our results.

Conclusions

HFNC performed similarly to aerosol mask in pediatric subjects with critical asthma. A multicenter randomized controlled trial is needed to confirm our results.

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