İstanbul Med J 2023; 24(3): 295–7
DOI: 10.4274/imj.galenos.2023.87404

Experience in Non-invasive Ventilation in Grade 3 Hepatic Encephalopathy

İlhan Ocak[1], Mustafa Çolak[1], Erdem Kınacı[2]

[1]University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Transplant Intensive Care, İstanbul, Turkey
[2]University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Hepato-Pancreato-Biliary Surgery and Liver Transplantation, İstanbul, Turkey

ABSTRACT

Introduction: Hepatic encephalopathy (HE) is a common complication of acute and chronic liver failure, which can lead to significant morbidity and mortality. Grade 3-4 HE patients are typically managed with routine intubation and mechanical ventilation. However, recent research suggests that routine intubation may increase the risk of complications and death for the preservation of the airway. This study investigated the use of non-invasive ventilation (NIV) in patients with grade 3 encephalopathy associated with acute and chronic liver failure.

Methods: This retrospective study included patients with grade 3 encephalopathy associated with liver failure who underwent NIV between January 2022 and March 2023 in a liver transplant intensive care unit. The patient demographic data, laboratory results, comorbidities, and outcomes were collected and analyzed. The results were compared to those of HE patients who were intubated as reported in the literature.

Results: A total of 41 children and adults with grade 3 HE who received NIV were included in this study. Compared with HE patients who were intubated as reported in the literature, the NIV group had significantly lower rates of complications and mortality. Additionally, there were no additional complications observed in patients who received NIV without intubation, such as infections, cardiovascular disorders, or cognitive impairments.

Conclusion: The use of NIV in grade 3 HE patients suggests that it is an effective alternative to intubation. These findings support the need for careful consideration when deciding to intubate HE patients and suggest that continuous support using NIV may provide potential benefits. Further studies are needed to investigate the optimal management of these patients to improve their outcomes.

Keywords: Hepatic encephalopathy, hepatic failure, non-invasive ventilation

Introduction

Hepatic encephalopathy (HE) is the critical stage of liver failure, especially in acute cases. Patients with grade 3 or 4 HE is often intubated and underwent mechanical ventilation to prevent life-threatening complications (1,2). However, there is no concrete evidence that routine intubation has benefit for patients with advanced delirium associated with HE (3,4). In contrast, this procedure has its own various risks, such as nosocomial pneumonia, hypotension, increased mortality, and prolonged hospital stays (5,6). Thus, mechanical ventilation in patients with grade 3-4 HE has been associated with increased in-hospital mortality due to compromised immunity, altered drug metabolism, and circulatory dysfunction (7,8). The aim of this study was to determine the effects of preferring non-invasive ventilation (NIV) instead of intubation in patients with grade 3 HE in the aspect of clinical outcome.

Methods

In this study, the records of patients followed in the University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital between January 2022 and March 2023 were retrospectively reviewed. Patients with grade 3 HE related to acute or chronic hepatic failure to respiratory impairment due to cardiovascular insufficiency were included in the study. All these patients underwent NIV and continued to receive extracorporeal liver support therapy (9). "Acute Physiology and Chronic Health Evaluation (APACHE II)", "West Haven Classification" and "Glasgow Coma Scale" were used to stage the clinical conditions. The ethical rules of this study were determined in accordance with the Declaration of Helsinki. All necessary precautions were taken to ensure the confidentiality and protection of data.

Address for Correspondence: İlhan Ocak MD, University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Transplant Intensive Care, İstanbul, Turkey
Phone: +90 532 452 10 52 **E-mail:** ilhanocak.md@gmail.com **ORCID ID:** orcid.org//0000-0003-1770-0794

Cite this article as: Ocak İ, Çolak M, Kınacı E. Experience in Non-invasive Ventilation in Grade 3 Hepatic Encephalopathy. İstanbul Med J 2023; 24(3): 295-7.

Received: 23.07.2023
Accepted: 01.08.2023

This study was approved by the Ethics Committee of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital (approval number: 336, date: 26.07.2023).

Statistical Analysis

Statistical analyzes were performed using SPSS 20 (IBM Corp., Armonk, NY). The normal distribution of study data was evaluated using the Kolmogorov-Smirnov analysis. Demographic characteristics, intensive care unit (ICU) length of stay, APACHE and PRISM scores, and NIV parameters of the patients were presented as median (range), while laboratory values at admission to the ICU were presented as mean (standard deviation).

Results

A total of 41 patients with grade 3 HE were included. Of these patients, 24 were female and 17 were male. Thirteen of the patients were children with a mean age of 8 (range: 0-16 years), while the mean age of the 28 adult patients was 57 (range: 49-70) years. NIV was applied to the 28 adult patients for a mean of 8 days (range: 3-13 days) and to the 13 pediatric patients for a mean of 9 days (range: 4-14 days) until recovery, liver transplantation, or progression to grade 4 HE occurred. The application was performed for 20 hours per day. Nine patients (22%) progressed to grade 4 HE due to a rapid increase in hepatic failure and required protracheal intubation. These nine patients who were not suitable for liver transplantation or could not find a suitable donor died. Recovery was achieved in the other 24 patients who received NIV, and no additional complications such as nosocomial pneumonia, respiratory disorders, hypotension, or cognitive impairment were observed. Eight other patients who received NIV underwent liver transplantation and achieved recovery. The demographic, etiological and intensive care scoring values of the patients are presented in Table 1, the NIV values in Table 2 and the laboratory values in Table 3.

Table 1. Demographics, etiology and intensive care scoring values

Child	**13 (n)**
*Age	8 (0-16)
*PRISM score	29 (22-36)
Adult	**28 (n)**
*Age	57 (49-70)
*APACHE II score	25 (20-28)
Gender	**n**
Male	17
Female	24
Etiology	**n (%)**
Mushroom intoxication	11 (26.8)
Autoimmune disease	5 (12.1)
Toxic hepatitis	5 (12.1)
Hepatitis B	4 (9.7)
Wilson's disease	4 (9.7)
Paracetamol intoxication	3 (7.3)
Idiopathic disease	3 (7.3)
Progressive familial intrahepatic cholestasis	2 (4.8)
Alveolar hydatid cyst	2 (4.8)
Budd chiari syndrome	1 (2.4)
Wolcott-Rallison syndrome (WRS)	1 (2.4)

*Median values (range), APACHE-II: Acute Physiology and Chronic Health Evaluation-II, PRISM: Pediatric Risk of Mortality

Discussion

HE, which worsens to grade 3-4 is typically managed with intubation and mandatory mechanical ventilation according to literature and algorithms (10). However, studies have shown that routine intubation for airway protection in patients with grade 3-4 HE may potentially be related to increased risk of complications and in-hospital mortality (11-13). In this study, survival rates of 78% and 22% were determined in 41 patients.

In this study, the expected complications of intubation, such as nosocomial infections, cardiovascular and cognitive disorders, and increased mortality were not seen in our patients undergoing NIV who had different demographic, etiological, mortality scoring, and laboratory results. The most remarkable and often cited complication of intubation, aspiration pneumonia, was observed to be prevented.

The data in the literature about the outcomes of NIV in patients with HE are very limited. Our study showed that NIV in HE patients could significantly reduce complications and mortality compared with the reported outcomes for intubated patients. The results of a recent study written by Saffo and Garcia-Tsao (14) support our results although our study excludes grade 4 HE. According to this comprehensive study, 40% of HE patients who were intubated within the first 48 h died in the hospital, while 19% of those who were not intubated died overall. The mortality rate for intubated patients reached 70% after the first

Table 2. Non-invasive ventilation values

NIV parameter	**Adult (range)***	**Child (range)***
PEEP (cmH_2O)	8 (6-10)	6 (4-8)
P support (cmH_2O)	14 (10-16)	8 (6-12)
FiO_2	0.40 (0.35-0.55)	0.40 (0.21-0.5)
NIV duration (days)	8 (3-13)	9 (4-14)
SpO_2 (%)	99 (97-100)	99 (97-100)

PEEP: Positive end-expiratory pressure, P support: Support pressure, FiO_2: Fraction of inspired oxygen, NIV: Non-invasive ventilation, SpO_2: Peripheral oxygen saturation
*Mean values

Table 3. Laboratory values by grade 3 of encephalopathy (child + adult)

	Child*	**Adult***
AST (IU/L)	2,250±1,356	6,316±3,367
ALT (IU/L)	2,158±1,285	5,929±4,423
T. Bil (mg/dL)	35±11.2	21.2±11.5
INR	3.21±0.64	4.2±0.6
Procalcitonin (ng/mL)	13.4±10.1	11±13.2
CRP (mg/L)	98±7.1	101±29.3

*Mean ± SD: Mean ± Standard deviation, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, T. Bil: Total bilirubin, INR: International normalized ratio, CRP: C-reactive protein

2 days. In the same study, hospital stay was found to be statistically significantly longer for intubated patients compared with those who were not intubated.

The mechanism of complications that occur in intubated patients with HE has a defined physiological basis, which is circulatory, neurological, and immune dysfunction seen in intubated patients (15). Endotracheal intubation can worsen cardiovascular, cognitive, and immune function due to its increased risk of shock, delirium, infection, and other complications in patients with liver failure (16,17).

Study Limitations

The exclusion of patients with grade 4 HE is the main limitation of this case series. Therefore, we compared our results with the outcomes of intubated HE patients reported in the literature (14,18). We also did not have any patients in our center with HE who were not underwent with non-invasive or invasive respiratory support. This is an understandable situation because our ICU is a part of a liver transplantation center and not an ICU for general supportive aims.

Conclusion

This study supports the use of NIV instead of intubation for grade 3 HE patients with acute and chronic liver failure. The lower risk of complications and mortality of NIV highlights the need for careful consideration when deciding whether to intubate grade 3 HE patients. However, the lack of a control group undermines our courage to declare the need for more detailed retrospective or prospective studies to improve the optimal management of these patients before making definitive clinical recommendations.

Acknowledgments: I would like to thank the Apheresis specialist technicians, Intensive Care Nurses, and Assistant Doctors for their participation

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital (approval number: 336, date: 26.07.2023).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices - İ.O., M.Ç.; Concept - İ.O., M.Ç.; Design - İ.O.; Data Collection or Processing - İ M.Ç., E.K.; Analysis or Interpretation - İ.O., M.Ç., E.K.; Literature Search - M.Ç., E.K.; Writing - İ.O., E.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Egly J, Custodio D, Bishop N, Prescott M, Lucia V, Jackson RE, et al. Assessing the impact of prehospital intubation on survival in out-of-hospital cardiac arrest. Prehosp Emerg Care 2011; 15: 44-9.
2. Mayglothling J, Duane TM, Gibbs M, McCunn M, Legome E, Eastman AL, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg 2012; 73(5 Suppl 4): S333-40.
3. Orso D, Vetrugno L, Federici N, D'Andrea N, Bove T. Endotracheal intubation to reduce aspiration events in acutely comatose patients: a systematic review. Scand J Trauma Resusc Emerg Med 2020; 28: 116.
4. Alshamsi F, Jaeschke R, Baw B, Alhazzani W. Prophylactic Endotracheal Intubation in Patients with Upper Gastrointestinal Bleeding Undergoing Endoscopy: A Systematic Review and Meta-analysis. Saudi J Med Med Sci 2017; 5: 201-9.
5. Kobayashi H, Uchino S, Takinami M, Uezono S. The Impact of Ventilator-Associated Events in Critically Ill Subjects with Prolonged Mechanical Ventilation. Respir Care 2017; 62: 1379-86.
6. Selim A, Kandeel N, Elokl M, Khater MS, Saleh AN, Bustami R, et al. The validity and reliability of the Arabic version of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU): A prospective cohort study. Int J Nurs Stud 2018; 80: 83-9.
7. Hatchimonji JS, Dumas RP, Kaufman EJ, Scantling D, Stoecker JB, Holena DN. Questioning dogma: does a GCS of 8 require intubation? Eur J Trauma Emerg Surg 2021; 47: 2073-9.
8. Li J, Luo Z, Li X, Huang Z, Han J, Li Z, et al. Effect of different transpulmonary pressures guided mechanical ventilation on respiratory and hemodynamics of patients with ARDS: a prospective randomized controlled trial. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2017; 29: 39-44.
9. Ocak I. Value of extracorporeal artificial liver support in pediatric acute liver failure: A single-center experience of over 10 years. Front Pediatr 2023; 11: 979619.
10. Nielsen K, Hansen CM, Rasmussen LS. Airway management in unconscious non-trauma patients. Emerg Med J 2012; 29: 887-9.
11. Guo L, Wang W, Zhao N, Guo L, Chi C, Hou W, et al. Mechanical ventilation strategies for intensive care unit patients without acute lung injury or acute respiratory distress syndrome: a systematic review and network meta-analysis. Crit Care 2016; 20: 226.
12. Gibbs JT, Louissaint J, Tapper EB. Rate of Successful Extubation in Mechanically Ventilated Patients with Cirrhosis and Hepatic Coma. Dig Dis Sci 2022; 67: 5336-44.
13. Levesque E, Saliba F, Ichaï P, Samuel D. Outcome of patients with cirrhosis requiring mechanical ventilation in ICU. J Hepatol 2014; 60: 570-8.
14. Saffo S, Garcia-Tsao G. Early mechanical ventilation for grade IV hepatic encephalopathy is associated with increased mortality among patients with cirrhosis: an exploratory study. Acute Crit Care 2022; 37: 355-62.
15. Ginès P, Fernández J, Durand F, Saliba F. Management of critically-ill cirrhotic patients. J Hepatol 2012; 56 Suppl 1: S13-24.
16. He Q, Wang W, Zhu S, Wang M, Kang Y, Zhang R, et al. The epidemiology and clinical outcomes of ventilator-associated events among 20,769 mechanically ventilated patients at intensive care units: an observational study. Crit Care 2021; 25: 44.
17. Mitasova A, Kostalova M, Bednarik J, Michalcakova R, Kasparek T, Balabanova P, et al. Poststroke delirium incidence and outcomes: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Crit Care Med 2012; 40: 484-90.
18. Sasso R, Lauzon S, Rockey DC. Cirrhotic Patients on Mechanical Ventilation Have a Low Rate of Successful Extubation and Survival. Dig Dis Sci 2020; 65: 3744-52.