TITLE:

Retrospective Application of New Pediatric Ventilator-Associated Event Criteria in a Tertiary Pediatric İntensive Care Unit

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ABSTRACT

Background: In January 2020 a modification is applied for pediatric ventilator associated events (Ped-VAE) surveillance by Center for Disease Control and Prevention. İn this study we investigate the potential impact of this newly criteria and determine whether the adult ventilator-associated conditions (VAC), infection-related ventilator-associated complications (İVAC) and possible ventilator-associated pneumonia (PVAP) criteria could be applied pediatric patients with ped-VAE

Methods: We analyzed data between January 2014 and December 2019 using the new ped-VAE criteria. We compared two different criteria for identifying VAE: the 2013 adult VAE criteria, and the newly ped-VAE criteria.

Result: The data of 91 VAE patients were evaluated, 42.8 % were not categorized as ped-VAE and 57.2% patients were compatible with the ped-VAE, 19.2% were categorized as adult VAC, 21.1% were categorized as IVAC, and 59.6% patients were categorized as PVAP. There was no significant difference between mortality and the diagnostic ventilator surveillance types.

Conclusions: Pediatric ventilator-associated event algorithm is a better tool for children than the VAE algorithm defined for adults and the new pediatric criteria are more effective in detecting ventilator assosiated complications in children. We think further studies will be needed for evaluate ped VAE criteria.

Keywords: Infection-related ventilator-associated complications, pediatric ventilator-associated event, possible ventilator-associated pneumonia, ventilator-associated conditions.

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İntroduction

In spite of increased use of non-invasive mechanical ventilation, and high-flow nasal oxygen in the pediatric intensive care unit (PICU), invasive mechanical ventilation is still used in a large proportion of critically ill patients that a life-saving treatment. Ventilator associated events (VAE) are among the most common complications of mechanical ventilation, and are associated with increased duration of mechanical ventilation, length of hospital stay, and cost [1]. However the diagnosis and surveilllance of VAE are different and difficult from the adults due the lack of an objective gold standard compared to adult patients.

In 2013, changes were introduced in the Center for Disease Control and Prevention (CDC) surveillance definitions, with ventilator-associated pneumonia (VAP) being replaced by "ventilator associated events" (VAE) for adults [2]. VAE definitions were developed to find adverse events by surveillance and to utilize objective criteria (eg, increased ventilator settings) rather than subjective criteria (eg, radiographic interpretation). VAE surveillance is a promising strategy to improve care for ventilated patients by providing hospitals with a broader picture of their true burden of morbid complications and an objective metric to measure the impact of care improvement initiatives.

The VAE surveillance definition algorithm implemented by the CDC in 2013 was initially available for use in adult locations only. İn this algorithm, subjective items (such as chest X-ray) were removed and the emphasis was placed on respiratory worsening, properly defined by two well-documented ventilator settings: ≥ 0.2 increase in fraction of inspired oxygen (FiO$_2$) or a positive end-expiratory pressure (PEEP) of ≥ 3 cm H$_2$0 sustained for ≥ 2 days. Later, a modification is applied for pediatric use in January 2020 by CDC [3]. Pediatric VAE definition using changes in mean airway pressure (MAP) instead of PEEP setting, in addition of changes in the FiO$_2$ was proposed and the CDC decided move forward with Pediatric VAE (PedVAE) development. PedVAE CDC definition differs from adult VAE apart from the use of MAP instead of PEEP (a sustained increase of the daily minimum MAP 4 cmH$_2$O versus PEEP increase 3 cmH$_2$O) also in the changes in the FiO$_2$ (increase in daily minimum FiO$_2$ of 0.25 instead of 0.20). In both cases, the respiratory worsening has to be sustained for at least 2 calendar days for meeting VAE criteria [3].

The adult VAE definition set includes subcriteria to identify the subset of ventilator-associated conditions(VAC's) that might be infection-related ventilator-associated complications (IVAC) and possible ventilator-associated pneumonia (PVAP). IVAC criteria require an abnormal temperature and white blood cell (WBC) count as well as the initiation of new antimicrobials for at least 4 days within 2 days of the increase in PEEP or FiO_2 [4]. PVAP requires detection of potentially pathogenic organisms via culture or other respiratory diagnostic tests. But PedVAE does not have these criterias for children abd neonates.

İn this study we investigate the potential impact of this newly criteria and determine whether the adult VAC, IVAC and PVAP criteria could be applied pediatric patients with pedVAE. We analyzed data from our VAE cases between January 2014 and December 2019 using the new pediatric VAE criteria. Our hypothesis was that a new Pediatric Ventilator-Associated Event (Ped-VAE) algorithm would prove to be a better tool for children than the VAE algorithm defined for adults.

Methods:

This retrospective, single-center cohort study was completed at The Dr. Behçet Uz Child Disease and Pediatric Surgery Training and Research Hospital that a 375-bed pediatric teaching hospital. This hospital is a referral center for pediatric patients in the Aegean Region of Turkey and had 24 bed PİCU. In this study all children diagnosed with VAE by adult VAE criteria in the PICU from January 1, 2014, to December 31, 2019, were included.

The data required for patients on VAE surveillance are on the day of the ventilator, minimum hourly PEEP and FiO_2 values. These datas were recorded daily by the infection control nurse and intensive care nurse in the "Intensive Care Surveillance Monitoring Form" for each patient in mechanical ventilation. The datas were also checked from the patients written medical files. Laboratory tests and clinical information for IVAP and PVAP criteria were obtained from the electronic medical record and infection control database.

The datas were reviewed by two of the investigators (A.A.K and E.S) to determine whether VAE or not according to the new pedVAE classification. All data were reviewed by another investigator (İ.D.), and final decision was made by consensus. According to this system, children met criteria for VAE if they had a sustained ($\geq$ 2 calendar days) increase in MAP by greater than or equal to 4 cm H_2O or FiO_2 greater than or equal to 0.25. Patients diagnosed with pedVAE who received antimicrobial therapy for greater than or equal to 4 days and had

an abnormal temperature and white blood cell were defined IVAC. Patients were further diagnosed with PVAP if they had positive respiratory cultures.

We compared two different criteria for identifying VAE in a retrospective cohort of PICU patients: the 2013 adult VAE criteria, and the newly pediatric VAE criteria (Table1).

Our objectives were 1) to determine the number of VAE cases identified by each of the criteria, 2) to determine the clinical outcomes of VAE cases diagnosed with new pediatric criteria by using adult VAC, IVAC and PVAP criteria (Table2)

Results

Demographic features:

During the study period, when all data were examined, 112 VAE compatible cases were found in accordance with the 2013 CDC criteria for adults. Among the VAE cases, 29 of them were excluded from the study because of absence of raw data. Thus, the data of 91 VAE patients were evaluated. The medain age of the patients was 13.0 months ranging from 1 months of age to 16 years. Demographic and patient characteristics of 91 patients included in the study are shown in table 3. Among 91 patients, 88 patients(96,7%) of the patients had underlying diseases. Most common underlying diseases were neurologic diseases((41.8%) including mostly spinal muscular atrophy, followed by congenital heart disease and cardiovascular surgery(18.7%) and metabolic disease (17.5%;). Twenty three patients(25.3%) had tracheastomy. Considering the mortality rate, it was detected as 25% in pedVAE cases and 15.3% in nonpedVAE cases.

Comparison with previous surveilance criteria with adult diagnostic criteria

In the 91 patients with VAE by the 2013 adult VAE criteria; 39 patients(42.8 %) were not categorized as pedVAE by newly pediatric VAE criteria and 52 (57.2%) patients were compatible with the pedVAE criteria. When 52 patients diagnosed with PedVAE according to the new criteria were evaluated in terms of adult VAC, IVAP and PVAP, 10(19.2%) were categorized as adult VAC, 11(21.1%) patients were categorized as IVAC, and 31(59.6%) patients were categorized as PVAP.(Table 4) The most common VAP organisms identified were gram negative bacteria (29/31;93.5%), predominantly *Klebsiella pneumoniae* (11/31;35.4%), and *Pseudomonas aeruginosa* (10/31;32.2%). The other organisms; *Acinetobacter baumannii* (6/31;19.3%), *Escherichia coli* (2/31;6.4%), *Staphylococcus aureus* (2/31;6.4%).

A Kruskal-Wallis Test revealed a statistically significant difference in ages across patients with IVAC; PVAP, VAC and patients without pedVAE due to new criteria (Gp1,n= 38: patients without VAE; Gp2, n=32: PVAP,

Gp3, n= 11: IVAC, Gp4, n=10, VAP), X2(3,n=91)=8,04, p=0.045). The further Mann-Whitney test revealed the median age of patients with IVAC (4 months) was significantly lower compared to the patients without VAP(33 mon ths of age)(p=0,009). The ages of other groups did not show any difference between other groups(p>0.05).

There was no significant difference between mortality and the diagnostic ventilator surveillance types. (p>0.286) (table-4)

Discussion

To our knowledge, this is the first study of CDC's new surveillance definitions published in 2020 to a pediatric population. We compared two different criteria for identifying VAE in a retrospective cohort of PICU patients: the 2013 adult VAE criteria, and the newly pediatric VAE criteria. As might be expected, as more stringent thresholds for Fio2 and MAP were applied, pediatric VAC rates according to the new criteria decreased across ICU types. In this study 41.7% patients were not categorized as pedVAE by newly pediatric VAE criteria. In a study conducted before the publication of the CDC 2020 new pedVAE criteria, that 9025 patients were evaluated using similar criteria (an increase in minimum daily FiO2 of ≥0.25 or an increase in MAP of ≥4 cm H2O for at least 2 days after 2 or more days of stable or decreasing daily minimum FiO2 or MAP on the ventilator) for pediatric VAE, 41.8 % were found as non pedVAE [5]. The findings of the previus study supported findings of our study.

We explored whether the criteria used for surveillance of VAEs in adults—a criteria that includes IVAC and PVAP—can be applied to pediatric patients. Nearly all VAE cases were associated with abnormal temperature or WBC measurements regardless of the thresholds used. Therefore, these findings are not sufficient for pediatric cases to start antibiotics and continue for 4 days. Already when we compared the new pediatric criteria with the adult criteria, none of the patients considered as non-pedvae met the IVAC and / or PVAP criteria. Therefore, we believe that the new pediatric criteria are more effective in detecting ventilator assosiated complications in children. İn our study, 21.1% patients were categorized as IVAC, and 59.6% patients were categorized as PVAP among the cases diagnosed with pedVAE (52 cases) according to the new pediatric criteria and there was no statistically significant difference in mortality rate. In other studies evaluating the usability of adult IVAC and PVAP criteria on children, were found increased hospital mortality compared with those not meeting those definitions [6,7].

Using the ventilator-associated event criteria is of interest for screening for ventilator-associated pneumonia in children. The data required for patients on VAE surveillance, minimum hourly MAP and FiO_2 values. At present, in our clinic, these data are recorded daily on the "Intensive Care Monitoring Form" for each patient under mechanical ventilation by the infection control nurse and/or the intensive care nurse. However, automated surveillance for ventilator-associated events has been developed and put into routine use in some centers due to the potential inaccuracies of manual monitoring and the loss of personnel time / workforce. The value of automated data extraction using the adult VAE surveillance definition is also worthy of further consideration. In an adult study, the automated data extraction showed that it is not only efficient but also increase reliability and objectivity [8]. Another adult study confirmed that automated data extraction is feasible with 100% sensitivity and accuracy when compared with the manual method [9]. The potential benefit of the adult studies can be adopted to the paediatric patients. We think further studies are needed for VAE automated data extraction to be used in children after that collaboration between clinicians and experts in medical information and systems technology may result in an innovative data.

There are several potential limitations for this study. First, the data were collected retrospectively manually from the 'Intensive Care Surveillance Monitoring Form', so there was missing data and excluded cases. In addition the single-centre design may limit the general applicability of our findings. In the future, we think that it is more appropriate to plan the same study prospectively, multi-center and using an automated data system.

In conclusion, Pediatric Ventilator-Associated Event (Ped-VAE) algorithm is a better tool for children than the VAE algorithm defined for adults. Further studies will be needed for determining whether these metrics can be useful in pediatric national benchmarking and quality improvement programs, establish the generalizability of our findings to a broader set of hospitals, calculation of risk adjustment to account for differences in populations and for prospective evaluation to determine the responsiveness of pediatric AVAC and pediatric PVAP definitions to quality improvement initiatives.

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