

# Early application of non-invasive ventilation for children with pulmonary edema after drowning

Nihan Şık<sup>1</sup>, Hüseyin Bahadır Şenol<sup>1</sup>, aykut caglar<sup>2</sup>, Durgül Yılmaz<sup>1</sup>, and Murat Duman<sup>1</sup>

<sup>1</sup>Dokuz Eylul University Faculty of Medicine

<sup>2</sup>Adnan Menderes University Faculty of Medicine

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## Abstract

**Background:** The present study aimed to assess the efficacy of non-invasive ventilation (NIV) on the clinical course, oxygenation, need for invasive mechanical ventilation (IMV), and outcomes for children with pulmonary edema after drowning. **Methods:** We conducted a retrospective chart review. Children who were referred to the pediatric emergency department due to drowning-related pulmonary edema and underwent NIV between May 2014 and October 2020 were included. Demographics, vital signs, clinical findings, and results of laboratory and radiologic investigations were recorded. Patients were divided into 6 groups using the Szpilman classification system. The need for IMV, the need for pediatric intensive care unit (PICU) admission, and the length of NIV treatment and stay in the PICU were recorded for each patient. **Results:** Twenty-five patients were enrolled. According to the Szpilman classification, 13 (52.0%) patients were evaluated as grade 3 and 12 (48.0%) as grade 4. All patients were treated with bi-level positive airway pressure in the spontaneous/timed mode. A significant increase in oxygen saturation (SpO<sub>2</sub>) and SpO<sub>2</sub>/fraction of inspired oxygen ratios was observed from the beginning of NIV treatment and this increase was also observed for the 2nd and 4th hours. There was a decrease in respiratory rate at the 4th hour of NIV treatment. No patient subsequently deteriorated to IMV. **Conclusion:** We have reported a favorable clinical course of drowning patients who underwent early use of NIV in the pediatric emergency department. Management of drowning patients with pulmonary edema by NIV with close follow-up can be successfully applied in selected cases.

## Early application of non-invasive ventilation for children with pulmonary edema after drowning

Nihan Şık, MD<sup>1</sup>, Hüseyin Bahadır Şenol, MD<sup>2</sup>, Aykut Çağlar, MD<sup>3</sup>, Durgül Yılmaz, Prof.<sup>1</sup>, Murat Duman, Prof.<sup>1</sup>

<sup>1</sup> Division of Pediatric Emergency Care, Department of Pediatrics, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey.

<sup>2</sup> Department of Pediatrics, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey.

<sup>3</sup> Division of Pediatric Emergency Care, Department of Pediatrics, Adnan Menderes University, Faculty of Medicine, Aydın, Turkey.

Corresponding author: Prof. Dr. Murat Duman, Division of Pediatric Emergency Care, Department of Pediatrics, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey. e-mail: mduman@deu.edu.tr.

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**Running head :** Non-invasive ventilation for drowning children

## INTRODUCTION

Drowning is still a common cause of accidental death worldwide. According to the World Health Organization, drowning accounts for approximately 450000 deaths per annum globally and 97% of these deaths occur in low- and middle-income countries <sup>1-3</sup>. It was estimated that a further 1.3 million disability-adjusted life years are lost per annum as a result of premature death or disability from drowning <sup>4</sup>. Over half of drowning deaths occur in the pediatric population; it is the leading cause of deaths from unintentional injury in children aged between 1 and 4 years and the second leading cause for children aged 5 to 14 years in the United States, with a mortality rate of 3 per 100000 events <sup>5</sup>. Drowning is defined as “a process resulting in primary respiratory impairment from submersion/immersion in a liquid medium” <sup>6</sup>. After submersion, the victim initially holds his or her breath before laryngospasm. In this process, the victim swallows large amounts of water as a result of breath-holding/laryngospasm, and hypoxia and hypercapnia develop. Eventually, these reflexes abate and the victim aspirates water into the lungs; this process leads to worsening hypoxemia. Without rescue and restoration of ventilation, cardiac arrest occurs as a consequence of hypoxia. Thus, the first and most important treatment is the alleviation of hypoxemia. The current definition for drowning highlights the role of acute respiratory failure (ARF) in the pathophysiology. Pulmonary edema and ARF are the main components of the pathophysiology of drowning, which frequently evolves to acute respiratory distress syndrome (ARDS). Due to the alveolar-capillary membrane damage from aspiration, transudation of proteinaceous fluid into the alveoli may occur. This process may result in non-cardiogenic pulmonary edema with alteration of the ventilation/perfusion ratio, increased intrapulmonary shunt, and decreased pulmonary compliance with increased respiratory work. Finally, pulmonary damage may evolve into ARDS, and sometimes cardiac arrest <sup>7</sup>.

Treatment strategies for a drowning patient emphasize the importance of rapidly reaching the patient to initiate respiratory support <sup>8</sup>. In an awake, alert patient with hypoxemia, the first line of therapy is administering supplemental oxygen. If supplemental oxygen fails to provide adequate oxygenation, then more aggressive therapy is required. Current practice recommends a lung-protective ventilation strategy similar to that used for patients with ARDS, on the basis that the pattern of lung injury is similar for drowning <sup>9</sup>. However, an optimal strategy to support the respiratory function is still lacking <sup>10,11</sup>.

Applications of non-invasive ventilation (NIV) have increased in recent years, with a highly variable frequency of use. Strong evidence supports NIV use for ARF to prevent invasive mechanical ventilation (IMV), to facilitate extubation in patients with acute exacerbations of chronic obstructive pulmonary disease, and to avoid IMV in cases of acute cardiogenic pulmonary edema and in immunocompromised patients. Weaker evidence supports NIV application for post-extubation or post-operative ARF or ARF due to asthma exacerbations <sup>12</sup>. However, there are limited data on the use of NIV treatment as a ventilation strategy for drowning patients.

Considering the lack of information about NIV use for drowning, we aimed to assess the efficacy of NIV on the clinical course, oxygenation, need for IMV, and outcomes for children who presented to the pediatric emergency department with pulmonary edema after drowning.

## MATERIALS AND METHODS

### Study design

We performed a single-center retrospective chart review in the pediatric emergency department of the Dokuz Eylul University Faculty of Medicine, a tertiary hospital with approximately 120000 pediatric emergency

department admissions per annum. The study was approved by the Institutional Review Board of the Dokuz Eylul University Faculty of Medicine (approval number: 2020/01-11).

Children aged between 0 and 18 years who were referred to the pediatric emergency department due to drowning-related pulmonary edema and underwent NIV treatment between May 2014 and October 2020 were included. The International Classification of Diseases (ICD) codes for drowning, near drowning, immersion, and submersion injuries were used to identify patients. We obtained information from a computer database, electronic medical records, medical charts, and nursing records of the cases. Patients were excluded if they had chronic pulmonary, cardiac, or neuromuscular diseases; if they were transferred from another hospital; and if there were insufficient data.

The following data were recorded: demographic data; initial body temperature and Glasgow Coma Scale (GCS) score; heart rate; respiratory rate (RR); peripheral oxygen saturation (SpO<sub>2</sub>); blood pressure; fraction of inspired oxygen (FiO<sub>2</sub>); SpO<sub>2</sub>/FiO<sub>2</sub> (S/F) ratio at 0, 1, 2, 4, 8, and 12 hours; clinical findings; and results of the laboratory and radiologic investigations and applied treatments. Using findings at arrival to the pediatric emergency department, patients were divided into 6 groups using the Szpilman classification system as follows: grade 1, normal pulmonary auscultation with coughing; grade 2, abnormal pulmonary auscultation with rales in some pulmonary fields; grade 3, pulmonary auscultation of acute pulmonary edema without arterial hypotension; grade 4, pulmonary auscultation of acute pulmonary edema with arterial hypotension; grade 5, isolated respiratory arrest; and grade 6, cardiopulmonary arrest <sup>13</sup>.

Non-invasive ventilation strategies were divided into two groups as continuous (CPAP) or bi-level (BiPAP) positive airway pressure [spontaneous, spontaneous/timed (ST), or timed mode for NIV ventilators (Philips Respironics V60 ventilator, USA); A/C pressure or PSV mode for conventional ventilators with NIV option (Maquet Servo I, Germany)].

The time between arrival to the pediatric emergency department and starting NIV application, total duration time and observed side effects during NIV treatment, need for IMV, need for pediatric intensive care unit (PICU) admission, and total length of stay in the PICU and in the hospital were recorded for each patient.

## Statistical analysis

All statistics were analyzed using SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). Data were presented as means with standard deviations (SDs) or medians with interquartile ranges (IQRs) and 25th-75th percentiles. The Mann-Whitney U test was used to compare nonparametric variables and Student's *t*-test was used for parametric data. The paired sample *t*-test and repeated measure ANOVA, followed by the post hoc Tukey test, were used to evaluate changes of variables. Values of *p* < 0.05 were considered statistically significant.

## RESULTS

There were 27 patients during the study period and, of them, 25 were enrolled. The median age was 6.7 years (IQR: 4.1-11.8). Of the patients, 18 (72.0%) were male. Seventeen (68.0%) drownings occurred in saltwater and 8 (32.0%) in freshwater. The initial GCS score was 15 for 14 (56.0%) patients, 14 for 6 (24.0%) patients, 13 for 3 (12.0%) patients, and 12 for 2 (8.0%) patients. According to the Szpilman classification, 13 (52.0%) patients were evaluated as grade 3 and 12 (48.0%) as grade 4. Four patients (16.0%) received CPR at any time between rescue from the scene and the hospital, the duration ranging between 1.5 and 5 minutes. The clinical and laboratory findings of the patients are summarized in Table 1. The chest X-rays of all patients revealed acute pulmonary edema. Treatment with 10-12 L/min oxygen by a non-rebreather face mask with a reservoir was administered for all children during the time interval between arrival to the pediatric emergency department and the start of NIV application.

All patients received BiPAP therapy in ST mode using oronasal or full-face masks, inspiratory positive airway pressure (IPAP) in the range of 8-18 cmH<sub>2</sub>O, and expiratory positive airway pressure (EPAP) in the range of 4-10 cmH<sub>2</sub>O. For 13 (52.0%) patients, BiPAP therapy was started in the first hour, while for 12 (48.0%) it was started between 1 and 4 hours after arrival to the pediatric emergency department. A significant

increase in S/F ratios was observed from the beginning of NIV treatment and this increase was also observed for the 2nd, 4th, 8th, and 12th hours ( $p < 0.05$ ) (Figure 1). A significant increase in SpO<sub>2</sub> values was also observed from the start of NIV use and the same increase was observed for the 2nd and 4th hours ( $p < 0.05$ ) (Figure 2). There was a decrease in RR at the 4th hour of NIV treatment ( $p < 0.05$ ) (Figure 3). The median length of NIV use was 7.0 hours (IQR: 5.2-12.5). No side effects were observed during NIV treatment. Of all NIV applications, no patient subsequently deteriorated to IMV.

Of the 25 patients, 10 (40.0%) were admitted to the PICU, and 15 (60.0%) of them were observed in the pediatric emergency department and then discharged. All patients who were admitted to the PICU had Szpilman scores of grade 4. Of the 15 patients who were discharged from the emergency department, 13 (86.6%) of them had a Szpilman score of grade 3 and 2 (13.4%) had a score of grade 4; children who were admitted to the PICU had higher Szpilman scores ( $p < 0.001$ ). The mean duration of NIV treatment was also longer in children who were admitted to the PICU (admitted:  $13.4 \pm 4.8$  hours, not admitted:  $6.1 \pm 2.6$  hours;  $p < 0.001$ ). There was no difference in PICU admission rates, duration of NIV treatment, or length of stay in the PICU or the hospital for drownings that occurred in fresh versus saltwater. The mean length of stay in the PICU was  $19.3 \pm 3.0$  hours and the median length of stay in the hospital was 28.0 hours (IQR: 20.0-53.0).

## DISCUSSION

Non-invasive ventilation has profoundly changed the approach to patients with ARF over the last 20 years, reducing hospital stay and avoiding the complications of IMV <sup>14</sup>. The overall effectiveness of NIV use in avoiding intubation was reported to range between 69% and 79% in randomized studies <sup>15</sup>. It was also reported that NIV had the potential to reduce the length of hospitalization and associated costs for adults with chronic obstructive pulmonary diseases and ARF <sup>16</sup>.

For drowning patients with Szpilman scores of grades 3 and 4, administering high-flow oxygen therapy and/or mechanical ventilation was proposed <sup>17</sup>. Despite the absence of recommendations for NIV use for cases of drowning-related ARF, NIV was previously applied with safety and efficacy for drowning patients <sup>10</sup>. Similar to IMV, NIV provides airway pressure to prevent atelectasis and support respiratory muscle use while preventing hypoxemia. Its value might be based on the use of positive end-expiratory pressure (PEEP) over oxygen supplementation in the clinical course <sup>10</sup>.

We could find very limited relevant data in the literature; to our knowledge, there is only one study evaluating adults and a few case reports of adults and children describing the use of NIV for drowning patients <sup>10,11,18-20</sup>. Our study has the largest number of pediatric cases to evaluate the efficacy of NIV treatment to date.

Michelet et al. evaluated adults with drowning-related ARF in intensive care units and assessed the efficacy of ventilator strategies used. They declared that their cases were grades 3 to 5 according to the Szpilman classification, and of the 25 patients who underwent NIV treatment, 4 were intubated due to respiratory or neurological deterioration. They reported similar neurological outcomes and correction of hypoxemia and acidosis comparing patients treated with NIV versus IMV after drowning. Furthermore, patients who were treated with NIV had a lower incidence of infection and decreased length of intensive care unit and hospital stay <sup>10</sup>.

In our study, all children were treated using BiPAP, and none of them deteriorated to require IMV. The Szpilman classification was grade 3 or 4 for our cases. Our results demonstrate that NIV treatment was associated with rapid improvement in the early phase of oxygenation. Considering drowning-related ARF, which is characterized by profound but reversible hypoxemia without relevant hypercapnia, early application of NIV may aid in the hastening of clinical improvement.

Our decision to use NIV was made on the basis of confidence that its early application could be a preventive treatment strategy, with the reversible nature of drowning, for eligible patients without complete loss of consciousness to reduce morbidity <sup>10,20</sup>. We preferred to use BiPAP to reduce the respiratory workload for patients who were tachypneic, whereas the application of PEEP was repeatedly suggested and CPAP was

used as frequently as BiPAP in pre-hospital settings <sup>10</sup>. However, the use of NIV for drowning patients with altered mental status should be considered with a high index of caution because there may be increased risk of vomiting and aspiration <sup>9</sup>. The initial neurological assessment appears to be of paramount importance to initially choose the ventilator strategy. The occurrence of neurological deterioration is an indication for IMV rather than NIV use. Gregorakos et al. evaluated adults with drowning-related ARF in the emergency department and concluded that IMV could be avoided in non-comatose patients <sup>18</sup>. The improvement of neurological status as well as the lower incidence of hemodynamic instability could facilitate alternative treatment choices such as NIV <sup>14-15</sup>. At this point, the Szpilman score, which is first based on neurological status and secondly on respiratory and hemodynamic status, could guide the physician for the choice of ventilation strategy.

Ruggeri et al. reported successful NIV use for a 45-year-old man who had ARF secondary to drowning after an epileptic crisis <sup>11</sup>. Dottorini et al. reported 13- and 19-year-old drowning patients without loss of consciousness who presented with radiographic appearance of pulmonary edema and were successfully treated with nasal CPAP therapy, highlighting the importance of neurological status in the choice of ventilation strategy <sup>19</sup>. Çağlar et al. also reported 5-, 12-, and 13-year-old drowning patients with pulmonary edema who were successfully treated with BiPAP therapy in the pediatric emergency department. The Szpilman classification was grade 3 or 4 for these patients <sup>20</sup>.

We acknowledge the limitations related to the retrospective nature of our study. Information was missing for some patients. Also, we only evaluated the patients who underwent NIV treatment. If we had a control group, we could have compared the hastening of clinical improvement, morbidity, complications, and length of stay in the hospital for NIV treatment.

We have reported a favorable clinical course of drowning patients who underwent early use of NIV in a pediatric emergency department. Management of drowning patients by NIV with close follow-up can be successfully applied in selected cases. The choice of NIV appears to be a valuable preventive ventilation strategy for reducing IMV and implicitly reducing morbidity resulting from the complications of IMV. Nevertheless, multicenter studies with larger case series are required to determine the effectiveness of choices for ventilator strategy and to reveal the benefits of early application of NIV for drowning patients in pediatric emergency settings, and to help shape treatment guidelines.

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