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Article

Effectiveness of Humidified High Flow Nasal Cannula Versus Continuous Nasal Positive Airway Pressure in Managing Respiratory Failure in Preterm Infants: An Emergency Department Study

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Abstract: BACKGROUND: Pneumonia is a significant cause of morbidity and mortality in neonates, particularly when accompanied by respiratory failure. This study aims to compare the effectiveness and outcomes of HHFNC and CPAP in improving respiratory outcomes and reducing adverse effects. **METHODS:** The 220 patients were enrolled in the study (110 in each group) from the neonatal unit, after obtaining written informed consent from their parents/guardians. Nasal CPAP was applied to patients in group A through nasal cannula with the following settings FiO₂: 40-60%, PEEP: 5-8 cm H₂O, flow: 4-6L/min. HHFNC was applied to patients in group B through the nasal cannula with the following setting FiO₂: 40-60%, flow: 4-6L/min. Study variables were recorded in the proforma and analyzed using SPSS version 23.0. **RESULTS:** The comparison of CPAP (Group A) and HHFNC (Group B) showed no significant differences in age, gestational age, or clinical parameters, except for a higher respiratory rate in HHFNC. The HHFNC group had significantly shorter durations of non-invasive ventilatory support and hospital stay. Adverse effects were more common in HHFNC, especially nasal mucosal injury, while sepsis was more frequent in CPAP. Treatment failure occurred more often in the HHFNC group. Neonatal outcomes were similar, with no significant differences in discharge rates, mortality, or intubation rates. **CONCLUSION:** The study found that the duration of non-invasive ventilator support, shown by HHFNC, was significantly less when compared to CPAP. This suggests that HHFNC might be preferred for providing extended respiratory support in this patient population. Nonetheless, both HHFNC and CPAP appear safe and effective in supporting neonates through their respiratory challenges.

Keywords: Continuous Nasal Positive Airway Pressure (CPAP); Humidified High Flow Nasal (HHFNC); pneumonia; respiratory failure

Introduction

The major age-related mortality with pneumonia occurs in neonates because of their poor lung defences and nonspecific clinical symptoms [1]. Pneumonia was the third largest cause of mortality among neonates, with 21.7 deaths per 100,000 live births in the first 7 days and 13.3 deaths per 100,000 live births from 7 to 27 days [2]. UNICEF estimates the number of pneumonia-related fatalities among children under the age of five in poor countries each year [3]. Pneumonia, a leading cause of respiratory failure and ICU admissions in paediatrics, is primarily attributed to hypoxemia due to ventilation-perfusion mismatch, increased breathing work, and hypercarbia [4].

Nasal continuous positive airway pressure (nCPAP) is the most popular non-invasive breathing assistance for preterm newborns, but its usage needs competent nursing care because of the bulky interfaces [5]. High-flow nasal cannula treatment (HFNC) is a gentler option that is becoming popular among newborns and children with respiratory diseases [6].

HFNC are tiny, thin binasal prongs that supply oxygen or oxygen/air mixes at flow rates greater than 1 L per minute. They are located inside the nares and can take up to half of the available space without a seal [7]. Patients may tolerate larger flow rates since the gas is appropriately warmed and humidified when given. These high flow rates can equal or surpass patients' inspiratory flow rates, limiting room air intake while ensuring that the percentage of oxygen (FiO₂) inspired by patients matches the FiO₂ given by the HFNC system. The heated, humidified high-flow delivered via nasal cannulae (HHFNC) approach is increasingly being employed for noninvasive respiratory support in preterm newborns, critically sick children, and adults [8].

Over the last six years, the usage of HHFNC in neonatal intensive care units (NICUs) in wealthy nations has expanded dramatically [9]. This is owing to its effectiveness, safety, and perceived advantages to nCPAP, such as a simpler, smaller nasal interface and more comfort for babies. However, data is only available from larger randomised controlled studies, with the majority comparing basic respiratory assistance in preterm newborns [10]. Over the previous two years, 6 randomised studies have included 936 preterm newborns [11,12].

Literature supports that HFNC can avoid extubation failure, improve respiratory function, and aid in weaning off CPAP [13]. Another research found that nasal cannulae flows of up to 2.5 L/min are equally effective as nasal CPAP for treating apnoea of prematurity without raising oxygen requirements [14].

Previous studies on the treatment of respiratory failure in pre-term neonates have focused on comparing Humidified High Flow Nasal Cannula (HHFNC) with CPAP [15,16]. This study aims to compare both treatment modalities, focusing on the mean duration of hospital stay and the mean duration of dependency on respiratory support, focusing on the ease of administration, improved compliance, and better patient outcomes compared to traditional ventilation methods.

Materials and Methods

Study Design and Patient Enrolment

The quasi-experimental study was conducted after the ethical approval and consent taken from the parent/guardian. Patients were enrolled from the Neonatal Unit, at the University of Lahore teaching hospital, Lahore, Pakistan. Non-probability, consecutive sampling was used to add 220 (110 in each group) patients to the study. The sample size is calculated by using the power of study equal to 80% and level of significance equal to 5%, taking treatment failure in the HHFNC group as 38.1% and in CPAP as 20.9% was 220 (110 in each group) patients were enrolled in the study [17].

Patient Selection and Grouping

Patients were assigned to two groups (group A applied to CPAP and group B applied to HHFNC) using a computerized random table generator to obtain a trial sequence which was hidden in sequentially numbered sealed opaque envelopes prepared by co-investigator.

The research looked at individuals aged 1 to 28 days who had type 1 respiratory failure and needed non-invasive ventilatory assistance, such as a High-Flow Nasal Cannula or nasal Continuous Positive Airway Pressure. Patients with congenital heart disease or neuromuscular abnormalities were excluded, as were newborns suffering from type 2 respiratory failure or requiring invasive mechanical ventilation or intubation. The study intended to maintain the study's integrity. Additionally, participation was limited to those whose parents or guardians consented to take part in the study. This approach helps create a focused and relevant cohort for better understanding and managing type 1 respiratory failure in neonates.

Training Session

The Training session was arranged by the principal researcher for fellow doctors and nurses of the neonatal unit in which they were given detailed training regarding data collection, procedures and interventions used in this study. Term neonates meeting inclusion criteria were inducted into the study. All patients were evaluated to rule out any exclusion criteria.

Data Collection

Written and informed consent was taken from parents/legal guardians for each patient after explaining the procedure and complications. The patient's history including gestational age was noted. Diagnosis of pneumonia and respiratory failure was established with the help of clinical findings, radiological findings, and arterial blood gas analysis. Baseline variables pH, PaCO₂, and PaO₂ were noted by arterial blood gases. The respiratory rate was recorded. Nasal CPAP was applied to group 1 through nasal cannula with the following settings FiO₂: 40-60%, PEEP: 5-8 cm H₂O, Flow: 4-6L/min. HHFNC was applied to group 2 through the nasal cannula with the following setting FiO₂: 40-60%, Flow: 4-6L/min. Any patient who could not maintain oxygen saturation (SpO₂ < 90% on pulse oximetry) with CPAP or HHFNC or ABG suggestive of type 2 respiratory failure, was intubated and shifted to invasive ventilation, which was counted as treatment failure and was excluded from the study. Data was recorded about the duration of hospital stay in days & duration of application of respiratory support i.e. nCPAP or HHFNC at the time of discharge. Arterial Blood Gases were performed daily or as per the requirement to check the PaO₂ and PaCO₂. Vitals were recorded on an hourly basis, and any change of nCPAP & HHFNC settings were recorded. The same Antibiotics (Cefotaxime 150mg/kg/24hr & Ampicillin 200mg/kg/24hr as 1st line) and other treatments including maintenance fluid were given to both groups as per requirement. All the data was recorded on a pre-designed proforma by the staff members and results were subjected to statistical analysis by the principal researcher to determine the significance of observed differences. The data collection continued until the enrolled neonates were discharged from the hospital.

The data collection aimed to analyse the following outcomes; Total. Duration of hospital stay in days, mean duration of application of respiratory support in hours, frequency of adverse events including sepsis, frequency of nasal mucosal injury, abdominal distension, feeding intolerance, outcome (discharged, expired, intubated and treatment failure) and neonatal outcomes (Discharge, Expired, Intubated).

Data Analysis

Collected data was entered and analyzed using Statistical Package for Social Science (SPSS) version 23.0. all the quantitative variables like age, APGAR score, gestational age of mother, duration of hospital, respiratory support, and total days of oxygen use up to the time of discharge for each group were reported by Mean±SD. All the qualitative variables like gender, neonatal outcomes (Discharge, Expired, Intubated), adverse events like sepsis, abdominal distention, feeding intolerance, and nasal mucosal injury) and outcome (discharged, expired, intubated and treatment failure) have been presented by frequency/percentages. Duration of hospital stay in days and mean duration of application of respiratory support in hours have been compared with Man Whitney U

test according to normality of data. The comparison of adverse effects among both groups was compared by the Chi-square test. A P-value less than or equal to 0.05 was considered significant.

Results

Baseline Characteristics of Study Sample

The comparison of characteristics between Group A and Group B reveals no significant differences in several variables. The mean age (14.72 ± 8.45 days for Group A vs. 15.07 ± 8.02 days for Group B) and gestational age (32.71 ± 2.52 weeks for Group A vs. 32.45 ± 2.94 weeks for Group B) were similar between the two groups, with p-values of 0.796 and 0.472, respectively, indicating no significant differences. The gender distribution also showed no notable difference ($p = 0.495$), with a slightly higher percentage of females in both groups. Regarding clinical parameters, the APGAR score, SpO₂, heart rate (HR), arterial pH, pO₂, and pCO₂ values were similar between the groups, with p-values of 0.971, 0.735, 0.765, 0.363, 0.941, and 0.344, respectively, suggesting no significant differences. However, the respiratory rate was significantly higher in Group B (55.75 ± 11.66) compared to Group A (52.29 ± 11.23), with a p-value of 0.028, indicating a statistically significant difference between the two groups. (Table 1)

Table 1. Comparison between the Groups at Baseline.

Characteristics	Group A (n=128)	Group B (n=128)	p-value
Age (1-28 days)	14.72±8.45	15.07±8.02	0.796 ^a
Gender			
Male	44 (40.0%)	49 (44.5%)	0.495 ^b
Female	66 (60.0%)	61 (55.5%)	
Gestational Age	32.71±2.52	32.45±2.94	0.472 ^a
APGAR Score	5.98±0.88	5.46±0.81	0.971 ^a
SPO2	69.69±18.2	70.43±17.38	0.735 ^a
Respiratory Rate	52.29±11.23	55.75±11.66	0.028 ^a
HR Rate	134.28±18.69	133.46±17/83	0.765 ^a
Arterial Ph	6.26±1.37	6.09±1.41	0.363 ^a
PO2	63.31±12.1	63.02±11.5	0.941 ^a
PCO2	40.56±5.42	39.87±5.23	0.344 ^a

^a Mann Whitney U test. ^b Chi Square test. Taking p-value≤0.05 as significant.

Comparison of Duration of Application of Non-Invasive Ventilatory Support (Hours) and Hospital Stay Between the Groups

The comparison of the duration of application of non-invasive ventilatory support and hospital stay between the two groups shows significant differences. The mean duration of non-invasive ventilatory support was significantly shorter in Group B (HHFNC) at 65.20 hours (± 15.9) compared to Group A (CPAP), which had a mean of 72.29 hours (± 20.7), with a p-value of 0.013, indicating statistical significance. Similarly, the mean duration of hospital stay was significantly shorter in Group B (HHFNC) at 20.14 days (± 3.50) compared to Group A (CPAP), which had a mean of 24.25 days (± 6.07), with a p-value of 0.000, confirming a significant difference. These finding suggest support that the HFNC may be associated with a shorter duration of both non-invasive ventilatory support and hospital stay compared to CPAP (Table 2). The most prevalent adverse impact in the CPAP group was sepsis, which was documented in eight instances, followed by nasal mucosal damage in seven. Feeding intolerance and stomach distention were reported in five and four patients, respectively. In contrast, the HHFNC group exhibited a greater rate of nasal mucosal damage (18

instances) compared to CPAP. Feeding intolerance and abdominal distention were recorded in 9 and 6 instances, respectively, whereas sepsis was diagnosed in 10 cases. These findings show that, while both groups suffered similar adverse effects, HHFNC was linked with a greater frequency of nasal mucosal damage, whereas sepsis was more common in the CPAP group (Figure 1).

Table 2. Comparison of Duration of Application of Non-invasive Ventilatory Support (hours) and hospital stay between the Groups.

Duration of Application of Non-invasive Ventilatory Support (hours)			
Study Group	Mean	Std. Deviation	p-value
CPAP (A)	72.29	20.7	0.013 ^a
HHFNC (B)	65.20	15.9	
Hospital stay in days			
CPAP (A)	24.25	6.07	0.000 ^a
HHFNC (B)	20.14	3.50	

^a Mann Whitney U test, Taking p-value≤0.05 as significant.

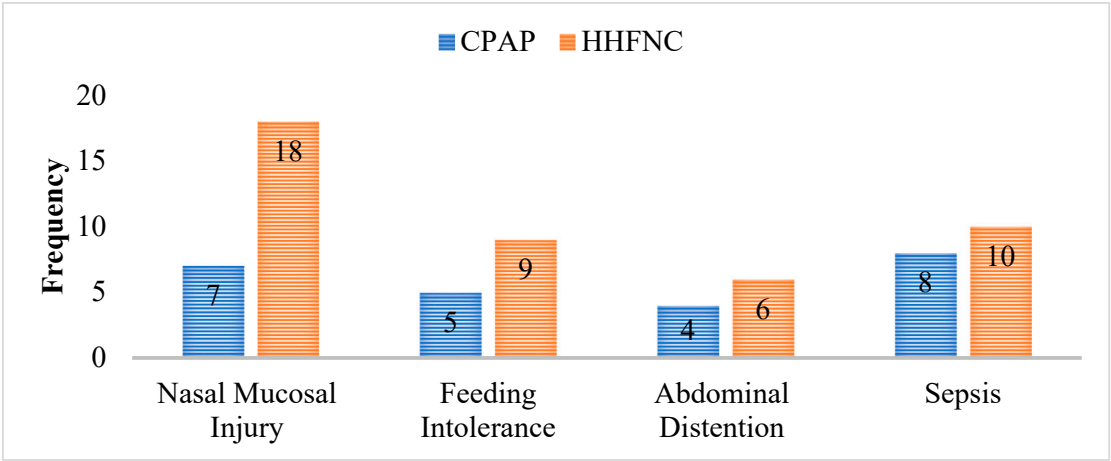


Figure 1. Comparison of adverse effects in both groups. ^bChi Square test. Taking p-value≤0.05 as significant.

Comparison of Treatment Failure in Both Groups

The incidence of treatment failure in the CPAP and HFNC groups. The 12 patients experienced treatment failure in the CPAP group, whereas 18 patients had treatment failure in HFNC. This suggests that a higher proportion of patients in the HFNC group experienced treatment failure compared to those in the CPAP group (Figure 2).

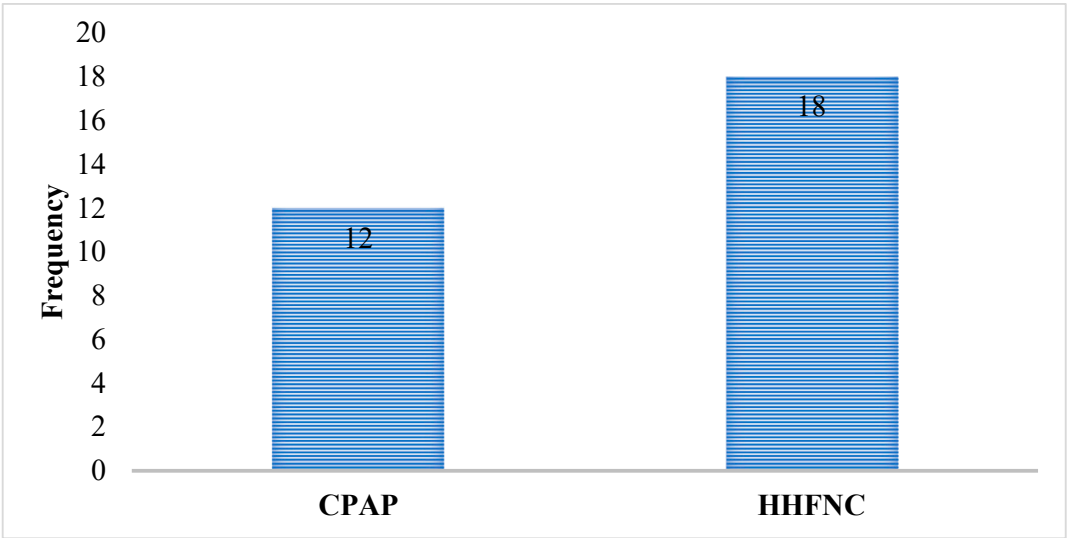


Figure 2. Comparison of Treatment failure in both groups. ^b Chi Square test. Taking p-value≤0.05 as significant.

Comparison of Duration of Neonatal Outcome Between the Groups

The neonatal outcomes for both CPAP and HHFNC groups were compared. Among the total of 220 neonates, 194 (88.2%) were discharged, with 100 (90.9%) in the CPAP group and 94 (85.5%) in the HHFNC group. The difference in discharge rates between the two groups was not statistically significant, with a p-value of 0.224. In terms of mortality, 9 neonates (4.1%) expired, with 5 (4.5%) from the CPAP group and 4 (3.6%) from the HHFNC group, indicating a similar low incidence of mortality across both groups. Regarding intubation, 17 neonates (7.7%) required intubation, with a higher incidence in the HHFNC group (12 cases, 10.9%) compared to the CPAP group (5 cases, 4.5%). However, the p-value suggests that these differences were not statistically significant (Table 3).

Table 3. Comparison of Duration of Neonatal outcome between the Groups.

Neonatal Outcome	Groups		Total	P-value
	CPAP	HHFNC		
Discharged	100(90.9%)	94(85.5%)	194(88.2%)	^b 0.224
Expired	5(4.5%)	4(3.6%)	9(4.1%)	
Intubated	5(4.5%)	12(10.9%)	17(7.7%)	
Total	110	110	220	

^b Chi Square test. Taking p-value≤0.05 as significant.

Discussion

CPAP serves as the primary respiratory support modality for the majority of neonates experiencing respiratory distress. Regardless of the underlying etiology, this effective therapeutic approach confers benefits to most newborns [18]. Prompt initiation of nCPAP, either in the delivery room or within the initial hour of respiratory distress onset, has been shown to reduce the reliance on mechanical ventilation and surfactant administration, particularly in very preterm infants [19]. Nevertheless, the application of nCPAP is associated with potential drawbacks, including nasal injury, frequent displacement of nasal prongs, increased nursing time, and a requirement for skilled nursing personnel. Additionally, nCPAP failure rates reach approximately 15-25% among neonates

receiving this mode of support [20]. In recent times, HFNC has growing acceptance as an alternative respiratory support modality for preterm infants. HFNC presents certain advantages over nCPAP, such as a reduced incidence of nasal trauma, utilization of patient and parent-friendly nasal prongs, and ease of use [21].

Owing to controversy in existing literature, the present study was aimed to compare two widely used respiratory support methods, HFNC and CPAP, in term neonates suffering from pneumonia with respiratory failure. The study involved term neonates with pneumonia and type 1 respiratory failure, with a mean age of 14.72 ± 8.45 days for Group A and 15.07 ± 8.02 days for Group B. Previous studies reported lower mean ages of 1-2 days respectively, for neonates with pneumonia and type 1 respiratory failure [22,23]. This considerable variation in mean age could potentially be attributed to differences in the age criteria used to include patients in the respective studies [24].

The gender distribution also showed no notable difference ($p = 0.495$), with a slightly higher percentage of females in both groups. Other studies reported the higher male-to-female ratios of 1.66:1 reported by Sarkar et al. (2018) [25] and Sharma (2018) reported an even higher proportion of male neonates (78.6%) in their study conducted in India [26]. The gestational age were similar between the two groups, indicating no significant differences. It is noteworthy that no previous study has been conducted specifically on term neonates in this particular comparison. However, studies conducted on preterm neonates have reported gestational ages of 32.5 ± 1.5 weeks by Shin et al. (2017) in Korea [27]

The mean SPO₂ at admission suggests that the patients in this study presented with lower oxygen saturation levels, indicating potential respiratory compromise or respiratory failure. The higher mean SPO₂ observed in the literature suggests better oxygenation levels in their study population, possibly reflecting more favourable respiratory status or different patient characteristics [28]. In contrast, the lower mean SPO₂ reported in the prior study implies that their sample population had insufficient oxygenation levels at admission, perhaps indicating more serious respiratory distress [29]. Maintaining proper oxygen levels is critical for controlling hypoxia which can cause organ malfunction and consequences. Differences in mean SPO₂ levels between studies might be attributed to patient characteristics, illness severity, or treatment procedures. Consistency in respiratory rate with previous research improves outcomes dependability and generalizability. However, increased respiratory rates may suggest changes in illness severity, patient characteristics, or clinical care strategies [30]. Similarly, the heart rate data from this investigation and the current literature add to the results' consistency and dependability, as well as their generalizability to comparable patient groups. Previous reports of increased heart rates may imply variations in illness severity, patient characteristics, or clinical care techniques in their individual research cohorts. [31].

The arterial pH findings reported in this study and other studies highlights consistency in the acid-base status of patients with similar respiratory conditions in different research settings. Acid-base disturbances are crucial indicators of the patient's overall physiological status and can help identify the underlying cause and guide appropriate management. The similarity in PO₂ values suggests comparable oxygenation levels in patients from both cohorts [32].

In this study, the mean duration of non-invasive ventilatory support and duration of hospital stay was significantly shorter in Group B compared to Group A. These results suggest that HHFNC may be associated with a shorter duration of both non-invasive ventilatory support and hospital stay compared to CPAP. These findings align with results reported previously where the mean duration of application was also higher in the CPAP group than the HHFNC group (69 ± 94.8 vs. 65 ± 99.9 hours), but the difference was not statistically significant [12]. However, it is important to note that other studies have reported different findings. Some studies showed an inverse relation, where the mean duration of application was less in the CPAP group than in the HHFNC group, but again the difference was not significant [33].

The longer mean duration of application in the CPAP group in this study suggests that CPAP may be utilized for a more extended period compared to HHFNC for providing non-invasive ventilatory support in this particular patient population. The variations in the duration of application

between different studies may be influenced by differences in patient selection criteria, disease severity, and clinical management approaches. The lack of statistical significance in some studies could be due to the relatively small sample sizes or other factors that contribute to the variability in results.

The higher incidence of treatment failure in the HFNC group (compared to CPAP) is noteworthy. As reported in the literature indicates that HFNC may be less effective in cases of severe respiratory distress, necessitating intubation or escalation of care [34,35]. This underscores the importance of patient selection when deciding between HHFNC and CPAP as initial interventions. Studies advocate for clear clinical criteria to minimize the risk of treatment failure in vulnerable neonates [36].

This study adds to the expanding body of evidence comparing HFNC and CPAP for treating respiratory insufficiency in preterm babies. While HHFNC has benefits such as shorter hospital stays and shorter ventilatory support duration, it may also be linked with increased rates of treatment failure and particular side effects such as nasal mucosal damage. These findings highlight the necessity of individualised therapy strategies based on clinical severity and patient-specific characteristics in optimising outcomes. The study's applicability to other healthcare settings may be restricted, and it may not address long-term effects such as chronic respiratory diseases. Future multicenter research including bigger, varied populations and standardised techniques are required.

Conclusions

The duration of non-invasive ventilator support, shown by HFNC, was significantly less while compared to CPAP. Moreover, length of hospital stay was also significantly short in HHFNC group than CPAP. This suggests that HHFNC might be preferred for providing extended respiratory support in this patient population. Nonetheless, both HHFNC and CPAP appear safe and effective in supporting neonates through their respiratory challenges. Ultimately, individual patient needs and clinical considerations should guide the selection of the most suitable respiratory support method. Further research is needed to confirm these findings and explore potential strategies for mitigating adverse effects associated with HHFNC.

Conflicts of Interest statement: All authors declare no conflict of Interest

Author's contribution: All Authors contributed equally to the work

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Informed consent: Informed consent was obtained from the Parents and the attendees of all participants included in the study.

Data Availability: The datasets generated for this study are available in the attachment

Ethics Statement: The studies involving human participants were reviewed and approved by the Human Research Ethics Committee at The University of Lahore, Pakistan. Written informed consent to participate in this study was provided by the participants.

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