

Bundle care approach to enhance the outcome of pediatric ventilator-associated pneumonia (PedVAP) in pediatrics

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Abstract

Ventilated patients are at high risk for complications and poor outcomes including death, ventilator-associated pneumonia (VAP), sepsis, acute respiratory distress syndrome (ARDS), pulmonary embolism, barotrauma, and pulmonary edema. Ventilator-associated pneumonia is one of the most frequent hospital-acquired infections in mechanically ventilated children. Care bundles were first developed over 20 years ago. They have been used in several different medical and surgical specialties and have been used particularly extensively in cardiology. Interest in the application of care bundles to critical care was developed in the 1990s and early years of the century. The ventilator bundle: it was the first set of interventions to be developed as an outcome of the Institute for Healthcare Improvement's 100,000 Lives Campaign. We reviewed the literature on the effectiveness of ventilator care bundles in critically ill children. As a multidisciplinary approach to infection prevention, the ventilator care bundles (VCBs) could reduce the occurrence of ventilator-associated pneumonia (VAP) and improve the patient's clinical outcomes in the ICUs. To improve healthcare quality, using care bundles is a multifaceted issue which was actively associated with incorporating staff education, adherence process, and as well as highest levels of bundle compliance. Although the preventive measures for VAP are well documented and evidence based, they are still poorly implemented in most ICUs. Furthermore, it seemed necessary to evaluate the VCB compliance rate and the effect of education on its improvement. The limitations of VAP surveillance definitions have implications for prevention. Valid surveillance data are necessary for assessing the effectiveness of prevention strategies.

Keywords: Education, Intensive Care Unit, Mechanical Ventilation, Ventilator-Associated Pneumonia, Ventilator Care Bundles.

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1. Introduction

Ventilated patients are at high risk for complications and poor outcomes including death, ventilator-associated pneumonia (VAP), sepsis, acute respiratory distress syndrome (ARDS), pulmonary embolism, barotrauma, and pulmonary edema [1]. A care bundle is defined as the implementation of a group of evidence-based interventions together for a defined patient population, which when each one of them is executed individually will result in improved patient's recovery process and outcomes, but when performed all together, they are providing better outcomes than implemented individually [2]. The ventilator bundle implementation has a significant reduction in VAP rates, duration of MV, antibiotic administration, length of PICU stay, and hospital costs. In conclusion, implementation of pediatric ventilator bundle is considered a practical approach for achieving better patient and clinic outcomes, with an evidence-based safe and multidisciplinary approach [3]. The new surveillance model of ventilator-associated events (VAEs) has shifted the focus from VAP to objective, generalized signs of pulmonary decompensation not specific

to VAP. This raises the question of whether the ventilator bundle also is effective in reducing VAE [4].

2. Mechanical Ventilation

The movement of gas into and out of the lung using automatic machine defined as ventilator connected directly to the patient [5]. It is a measure to assist or replace spontaneous breathing when respiratory failure develops and other measures like oxygen therapy and airway suctioning are not effective to improve oxygenation and ventilation [6]. Mechanical ventilation is an essential, life-saving therapy and one of the most used interventions in pediatric intensive care units (PICUs) [7].

3. Types of Mechanical Ventilation

3.1. Negative pressure ventilation (NPV)

Negative-pressure ventilators provide ventilatory support using a device that encases the thoracic cage starting from the neck, and devices range from a whole-body tank to a cuirass shell [8]. The general principal is the same with a

vacuum device, which lowers the pressure surrounding the thorax, creating subatmospheric pressure and thereby passively expanding the chest wall with diaphragmatic descent, all leading to lung inflation. Exhalation occurs with passive recoil of the chest wall [9].

3.2. Positive pressure ventilation (PPV)

It refers to the process of forcing air into lung of the patient utilizing a positive pressure, so the flow of air into the lung depends on the pressure difference between upper airways and the alveoli [10]. PPV is the most widely used type of ventilation due to its low cost, easy patient accessibility for examination and procedures and easy monitoring and nursing care [10]. It can be delivered in two forms: Non-invasive positive pressure ventilation (NIPPV): Which is delivered through a nasal or special face mask with a tight seal (air travels through anatomical airways) [8]. Invasive positive pressure ventilation (IPPV): Which involves the delivery of positive pressure to the lungs through an endotracheal tube or tracheostomy (or any other device that delivers gas bypassing parts of the anatomical airway) [10]. PPV can be continuous positive airway pressure (CPAP), intermittent positive airway pressure or combined [11].

4. Classification of mechanical ventilators

Conventional mechanical ventilators: cycle at low rates (up to 60 cycles/min.) [12].

Pressure- controlled ventilation: the pressure is the control (limit) variable once set it can never be exceeded during inspiration. VT is therefore variable and changes suddenly as patient's compliance and/or resistance changes.

Volume controlled ventilation: Tidal volume is the limit variable, so it is constant whatever the degree of lung pathology. The pressure therefore variable changes as patient's compliance and/or resistance changes.

Dual controlled ventilation: this method permits simultaneous control of pressure and volume thus combines features of the above-mentioned types.

High frequency positive pressure ventilators: These ventilators can cycle at very rapid rates (from 180 to 1200/min.). potential advantages over conventional ventilators include their ability to provide adequate gas exchange using much lower tidal volumes which reduce lung injury and volutrauma. There are mainly four types of HFV [13]: High-frequency oscillatory ventilation (HFOV), High-frequency positive pressure ventilation (HPPV), High-frequency jet ventilation (HJV) and High-frequency percussive ventilation (HFPV)

Indications of Mechanical Ventilation: Mechanical ventilation is indicated when the patient's spontaneous ventilation is inadequate to sustain life. Also, when other simple respiratory managements (oxygen, aerosol, chest physiotherapy, and suctioning) fail to improve oxygenation and/or ventilation [14]. Indications are divided into two categories: absolute and relative requirement, as well as

system involvement (respiratory, cardiovascular, and neurologic) [15].

According to necessity

(a) Absolute indications: Type 1 respiratory failure (persistent hypoxemia): $Pao_2 < 60\text{mmHg}$ and $PH < 7.30$, Type 2 respiratory failure (hypercapnia): $PaCO_2 > 50\text{mmHg}$ and $PH < 7.30$, Persistent and frequent apnea and markedly elevated intracranial pressure.

(b) Relative indications: Coma $GCS < 8$, Shock states, Refractory status epilepticus, Excessive work of breathing and inability to protect the airways.

5. Complications of Mechanical Ventilation

Patients who receive mechanical ventilation are at high risk for many complications and poor outcomes, including ventilator-associated pneumonia (VAP), sepsis, barotrauma, acute respiratory distress syndrome (ARDS), pulmonary embolism, pulmonary edema and death. Such complications can lead to longer duration of mechanical ventilation, longer stays in the ICU and hospital, increased healthcare costs and increased risk of disability and death [16].

5.1. Ventilator-associated lung injury

With ventilator-associated lung injury, the alveolar epithelium is at risk for barotrauma, volutrauma, atelectasis and biotrauma [17].

Barotrauma: Pulmonary barotrauma is a side effect of mechanical ventilation that has been linked to an increased risk of mortality and morbidity [18]. Pneumothorax, pneumomediastinum, and subcutaneous emphysema are all possible complications of too much alveolar air [19].

Volutrauma: The increased local inflammation lowers the patient's potential to recover from ARDS. The inflammatory cascade occurs locally and may augment the systemic inflammatory response as well. Thus, it is possible to develop this atelectrauma without high tidal volumes, indicating the need to have a high index of suspicion for this complication [14].

Atelectasis: The use of high fractions of inspired oxygen (FIO₂) can result in direct pulmonary toxicity as well as lung problems including absorption atelectasis [20].

Biotrauma: Several inflammatory cytokines are released with physical stress. IL-8, TNF, IL-1 β , and IL-17 would increase with high physical stress, and they are recruiters of neutrophils; the activation and recruitment of neutrophils to the site of pulmonary injury is a key process during the pathophysiology process [17].

5.2. Oxygen toxicity

Oxygen toxicity is an outcome of increased FIO₂ and its duration of use. Oxygen toxicity is due to the production of oxygen free radicals, such as hydroxyl radical, superoxide

anion and hydrogen peroxide. Oxygen toxicity can cause a variety of complications ranging from mild absorptive atelectasis and to diffuse alveolar damage that is indistinguishable from ARDS [21].

5.3. Ventilator-associated pneumonia (VAP)

Centers for Disease Control and Prevention had defined ventilator-acquired pneumonia as hospital-acquired pneumonia that develops in patients who have been treated for 48hs or longer with mechanical ventilation and who had no signs or symptoms of lower respiratory infection before they were intubated and MV initiated [22]. In PICUs, VAP is thought to be the most common infection. Many published reports showed that the occurrence of VAP is 6–10% of patients who were ventilated in the pediatric intensive care unit (PICU) [23].

5.4. Pediatric Ventilator-Associated Events (PedVAEs)

PedVAEs are defined by the deterioration in respiratory status after a period of stability or improvement on the ventilator. The baseline period of stability or improvement on the ventilator must be characterized by more than two calendar days of stable or decreasing daily minimum FiO₂ or mean airway pressure (MAP) values.

7. Ventilator Care Bundle (VCB)

A care bundle is defined as the implementation of a group of evidence-based interventions together for a defined patient population, which when each one of them is executed individually will result in improved patient's recovery process and outcomes, but when performed all together, they are providing better outcomes than implemented individually. There are two main types of bundles: ventilator and severe sepsis bundles [24]. The ventilator bundle: it was the first set of interventions to be developed as an outcome of the Institute for Healthcare Improvement's 100,000 Lives Campaign. The bundle was created to prevent complications associated with mechanical ventilation, specifically ventilator associated pneumonia (VAP) [25].

7.1. Components of ventilator care bundle (VCB)

Ventilator bundles are standardized practices based upon evidence of varying quality.4 Although they differ in components, most include core practices such as semi-recumbent positioning, oral care, avoidance of nasogastric tubes, limited use of orogastric tubes and strategies to limit the duration of mechanical ventilation by incorporating daily sedation interruptions (DSI) and spontaneous breathing trials (SBT) [26].

7.2. Infection control measures

Hand hygiene: Several time-series studies showed the importance of hand hygiene in reducing VAP. Of these, Rello et al., [27] reported reduced VAP risk. Introducing oral care and hand hygiene measures alone reduced early-onset

VAP by 59% [28]. Body-worn hand gel devices reduced VAP from 6.9 cases per 1000 to 3.7 cases/ per 1000 of mechanical ventilation [29]. In another study, hand hygiene alone reduced all respiratory tract infections by 36.3 infections per 1000 device days [30]. Central line bundle consists of Visanth and Sancha, [25]: Practice meticulous hand hygiene, Use full barrier precautions during central line insertion, apply chlorhexidine to the patient's skin as a cleansing agent, avoid central line insertion into the femoral vein and remove unnecessary I.V. catheters.

7.3. Elevation of the patient's head from the bed to at least 30 to 45 degree

Reduce the potential for gastric reflux and aspiration of contaminated orogastric secretions [26]. In the past, mechanically ventilated patients were kept supine and frequently had nasogastric tubes in place. A seminal study found that this was associated with higher incidences of orogastric secretion aspiration, microbial colonization and VAP compared to the semi-recumbent positioning at a 45° angle [31]. Enteral feedings also are associated with VAP such that being in the supine position while feeding magnifies the incidence of VAP. Yet, sustained positioning at 45° was found impractical compared to positioning at 25–30° [32]. Wang et al., [33] made a systematic review comparing supine positioning with semi-recumbent positioning and found no difference in clinically suspected or microbiologically confirmed VAP between positioning at 45° versus 25–30° (relative risk 0.74 [IQR 0.35–1.56] and 0.61 [IQR 0.20–1.84], respectively).

7.4. Reduce use of nasogastric and orogastric tubes

Nasogastric tubes are associated with sinusitis, and this is enhanced substantially when an ETT is present. Sinusitis itself substantially increases the risk of VAP [34].

7.5. Daily sedative interruption and daily assessment of readiness to extubate

Although the Institute for Healthcare Improvement (IHI) does not recommend daily interruption of sedation in pediatrics due to high risk of accidental extubating, Vet et al., [35] found no safety issues during daily sedation interruption. Further, daily interruption of sedation in addition to protocolized sedation did not improve clinical outcomes.

7.6. A structured oral care protocol

Including oral care with chlorhexidine solution 0.12% every 6 h and tooth brushing with a standard toothpaste every 12 h.: reduce the introduction and load of potentially pathogenic microbes into the oropharynx and, by extension, colonization of the lower respiratory tract [26]. During critical illness, the stomach often becomes colonized with gram-negative bacteria. Frequent gastroesophageal reflux causes the oral cavity to be colonized with these and other pathogenic microorganisms (eg, Streptococcus species, Candida albicans) [36]. In VAP, the same bacteria often are isolated from both the oral cavity and sputum. In addition,

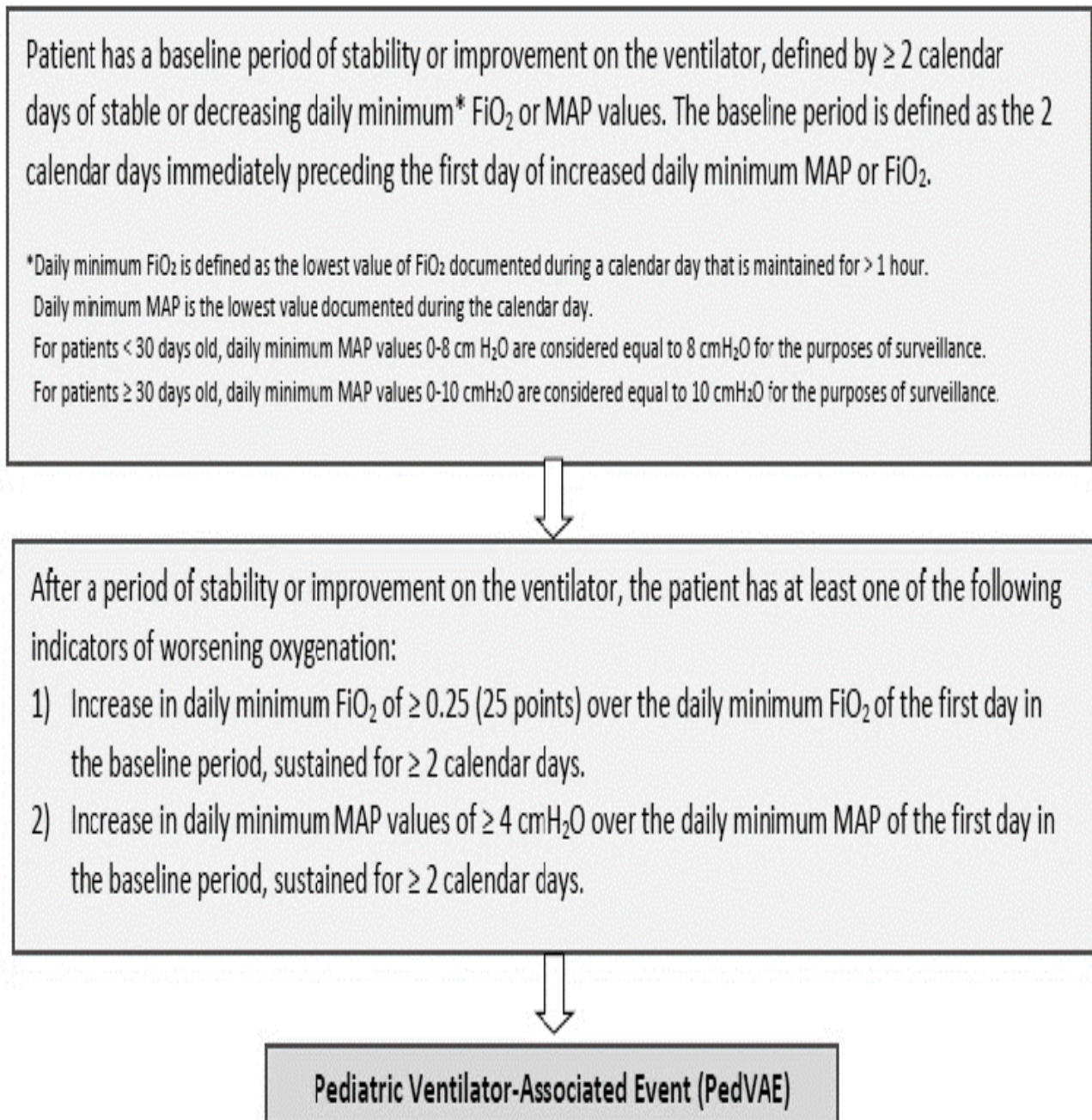


Figure 1. Pediatric Ventilator-Associated Events (PedVAE) Surveillance Algorithm

preexisting dental disease is associated with both community-acquired and hospital-acquired pneumonia [36].

In systematic reviews, oral care with chlorhexidine solution or gel reduces VAP risk by 25% to 40%, with uncertain or no additional benefit from augmenting oral care with tooth brushing [37].

8. Cuffed endotracheal tubes use when not contraindicated

8.1. Maintenance of tracheal tube/tracheostomy cuff pressure between 20 and 30 cm H₂O

Under-inflated ETT cuffs producing insufficient cuff pressures (ie, < 20 cm H₂O) are independently associated with VAP.³³ In relatively small, single-center trials, continuous control of cuff pressures between 20–30 cm H₂O reduced VAP by approximately 50–60%. Currently, 2 large, multi-center RCTs are underway to examine whether continuous versus intermittent monitoring and control of ETT cuff pressure reduces VAP [38].

8.2. Circuit changes only if the circuit becomes soiled or damaged. Prophylaxis of peptic ulcer

Hill and Muszynski added peptic ulcer prophylaxis to the VCB [39]. Babcock and Gurskis added the avoidance of peptic ulcer prophylaxis to the VCB [40]. Peptic ulcer prophylactics (H₂ antagonists and antacids) raise the gastric pH and may increase colonization with pathogenic organisms and therefore increase the risk of VAP. In adults, the use of sucralfate as peptic ulcer prophylaxis, which does not alter the gastric pH, was associated with a significant reduction in the incidence of VAP compared with the use of H₂ antagonists [41]. A recent study of Albert et al [42] found a significant increase of VAP rates with the use of acid-suppressive medication (odds ratio, 2.0; 95% CI, 1.2–3.6; p = 0.011). A recent meta-analysis showed that ventilator bundles were beneficial in adult ICU patients. The implementation of a ventilator care bundle was associated with a 10% relative reduction in mortality [43]. Also, a combination of the bundle components elevation of head of bed, daily oral care, and daily assessment of readiness to extubate and sedation vacation was found the most beneficial [43]. The optimal composition of the bundle is not known [44]. Further, quality improvement and implementation will be more successful with understanding of the complexity of the innovation and a setting's culture [45]. Ongoing attention must be given to sustaining compliance and the positive effects in the post-implementation phase. It is equally important to pay attention to compliance with the separate components; this gives information about compliance failure and changes for improvement [46].

9. Conclusions

VAP is a serious complication of Mechanical ventilation that significantly increases the length of PICU stay and mortality. Application of care bundle was found to be effective in decreasing the VAP rate in the PICU patients. Valid and reliable surveillance data are necessary for assessing the effectiveness of different components of care bundle.

References

- [1] Centers for Disease Control and Prevention (CDC). Pediatric Ventilator-Associated Event (PedVAE). Device-associated Module PedVAE. 2020; 11-1.
- [2] Alcan AO, Korkmaz FD. Prevention of ventilator-associated pneumonia: Care package approach. Izmir University Medical Journal 2015; 3: 38-47.
- [3] Alcan AO et al. Effect of patient position on endotracheal cuff pressure in mechanically ventilated critically ill patients. Australian Critical Care. 2017; 30:267–72.
- [4] Richard H. Ventilator Bundles in Transition: From Prevention of Ventilator-Associated Pneumonia to Prevention of Ventilator-Associated Events. Respiratory Care. 2019; 64(8).
- [5] S.R. Wilcox, A. Aydin, E.G. Marcolini. (2022). Terminology and Definitions. Mechanical Ventilation in Emergency Medicine. Cham: Springer International Publishing.
- [6] J.P. Goldsmith, E.H. Karotkin. (2003). Introduction to assisted ventilation. Assisted ventilation of the neonate. 3.
- [7] M. Klompas, R. Branson, K. Cawcutt, M. Crist, E.C. Eichenwald, L.R. Greene, S.M. Berenholtz. (2022). Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 Update. Infection Control & Hospital Epidemiology. 43 (6) 687-713.
- [8] G.W.S. Hoo. (2003). Nonpharmacologic adjuncts to training during pulmonary rehabilitation: the role of supplemental oxygen and noninvasive ventilation. Journal of Rehabilitation Research & Development. 40 (5).
- [9] J. Masip, W.F. Peacock, S. Price, L. Cullen, F.J. Martin-Sanchez, P. Seferovic, Acute Heart Failure Study Group of the Acute Cardiovascular Care Association and the Committee on Acute Heart Failure of the Heart Failure Association of the European Society of Cardiology. (2018). Indications and practical approach to non-invasive ventilation in acute heart failure. European heart journal. 39 (1) 17-25.
- [10] I. Potchileev, M. Doroshenko, A.N.J.S. Mohammed. (2021). Positive Pressure Ventilation.
- [11] P.C. Rimensberger, S.M. Schulzke, D. Tingay, B.S. Von Ungern-Sternberg. (2015). Pediatric and neonatal mechanical ventilation. From Basics to Clinical.
- [12] H.S. Jeffrey. (2015). Mechanical Ventilation, Conventional.
- [13] P.R. Murthy, A.K. AK. (2020). High Frequency Ventilation.
- [14] D. Christopher Jackson. (2020). Mechanical Ventilation.
- [15] M.C. AL, J.I. Mora. (2017). Ventilator management.
- [16] H. Wunsch, W.T. Linde-Zwirble, D.C. Angus, M.E. Hartman, E.B. Milbrandt, J.M. Kahn. (2010). The epidemiology of mechanical ventilation use in the

- United States. *Critical care medicine*. 38 (10) 1947-1953.
- [17] C. Pan, H. Qiu. (2020). Ventilator-Associated Lung Injury (VALI). *Burn and Trauma Associated Lung Injury*. 77-86.
- [18] T. Kien Nguyen, D.H. Mai, A.N. Le, Q.H. Nguyen, C.T. Nguyen, T.A. Vu. (2021). A review of intraoperative lung-protective mechanical ventilation strategy. *Trends in Anaesthesia and Critical Care*. 37 9-17.
- [19] T.S. Elhakim, H.S. Abdul, C.P. Romero, Y. Rodriguez-Fuentes. (2020). Spontaneous pneumomediastinum, pneumothorax and subcutaneous emphysema in COVID-19 pneumonia: a rare case and literature review. *BMJ case reports*. 13 (12).
- [20] I.K. Song, Y.E. Jang, J.H. Lee, E.H. Kim, S. Yoo, H.S. Kim, J.T. Kim. (2019). Effect of different fraction of inspired oxygen on development of atelectasis in mechanically ventilated children: a randomized controlled trial. *Pediatric Anesthesia*. 29 (10) 1033-1039.
- [21] B.T. Reidy, P. Whyte, P.J. Neligan. (2019). Is Oxygen Toxic?. *Evidence-Based Practice of Critical Care E-Book*. 36.
- [22] M.F. Alsoda, M.M. Al-Shahat, S.M.K. Reda, A.Y. Alsawah, M.A.M. Abboud, A.E. Elgendy. (2019). Implementation of ventilator bundle for prevention of ventilator-associated pneumonia in pediatric intensive care unit. *Journal of Medicine in Scientific Research*. 2 (4) 265.
- [23] E.W. van der Jagt, S.R.P. Short. (2021). *Healthcare-Associated Infections. Pediatric Critical Care: Text and Study Guide*. 1105-1143.
- [24] A.O. Alcan, K. FD. (2015). Ventilator ilişkili pnömoninin önlenmesi: Bakım paketi yaklaşımı. *İzmir Üniversitesi Tıp Dergisi*. 3 38-47.
- [25] V.S. Visanth, A. Sancha. (2017). *research studies*. 2347-4793.
- [26] R.H. Kallet. (2019). Ventilator bundles in transition: from prevention of ventilator-associated pneumonia to prevention of ventilator-associated events. *Respiratory care*. 64 (8) 994-1006.
- [27] J. Rello, E. Afonso, T. Lisboa, M. Ricart, B. Balsera, A. Rovira, FADO Project Investigators. (2013). A care bundle approach for prevention of ventilator-associated pneumonia. *Clinical Microbiology and Infection*. 19 (4) 363-369.
- [28] K.C. Su, Y.R. Kou, F.C. Lin, C.H. Wu, J.Y. Feng, S.F. Huang, S.C. Chang. (2017). A simplified prevention bundle with dual hand hygiene audit reduces early-onset ventilator-associated pneumonia in cardiovascular surgery units: An interrupted time-series analysis. *PLoS One*. 12 (8) e0182252.
- [29] M.D. Koff, H.L. Corwin, M.L. Beach, S.D. Surgenor, R.W. Loftus. (2011). Reduction in ventilator associated pneumonia in a mixed intensive care unit after initiation of a novel hand hygiene program. *Journal of critical care*. 26 (5) 489-495.
- [30] G. Finco, M. Musu, G. Landoni, M. Campagna, A. Lai, L. Cabrini, M. Galletta. (2018). Healthcare-associated respiratory infections in intensive care unit can be reduced by a hand hygiene program: A multicenter study. *Australian Critical Care*. 31 (6) 340-346.
- [31] M.B. Drakulovic, A. Torres, T.T. Bauer, J.M. Nicolas, S. Nogué, M. Ferrer. (1999). Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *The Lancet*. 354 (9193) 1851-1858.
- [32] V. Artinian, H. Krayem, B. DiGiovine. (2006). Effects of early enteral feeding on the outcome of critically ill mechanically ventilated medical patients. *Chest*. 129 (4) 960-967.
- [33] L. Wang, X. Li, Z. Yang, X. Tang, Q. Yuan, L. Deng, X. Sun. (2016). Semi-recumbent position versus supine position for the prevention of ventilator-associated pneumonia in adults requiring mechanical ventilation. *Cochrane Database of Systematic Reviews*. (1).
- [34] N.A. Metheny, L.J. Hinyard, K.A. Mohammed. (2018). Incidence of sinusitis associated with endotracheal and nasogastric tubes: NIS database. *American Journal of Critical Care*. 27 (1) 24-31.
- [35] N.J. Vet, S.N. de Wildt, C.W. Verlaat, C.A. Knibbe, M.G. Mooij, J.B. van Woensel, M. de Hoog. (2016). A randomized controlled trial of daily sedation interruption in critically ill children. *Intensive care medicine*. 42 233-244.
- [36] F.F. Tuon, O. Gavrilko, S. de Almeida, E.R. Sumi, T. Alberto, J.L. Rocha, E.A. Rosa. (2017). Prospective, randomised, controlled study evaluating early modification of oral microbiota following admission to the intensive care unit and oral hygiene with chlorhexidine. *Journal of global antimicrobial resistance*. 8 159-163.
- [37] Z. Shi, H. Xie, P. Wang, Y. Wu, E. Chen, L. Ng, I. Needleman. (2010). Oral hygiene care for critically ill patients to prevent ventilator associated pneumonia [Intervention Protocol]. *Cochrane Database of Systematic Reviews*. (2) 1-14.
- [38] V.Q. Dat, R.B. Geskus, M. Wolbers, H.T. Loan, L.M. Yen, N.T. Binh, B. Nadjm. (2018). Continuous versus intermittent endotracheal cuff pressure control for the prevention of ventilator-associated respiratory infections in Vietnam: study protocol for a randomised controlled trial. *Trials*. 19 (1) 1-10.
- [39] J.A. Muszynski, J. Sartori, L. Steele, R. Frost, W. Wang, N. Khan, O. Ayad. (2013). Multidisciplinary quality improvement initiative to reduce ventilator-associated tracheobronchitis in the PICU. *Pediatric critical care medicine: a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*. 14 (5).
- [40] V. Gurskis, J. Ašembergienė, R. Kėvalas, J. Miciulevičienė, A. Pavilonis, R. Valintėlienė, A. Dagys. (2009). Reduction of nosocomial infections and mortality attributable to nosocomial infections in pediatric intensive care units in Lithuania. *Medicina*. 45 (3) 203.

- [41] M. Klompas, A.C. Kalil. (2018). Rethinking ventilator bundles. *Critical care medicine*. 46 (7) 1201-1203.
- [42] B.D. Albert, D. Zurakowski, L.J. Bechard, G.P. Priebe, C.P. Duggan, D.K. Heyland, N.M. Mehta. (2016). Enteral nutrition and acid-suppressive therapy in the pediatric intensive care unit: Impact on the risk of ventilator-associated pneumonia. *Pediatric critical care medicine: a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*. 17 (10) 924.
- [43] C. Pileggi, V. Mascaro, A. Bianco, C.G. Nobile, M. Pavia. (2018). Ventilator bundle and its effects on mortality among ICU patients: a meta-analysis. *Critical Care Medicine*. 46 (7) 1167-1174.
- [44] M. Klompas, A.C. Kalil. (2018). Rethinking ventilator bundles. *Critical care medicine*. 46 (7) 1201-1203.
- [45] M. Dixon-Woods, M. Leslie, C. Tarrant, J. Bion. (2013). Explaining Matching Michigan: an ethnographic study of a patient safety program. *Implementation science*. 8 (1) 1-13.
- [46] J. Brierley, L. Highe, S. Hines, G. Dixon. (2012). Reducing VAP by instituting a care bundle using improvement methodology in a UK paediatric intensive care unit. *European journal of pediatrics*. 171 323-330.