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Delirium during Noninvasive Positive Pressure Ventilation: A Prospective Observational Study

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Abstract

Background: Noninvasive positive pressure ventilation (NPPV) has been used to treat acute respiratory failure in intensive care units (ICU), while some patients need tracheal intubation because of not only underlying diseases but also delirium. Delirium in patients being mechanically ventilated via endotracheal tubes has been subject to concern and investigated in numerous studies, however in patients receiving NPPV has been little studied. The aim of the study was to discover the incidence of delirium in NPPV patients.

Methods: Adult patients who received NPPV were enrolled. Basic profiles of patients, underlying diseases, indication of NPPV, duration of NPPV, length of stay in ICU, NPPV settings, administration of sedative agents and outcome were collected. Delirium was diagnosed with the Confusion Assessment Method for the ICU (CAM-ICU) by attending nurses.

Results: Forty-three adult patients who received NPPV were enrolled. For all patients, NPPV was applied via full face mask. The diagnosis of 30 patients (69%) was cardiogenic pulmonary edema. Delirium was observed in 16 patients (37%). Patients with delirium were older than those without (78.4 vs. 69.5 years old, p = 0.031). Thirty-one patients (72%) were successfully weaned from NPPV. NPPV failure rate was 38% for patients with delirium and 22% for patients without (p = 0.313). Dexmedetomidine was administered to 26 (61%) patients during NPPV.

A few studies reported the incidence of delirium during NPPV for hypercapnic respiratory failure. We found an incidence of delirium similar to patients with hypercapnic respiratory failure. Dexmedetomidine was most frequently administered because it carried minimal risk of respiratory depression, while we are unable to unconditionally rely on the safety of dexmedetomidine during NPPV.

Conclusions: The incidence of delirium in patients who received NPPV for normocapnic respiratory failure was as high as NPPV for hypercapnic patients. While it was lower than for patients receiving invasive mechanical ventilation.

Keywords: CAM-ICU; Dexmedetomidine; Cardiogenic pulmonary edema

Background

For two decades, noninvasive positive pressure ventilation (NPPV) has been used to treat acute respiratory failure in intensive care units (ICU). Use of NPPV prevents intubation and decreases mortality, especially for patients with cardiogenic pulmonary edema (CPE) or acute exacerbation of chronic obstructive pulmonary disease (COPD) and for immunocompromised patients with respiratory failure. Some patients need tracheal intubation, however, not only to treat underlying diseases but also for other conditions, including delirium [1,2].

Delirium, which is generally reversible, occurs when there are rapid changes in brain functioning. The pathophysiology of delirium in critical illness is associated with a variety of causes, but evidence shows that delirium is associated with increased morbidity and mortality both in the ICU and in the wider hospital. In addition, delirium disturbs the daily life of patients after hospital discharge [3]. Recently, delirium in patients being mechanically ventilated via endotracheal tubes has been subject to concern and investigated in numerous studies, which report delirium in of 60% to 80% of such patients [4-7]. Benzodiazepine is considered to increase the risk of delirium: in general, it is less frequently administered to NPPV patients. Even so, delirium in patients receiving NPPV has been little studied, and neither has the use of analgesics and sedatives and their efficacy during NPPV been comprehensively evaluated.

We undertook this study to discover the incidence of delirium in our NPPV patients and to reveal our own patterns of administration of analgesics and sedatives to them.

Methods

This prospective observational study was carried out from February 2012 to January 2014 at a medical/surgical ICU in a university hospital. The study protocol was approved by the institutional review board of Tokushima University Hospital. Informed consent was not required because all measurements and procedures were part of daily routine practice.

Adult patients who were admitted to the ICU and received NPPV were enrolled. Exclusion criteria were younger than 20 years old, post-extubation respiratory failure, administration of ambulatory NPPV therapy, and signs of neuromuscular disorder. Patients who required intubation within two hours were also excluded.

Initial administration of NPPV was decided by attending physicians, who recorded underlying diseases and initial NPPV settings. IPAP level for spontaneous/timed mode, PEEP level for continuous positive airway pressure mode, and F_IO_2. For all patients, BiPAP Vision or V60

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(both Respironics Inc., Murrysville, PA) were used for NPPV via full face mask. Acute physiology and chronic health evaluation (APACHE) II scores were also recorded. Arterial blood gases were measured at start of NPPV. At 8-hour intervals until NPPV was discontinued, nurses recorded the need of physical restraint and carried out evaluation using the Confusion Assessment Method for the ICU (CAM-ICU). In data analysis, we also included the types of analgesics and sedatives administered and any recorded adverse effects, the duration of NPPV, the length of ICU stay, and respiratory status at ICU discharge. The sedation protocol we normally use for intubated patients was not applied to NPPV patients: administration of analgesics and sedatives was decided by attending physicians.

For statistical analysis, continuous variables were expressed as mean ± standard deviation and compared using unpaired t-test. Categorical variables were expressed as numbers and percentages and compared using Fisher's exact test. Differences of p less than 0.05 were considered statistically significant.

Results

Patient characteristics

During the study period, 43 patients were included (Table 1). All patients began NPPV on the day of ICU admission. The diagnosis of the majority (69%) of these patients was cardiopulmonary edema.

Incidence of delirium, analgesics and sedatives, and physical restraint

Delirium was observed in 16 patients (37%): for 13, delirium developed during the first night in the ICU. Patients with delirium were older than those without (78.4 vs. 69.5 years old, p = 0.031). No differences between those with and without delirium were found in relation to sex, APACHE II score, diagnosis at admission, arterial blood gas, and initial NPPV settings (Table 2).

None of the patients received analgesics. Sedatives were administered to 26 patients (61%), most of whom received dexmedetomidine (DEX): 22, only DEX; 1, DEX and haloperidol; and 2, DEX, haloperidol, and midazolam. Haloperidol alone was administered to the remaining patient. Sedatives were administered only at night to 15 patients, and the other 11 also received them during the day. Sedatives were given to 15 patients before signs of delirium, either owing to restlessness or because the patient, wanting to go to sleep, requested sedation. Two patients sedated without delirium later developed it.

Six patients (14%) were physically restrained. Physical restraint and sedation were started concurrently in 4 patients. Physical restraint was applied prior to sedation in 2 patients.

Outcomes

Thirty-one patients (72%) were successfully weaned from NPPV and discharged from the ICU. Ten patients were switched to invasive ventilation, but this was owing to respiratory failure or fatigue rather than to delirium. Of the patients who required intubation, 5 were successfully extubated, 2 were tracheostomized, and 3 died. Two discharged patients were withdrawn from the ICU (Table 3). NPPV failure rate was 38% for patients with delirium and 22% for patients without (p = 0.313).

The duration of NPPV was 1.6 ± 1.2 days and the length of ICU stay was 5.8 ± 8.3 days. While patients with delirium underwent NPPV for longer than patients without (2.2 vs. 1.3 days, p = 0.042), no statistically significant difference was found in length of ICU stay (7.6 vs. 4.8 day, p = 0.295).

DEX was discontinued for 3 patients who showed hypotension.

Age (year)	72.8 ± 13.2
Gender, male/female	27/16
APACHE II score	21.0 ± 5.9
Diagnosis, n (%)	
Cardiogenic pulmonary edema	30 (69)
Acute exacerbation of COPD	2 (5)
Others	11 (26)
pH	7.390 ± 0.097
$PaCO_2$, mmHg	41.2 ± 17.1
PaO_2, mmHg	106.6 ± 64.7
PaO_2/F_IO_2, mmHg	197.3 ± 90.3
NPPV initial setting	
IPAP, cmH_2O	8.1 ± 1.9
F_IO_2	0.61 ± 0.21

Table 1: Patient characteristics at admission.

Incidence of delirium, n (%)	16 (37)
Sedative agents, n (%)	26 (61)
DEX, n	22
DEX+haloperiol+midazolam	2
DEX+haloperidol	1
Haloperidol	1
Physical restraint, n (%)	6 (14)

Table 2: Incidence of delirium, use of sedation, and physical restraint.

Successfully weaned from NPPV, n (%)	31 (72)
Switched to invasive ventilation, n (%)	10 (23)
Extubated, n	5
Tracheostomy, n	2
Dead, n	3
Withdrawn, n (%)	6 (14)

Table 3: Outcome at ICU discharge.

Respiratory depression, including upper airway obstruction and impaired secretion clearance was not observed.

Discussion

We observed delirium during NPPV in 16 (37%) of 43 patients. Sedation, most often DEX, was administered to 61% of the patients.

NPPV is widely used in the ICU, but the failure rate is relatively high. Delirium, common in the ICU, is associated with NPPV failure [1,2]. In reports, the general incidence of delirium in the ICU is in the range of 16% to 46% [8-10]. For patients receiving invasive mechanical ventilation, the incidence is higher: 60% to 80% [4-7]. Delirium in during NPPV, however, is less well known. Without describing diagnostic criteria, Rozzini and colleagues have reported an incidence of 38% (44 of 115 patients). Meanwhile, Campo and colleagues assessed 27 patients using CAM-ICU, and observed delirium in 9 patients (33%). Even though these studies were of NPPV used for hypercapnic respiratory failure, the incidence of delirium was similar to the present study, which, as far as we know, is the first observational study of delirium during NPPV for normocapnic respiratory failure. While we found an incidence of delirium similar to patients with hypercapnic respiratory failure, it was lower than for patients receiving invasive mechanical ventilation.

Sedative agents are frequently administered to intubated delirious patients. During NPPV, however, respondents to a Web-based survey [11] generally reported infrequent administration of sedatives. During NPPV, physicians are most concerned about sedation causing or exacerbating respiratory depression, including upper airway obstruction

and impaired secretion clearance. DEX is widely used because it carries minimal risk of respiratory depression. In addition, delirium is less often observed in patients undergoing invasive ventilation if DEX rather than midazolam is administered [12,13]. Because there have been so few case reports, we are unable to unconditionally rely on the safety of DEX during NPPV [14]. In our study, however, no patients experienced respiratory depression: this suggests that DEX may be appropriate for sedation during NPPV.

There are some limitations in this study. First, sedation was used in 15 patients who showed no signs of delirium. In this group, only 2 patients (13.3%) developed delirium. If sedation had not been used, the overall incidence might have been higher. Second, there were no protocols for NPPV weaning or criteria for switching to intubation. This lack might make our results for duration of NPPV less sound. Third, we did not collect data to evaluate delirium in patients in our ICU who received invasive mechanical ventilation during the study period, and we are not sure if the incidence of delirium during NPPV was lower than that during invasive mechanical ventilation.

In summary, the incidence of delirium in patients who received NPPV for normocapnic respiratory failure was lower than has been reported for patients receiving invasive mechanical ventilation. DEX may be effective in preventing delirium for NPPV patients who do not have respiratory depression.

Author Contributions

Literature search: MO and MN; Data collection: MO; Study design: MO, and MN; Analysis of data: MO, NO, MI, and MO; Manuscript preparation: MO, NO, MI, and MN; Review of manuscript: MN. All authors read and approved the final manuscript.

Competing Interest

The authors declare that they have no competing interests.

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