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RESPIRATORY SUPPORT IN SEVERE TRAUMATIC BRAIN INJURY (literature review)

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Ключевые слова: *респираторная поддержка, черепно-мозговая травма, механическая вентиляция легких, искусственная вентиляция легких, отлучение от респиратора, газовый состав крови*

Abstract. Respiratory support in severe traumatic brain injury (literature review). Krishtafor D.A., Klygunenko O.M., Kravets O.V., Yekhalov V.V., Krishtafor A.A. *Patients with traumatic brain injury (TBI) are the largest group of victims at the emergency departments. Up to 20% of patients with severe TBI require endotracheal intubation and prolonged mechanical ventilation. The ventilation parameters choice should be focused on the normal arterial blood gas composition. Hypoxia causes secondary damage to the brain tissue, and hyperoxia carries risks of oxygen toxicity. Hypercapnia leads to cerebral vasodilatation, increased intracranial pressure (ICP) and the risk of cerebral edema. Hypocapnia promotes cerebral vasoconstriction, which reduces cerebral blood flow and ICP, but also leads to cerebral tissue ischemia, so prolonged hyperventilation in TBI is not currently recommended. Patients with TBI often require sedation to synchronize with the respirator. The drugs of choice are propofol and midazolam. Routine use of muscle relaxants is not recommended. The initial ventilation mode should provide a certain respiration rate to achieve normocapnia, while allowing the patient to make breathing attempts. Support ventilation modes are used while weaning from mechanical ventilation. Promising in predicting extubation success is the assessment of the VISAGE score, which includes visual pursuit, swallowing, age, and the Glasgow coma score. Modern principles of respiratory support in severe TBI include: tracheal intubation by Glasgow coma score ≤8 ; early mechanical ventilation; PaO_2 80-120 mm Hg (SaO_2 ≥95%); $PaCO_2$ 35-45 mm Hg; tidal volume ≤8 ml/kg; respiratory rate ≈20/min; PEEP ≥5 cm H_2O; head elevation by 30°; sedation in poor synchronization with the respirator; weaning through support ventilation modes; extubation when reaching 3 points on the VISAGE scale; early (up to 4 days) tracheotomy in predicted extubation failure.*

Реферат. Респіраторна підтримка при тяжкій черепно-мозковій травмі (огляд літератури). Кріштафор Д.А., Клигуненко О.М., Кравець О.В., Єхалов В.В., Кріштафор А.А. *Пацієнти з черепно-мозковою травмою (ЧМТ) є найбільшою групою постраждалих у відділеннях невідкладної допомоги. До 20% з них потребують ендотрахеальної інтубації та тривалої механічної вентиляції легень. При виборі параметрів вентиляції орієнтуватися слід на нормальний газовий склад артеріальної крові, щоб уникнути вторинного пошкодження мозкової тканини. Для синхронізації з респіратором пацієнти з ЧМТ нерідко потребують седації. Препаратами вибору є пропофол та мідазолам. Рутинне застосування міорелаксантів не рекомендоване. Початковий режим вентиляції має забезпечувати певну частоту дихання для досягнення нормокапнії, у той же час дозволяючи пацієнту робити самостійні вдихи. Допоміжні режими використовуються при відлученні від респіратора. Перспективною щодо прогнозування успіху екстубації є шкала VISAGE, яка включає стеження поглядом, ковтальний рефлекс, вік та оцінку за шкалою ком Глазго. Сучасні принципи респіраторної підтримки при тяжкій ЧМТ включають: інтубацію трахеї при оцінці за шкалою ком Глазго ≤8 балів; ранню механічну вентиляцію; PaO_2 80-120 мм рт. ст. (SaO_2 ≥95%); $PaCO_2$ 35-45 мм рт. ст.; дихальний об'єм ≤8 мл/кг; ЧД≈20/хв; PEEP≥5 см H_2O; приподнятий на 30° головний кінець ліжка; седацію при поганій синхронізації з респіратором; відлучення від респіратора через допоміжні режими вентиляції; екстубацію при досягненні 3 балів за шкалою VISAGE; ранню (до 4 діб) трахеотомію при прогнозованих труднощах з екстубацією.*

Patients with traumatic brain injury (TBI) are the most common group of trauma victims admitted to the emergency departments. Many patients with severe TBI die at the prehospital phase: in fact, about

90% of prehospital trauma deaths are due to the fatal TBI. In the overall structure of mortality from trauma, TBI accounts for 68%. Survivors often have neurological disorders that affect their work and social activity and can lead to disability [2, 5].

Severe TBI is clinically determined by depression of consciousness by a Glasgow score of 8 or less [5]. Due to the suppression of swallowing and cough reflexes, the risk of aspiration increases significantly, which requires airway protection. In addition, the ability of the respiratory center to respond to changes in metabolic needs of the brain is impaired, leading to central respiratory disorders and inability to maintain normal blood gas composition, even if spontaneous breathing is preserved [11]. During the first days after injury, hypoxemia and hypo/hypercapnia lead to secondary brain damage, which worsens the prognosis. Possible severe psychomotor agitation, which requires deep sedation, should also be considered. As a result, 20% of patients with brain damage require endotracheal intubation and mechanical ventilation [32].

The aim of this review was to determine modern principles of respiratory support in severe TBI.

Duration of mechanical ventilation in TBI patients is significantly longer than in non-neurological patients [8, 13, 14]. Brain damage leads to a systemic inflammatory response in which inflammatory cells migrate to the airways and alveolar spaces. Neurogenic pulmonary edema, neurotransmitter release, or side effects of the neuroprotective drugs are also additional potential mechanisms of lung injury [12, 23]. These pathophysiological changes and prolonged ventilation lead to an increased risk of acute respiratory distress syndrome (ARDS) and ventilator-associated pneumonia (VAP), which, in turn, prolong the duration of the intensive care unit (ICU) and hospital stay, and increase mortality [8, 12-14].

Protective ventilation strategy in ARDS allows permissive hypoxemia, when the target levels of PaO_2 and SaO_2 are reduced so as to prevent tissue hypoxia, but at the same time to minimize the toxic effects of high oxygen concentrations [10, 16]. This implies maintaining SaO_2 at least at 82%-88%, which roughly corresponds to PaO_2 of 48-57 mm Hg [10, 26]. But with brain damage, hypoxia should be avoided because it causes secondary damage to the brain tissue [10]. Oxygenation management in brain injury involves an increase in FiO_2 to obtain PaO_2 >60 mm Hg [11].

The question of how hyperoxia affects brain damage still remains open. Most authors define safe PaO_2 limits between 60 and 300 mm Hg, which corresponds to SaO_2 ≥90% [26, 27, 35]. Thus, if PaO_2 exceeds 300 mm Hg, FiO_2 must be reduced. Optimal PaO_2 levels are between 80 and 120 mm Hg (SaO_2 ≥95%) [26, 32].

$PaCO_2$ is the most important determinant of cerebral blood flow (CBF). Normally, CBF has a linear correlation with $PaCO_2$ at its levels from 20 to 80 mm Hg [11]. Hypercapnia leads to cerebral vasodilatation, increased intracranial pressure (ICP) and the risk of cerebral edema. Hypocapnia promotes cerebral vasoconstriction, which reduces CBF (by an average of 3% for every 1 mm Hg) and ICP [19]. Therefore, traditionally, in order to reduce ICP in patients with severe TBI, it was recommended to use moderate hyperventilation with a target $PaCO_2$ of about 25 mm Hg. This was achieved mainly by increasing tidal volume to 9-10 ml/kg [32]. But in addition to a decrease in ICP, decreased CBF and vasoconstriction also lead to cerebral tissue ischemia. Traditionally, it has been considered that in patients with severe TBI cerebral edema predominates over ischemia. However, recent studies have shown a high incidence of cerebral ischemia in patients with severe TBI, which is exacerbated by hypocapnia [24]. Moreover, in severe TBI the cerebral vessels response to $PaCO_2$ changes may be exaggerated, and the $PaCO_2$ excursion from the normal range can have critical consequences [19].

According to the latest version of the Guidelines for the management of severe TBI [11], prolonged prophylactic hyperventilation with $PaCO_2$ ≤25 mm Hg is not recommended in TBI patients. Patients with severe TBI must receive normoventilation with target $PaCO_2$ of 35-45 mm Hg. Short-term hyperventilation is acceptable only in cases of rapid clinical deterioration, which indicates the risk of brainstem herniation. At the same time, a protective ventilation strategy should be followed, increasing the minute ventilation not with the tidal volume, but with the respiratory rate [7].

Protective ventilation with small tidal volumes has shown many benefits for patients with and without ARDS [15]. But ARDS ventilation strategy involves permissive hypercapnia ($PaCO_2$ up to 67 mm Hg), which is unacceptable in TBI [16, 17]. Because of this, such patients were excluded from all large clinical trials for protective ventilation [20]. Observational studies have shown that an increase in tidal volume over 8 ml/kg in patients with TBI leads to ventilator-induced lung injury, ARDS and worse prognosis [28]. Thus, a protective ventilation strategy can be used in patients with TBI if it provides a normal arterial blood gas.

It is believed that an increase in intrathoracic pressure with increasing PEEP can cause an ICP increase due to direct pressure transfer, decreased venous return, increased venous pressure and decreased cardia output. As a result, traditional ventilation strategies in brain injury involved low or

zero PEEP. But there is very little evidence to support this approach. At the same time, in many studies, an increase in PEEP above 5 cm H_2O did not correlate with ICP, but improved brain tissue oxygenation [7]. Thus, the practice of "zero PEEP" in patients with TBI is not justified. The European Society of Intensive Care Medicine consensus recommends using the same PEEP levels in patients with brain damage as in those without it. Also, 30º head elevation promotes intracranial venous drainage, and tight endotracheal tube fixation around the neck and extremes of neck rotation should be avoided [32].

As noted above, patients with TBI often require sedation. The range of indications for sedation in TBI is quite wide: induction for safe endotracheal intubation on admission; control of psychomotor agitation in concomitant alcohol or drugs intoxication; reduction of ICP; seizure control; respirator synchronization and ventilation optimization; target temperature management; reduction of paroxysmal sympathetic activity [11, 29]. In a study by Luo X.Y. et al (2020) episodes of respirator asynchrony were present in 96% of patients with acute brain damage [25]. Poor synchronization with the respirator can cause both baro- and volutrauma, as well as undesirable increases in ICP due to intrathoracic pressure changes [4, 33, 34].

Propofol and midazolam moderately reduce ICP and CBF, while maintaining CBF autoregulation. Barbiturates significantly reduce ICP and CBF. Dexmedetomidine has almost no effect on ICP, but experience with its use in neurosurgery is still limited. Ketamine has minimal effect on ICP and CBF, has analgesic properties and does not suppress respiration, but its use is limited due to its side effects. Based on this, the drugs of choice for sedation in TBI patients are propofol and midazolam, and barbiturates in refractory intracranial hypertension [11, 29].

Muscle relaxants can improve synchronization with the respirator, if it can not be achieved by sedation only [33]. However, routine use of muscle relaxants in neurosurgical patients is not recommended. They complicate the neurological assessment, mask seizure manifestations, and their long-term use carries the risk of polyneuropathies and myopathies [6, 30]. If the administration is indicated, non-depolarizing benzylisoquinoline muscle relaxants, such as atracurium, should be preferred. Depolarizing agents increase ICP, and when the blood-brain barrier is damaged, aminosteroid non-depolarizing agents (pancuronium, vecuronium) may have an epileptogenic effect due to the accumulation of cytosolic calcium [33].

The initial ventilation mode in a TBI patient should provide a certain RR to achieve the target $PaCO_2$, while allowing the patient to make breathing attempts on their own. Support ventilation modes are used as a stage of weaning from mechanical ventilation and in patients with preserved spontaneous breathing and normal blood gas levels, who are intubated for airway protection [31].

Final weaning from respirator and extubation in TBI are also a significant problem. The extubation failure rate in these patients reaches 31%-38% [18]. As a result, the unjustifiably delayed extubations rate is very high in this population [1, 3]. Instead of waiting for complete consciousness recovery, more promising is the assessment of the VISAGE score: VISual pursuit, Swallowing, AGE, Glasgow coma score (Table).

VISAGE score [9]

Factor	Score
Age <40 years old	**1**
Visual pursuit	**1**
Swallowing attempts	**1**
Glasgow coma score >10	**1**

Note. A score of 3 or greater is associated with 90% extubation success.

Early tracheotomy (4 days after trauma) also allows to simplify the process of weaning from mechanical ventilation and is associated with increase in days without mechanical ventilation, a lower pneumonia rate, shorter ICU stay length [2, 22, 36].

CONCLUSION

Thus, the current principles of respiratory support in severe TBI include:

1. Tracheal intubation by Glasgow coma score ≤8;
2. Early mechanical ventilation;

3. PaO_2 80-120 mm Hg (SaO_2 ≥95%);
4. Acceptable PaO_2 60-300 mm Hg (SaO_2 ≥90%);
5. $PaCO_2$ 35-45 mm Hg;
6. Tidal volume ≤8 ml/kg;
7. RR ≈20/min;
8. PEEP ≥5 cm H2O;
9. Head elevation by 30°;
10. Sedation in poor synchronization with the respirator;
11. Weaning from mechanical ventilation through the use of support ventilation modes;
12. Extubation when reaching 3 points by the VISAGE scale;
13. Early (up to 4 days) tracheotomy in predicted extubation failure.

Contributors:
Krishtafor D.A. – conceptualization, writing – original draft;
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Yekhalov V.V. – methodology, resources;
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