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Clinical outcomes related to the incidence of ventilator-associated pneumonia in adults – a cohort study

Desfechos clínicos ligados à incidência de pneumonia associada à ventilação mecânica no adulto – estudo de coorte

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Abstract

Introduction: Ventilator-Associated Pneumonia (VAP) is a common complication found in the Intensive Care Unit (ICU) and is associated with increased mortality, length of hospital stay and mechanical ventilation (MV) time. **Objective:** To determine the incidence of VAP and its impact on the clinical course of the subject undergoing invasive MV in the ICU. **Methods:** This is a cohort study of hospitalized subjects in the general adult ICU of the State Hospital of Bauru / SP. The clinical information for the period of 19 months were collected. Stratification for the groups was based on the presence or absence of VAP, free_VAP and VAP, respectively. The Hotelling T^2 with 95% confidence, chi-square and the Mann-Whitney tests were executed using the "R" software and the results showed as mean ± standard deviation and

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absolute and relative distribution ($p < 0.05$). **Results:** The sample was of 322 subjects; the VAP group consisted of 73 (22.67%), 54.79% male, age: 62.31±16.96 years and the APACHE II: 29.98 ± 8.64. The VAP group had longer time of the MV and of the ICU compared to free VAP group; even in this group, the highest incidence of death in the ICU occurred between the 16th and 20th day of hospitalization. The free VAP group was older and 50% of the patients discharged from hospital. **Conclusion:** VAP and their interfaces still impact on the clinical evolution of the subjects mainly on the time factor of MV and ICU stay. The highest incidence of death in the ICU occurs in the first weeks.

Keywords: Ventilator-Associated Pneumonia. Pulmonary Medicine. Cohort Studies.

Resumo

Introdução: *A Pneumonia Associada à Ventilação Mecânica (PAV) é uma complicação comumente encontrada na Unidade de Terapia Intensiva (UTI) e está associada à maior mortalidade, tempo de internação e ventilação mecânica (VM).* ***Objetivo:*** *Verificar a incidência da PAV e seu impacto sobre a evolução clínica dos sujeitos submetidos à ventilação mecânica invasiva na UTI.* ***Métodos:*** *Trata-se de um estudo de coorte com sujeitos internados na UTI geral adulto do Hospital Estadual de Bauru/SP. Foram coletadas as informações clínicas referentes ao período de 19 meses. A estratificação para os grupos foi realizada com base na ocorrência ou não da PAV, sem_PAV e PAV, respectivamente. Foi aplicado o teste T^2 de Hotelling com 95% de confiança e Qui-Quadrado utilizando o Software "R" e os resultados apresentados em média ± desvio padrão e distribuição absoluta e relativa ($p < 0,05$).* ***Resultados:*** *A casuística foi de 322 sujeitos; o grupo PAV constou de 73 (22,67%), sendo 54,79% do sexo masculino, idade: 62,31 ± 16,96 anos e APACHE II: 29,98 ± 8,64. O grupo NAV teve maior tempo de VM e na UTI se comparado ao grupo sem_NAV; ainda neste grupo, a maior incidência de óbito na UTI ocorreu entre o 16° ao 20° dia de internação. O grupo sem_PAV era mais velho e 50% deste tiveram alta hospitalar.* ***Conclusão:*** *A PAV e suas interfaces ainda causam impacto sobre a evolução clínica dos sujeitos principalmente quanto ao fator tempo de ventilação mecânica e de internação na UTI. A maior incidência de óbito na UTI ocorre nas primeiras semanas.*

Palavras-chave: *Pneumonia Associada à Ventilação Mecânica. Pneumologia. Estudos de Coortes.*

Introduction

The evolution of mechanical ventilation (MV) in recent years has been fundamental to increase the survival of subjects with respiratory failure, but its use is accompanied by undesirable effects, such as hemodynamic instability, lung injury, and respiratory infections. These changes can lead to morbidities, increasing the time and cost of hospitalization and raising the mortality rate [1 – 3].

One of these effects is the Ventilator-Associated Pneumonia (VAP), defined as a nosocomial infection that develops after 48 - 72 hours after the endotracheal intubation and the institution of invasive MV [4]. The VAP is one of the most feared deleterious effects in the Intensive Care Unit (ICU) because it can reach up to 33% of the subjects hospitalized in the unit [1, 2]. The difficulty in the VAP diagnosis criteria can lead to the low prevalence of the disease due to lack of diagnosis since the established criteria are clinical and laboratory, presenting little accuracy. The VAP is suspected when pulmonary infiltrate occurs on chest radiography, associated with fever, leukocytosis or leukopenia, and purulent tracheal secretion [5]. Also, the VAP can be classified as precocious (occurring up to the fourth day of intubation and onset of MV) and late (from the fifth day) [6]. Its prevalence is higher in the elderly, in those with higher severity scores at ICU admission, immunosuppressed, undernourished, smokers, and patients with comorbidities, as well as previous surgeries [6 – 8]. Also, factors that can be modified are also responsible for the prevalence of VAP in some populations [2]. The aspiration of pathogenic microorganisms of the oropharynx and gastric and the time of intubation increase

the chances of developing the VAP. Finally, the indiscriminate use of antibiotics likewise potentiates the occurrence of VAP [2, 3, 9, 10]. The VAP is associated with 43.65% of resistant pathogens, and its incidence contributes to high rates of mortality and morbidity [11].

Therefore, the aim of this study was to verify the clinical outcomes of subjects under MV hospitalized at the ICU with or without VAP.

Methods

This study was submitted to the Ethics and Research Committee of the Universidade do Sagrado Coração, Bauru-SP (protocol n° 122/09). It is a cohort study, comprised of subjects hospitalized in the Adult ICU of the State Hospital of Bauru / SP. During 19 months, clinical information was collected from the subjects submitted to MV by an endotracheal cannula or tracheostomy, independently of the underlying pathology, aged equal or greater than 18 years old, of both genders. Subjects with MV time lower than 48 hours, tracheostomy before admission to the ICU, and those who for any reason presented uncertain or incomplete information in their charts were excluded. Information was collected through electronic records of the "*e-pront*" system and from the database of the Hospital Infection Control Service.

For data collection, a standard form was used to record sociodemographic information, gender, and age, which was obtained considering the registration at the ICU. For clinical data, the following were recorded: primary cause of intubation, time of MV (days), medical diagnosis of VAP [12], time of MV (days) until the occurrence of VAP, overall lowering of consciousness (medical record – Glasgow scale score lower than eight [13], cause of reintubation, need for tracheostomy, time (days) of MV after tracheostomy, time (days) of ICU and hospital ward, death, disease severity and in-hospital mortality prediction - APACHE II (Acute Physiology and Chronic Health Evaluation) [14]. This classification allows a maximum score of 71 points, involving the factors: age, health status, and surgery.

After data collection, the stratification for the groups was performed based on the occurrence or not of VAP, as follows, respectively: VAP and free_VAP.

The statistical treatment was performed using the "R" software (Oswaldo Cruz Foundation, Rio de Janeiro, Brazil, 2014) by the tests T^2 of Hotelling's T-Square, Qui-Square and Mann-Whitney ($p < 0.05$). Thus, the results are presented using descriptive statistics in mean±standard deviation and by absolute and relative distribution.

Results

During the study, 722 admissions were registered in the ICU, from which only 322 subjects were submitted to the MV for more than 48 hours. The VAP occurred in 73 (22.67%) subjects, and 249 (77.32%) subjects did not manifest it. The mean duration of MV until the diagnosis of VAP was 11.18 ± 8.11 days.

Table 1 shows the demographic and clinical data of the VAP and free_VAP groups. It is possible to identify a predominance of male subjects in both groups; and concerning the age, the free_VAP group was older.

Table 1 - Demographic and clinical data

Demographic and Clinical Data		free_VAP Group (n: 249)	VAP Group (n: 73)
Gender (M/F)		152 (61.0%) / 97 (38.9%)	40 (54.7%) / 33 (45.2%)
Age (years)		63.35 ± 16.35	58.94 ± 18.64*
APACHE II		30.29 ± 8.82	28.90 ± 7.94
Causes for indication of MV	Respiratory failure	118 (47.38%)	27 (36.98%)
	Overall lowering of consciousness	53 (21.28%)	20 (27.39%)
	Hemodynamic Instability	39 (15.66%)	12 (16.43%)
Extubation Failure		32 (12.85%)	16 (21.92%)
Tracheostomy		66 (26.50%)	40 (54.79%)

Note: M: male; F: female; MV: mechanical ventilation; *comparison between groups ($p<0.05$); VAP: Ventilator-Associated Pneumonia.

Table 2 shows the data referring to the particular clinical evolution for each group that developed, or not, VAP during ICU admission.

Table 2 - Temporary data regarding clinical evolution of the groups as to the mechanical ventilation and hospital stay

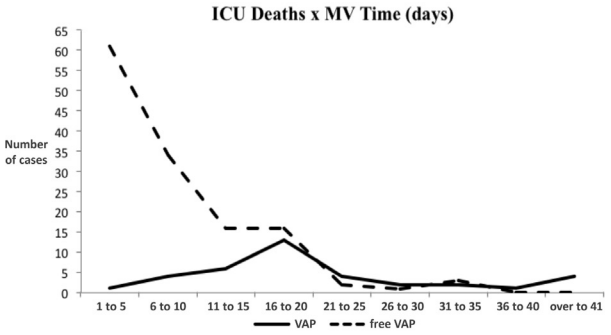
Time Variables (days)	Groups	
	free_VAP	VAP
MV Total time†	12.76 ± 18.40	25.04 ± 22.96*
Time of MV after tracheostomy	13.86 ± 29.56	19.48 ± 25.87
ICU Time	12.45 ± 9.64	25.00 ± 18.60*
Ward Time	20.98 ± 26.88	22.03 ± 19.83

Note: *comparison between groups (p< 0.05); MV: mechanical ventilation; OC: Orotracheal Cannula; ICU: Intensive Care Unit; VAP: Ventilator-Associated Pneumonia; †: the total of MV time evolves both orotracheal intubation and tracheostomy.

The primary cause for the return to ventilator prosthesis in the free_VAP group was the increase in respiratory work, characterized by an increase in the respiratory rate greater than 35 breaths/min. and presence of retractions, observed in 21 (65.62%) subjects. Subsequently, in the VAP group, the primary cause was the neurological lowering with a level of consciousness lower than eight, using as reference the Glasgow Consciousness level that occurred in 7 (43.75%) subjects.

Regarding the end outcome, many of the patients remained in the ICU and others were successful in intensive care and were transferred to the hospital ward, but some of them died. The deaths computed in the ICU were 133 (53.41%), in the free_VAP group, and 37 (50.68%) in the VAP group; at the hospital ward 33 (29.46%) died in the free_VAP group and 11 (31.42%) in the VAP group.

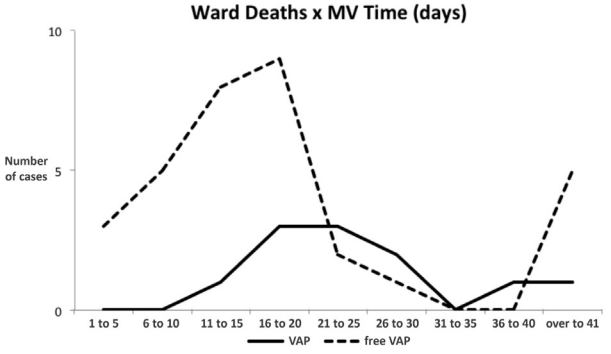
Figures 1 and 2 present the incidence of deaths between the groups according to ICU or hospital ward and time of MV. There was no statistically significant difference comparing the two groups. It is possible to visualize that subjects with a short duration of MV evolved to death; however, patients who remained more than 11 days in the ICU had a reduction for this event in the free_VAP group. In the VAP group, the highest incidence of death occurred when the patient remained in the MV from the 16th to the 20th day (p < 0.001).



Note: ICU: Intensive Care Unit; MV: mechanical ventilation; VAP: Ventilator-Associated Pneumonia; *: comparison intragroup (p < 0.05).

Figure 1 - Number of deaths verified in the Intensive Care Unit during the time subjects were submitted to mechanical ventilation, in both groups.

Subjects who remained in the MV around the 11th to the 20th day and who were discharged to the hospital ward had a higher incidence of death in the free_VAP group (p < 0.05). (Figure 2). In the VAP group, the increase was high between 16th and 25th days.



Note: MV: mechanical ventilation; VAP: Ventilator-Associated Pneumonia; *: comparison intragroup (p< 0.05).

Figure 2 - Number of deaths verified at the hospital ward unit versus time of mechanical ventilation in both groups.

Subjects of the VAP group had a high percentage (31.42%) regarding the need for hospital transfer after discharge from the ICU compared to the free_VAP group (19.64%). Regarding hospital discharge, for the VAP and free_VAP groups, respectively, the incidence was 13 (37.14%) and 57 (50.89%).

Discussion

This study demonstrated that the occurrence of VAP was compatible with what is described in the literature. The average incidence rate of VAP is approximately 20% in intubated individuals, which may vary from 6% to 67% depending on risk factors, population, and model of study [15, 16]. Furthermore, the subjects with VAP presented a longer stay and invasive MV time. Death occurred with greater prevalence around the 18th day of hospitalization, and the minority of the subjects left the hospital during the study period.

The risk of VAP as well as the risks of morbidity and mortality rise with an increase in age. Also, the incidence of chronic diseases, mainly cerebrovascular and neurological dysfunctions, is greater in subjects with aggregated risk factors, and their physiological reserves are smaller [17, 18]. The diseases of the hospitalized subjects in the unit in which this study was conducted were predominantly ischemic stroke, exacerbation of chronic respiratory diseases, and postoperative complications. The VAP group was expected to have more risk factors for its development, including the advanced age. However, it did not happen in this study. Therefore, it is possible to infer that other factors would also be contributing to VAP and not precisely the age.

In both groups, there was a predominance of the male gender. Gender is a variable that is little discussed in the literature about this subject. However, the male gender is a non-modifiable risk factor for VAP [19]. Moreover, its predominance in subjects affected by VAP is greater [20]. As it was already mentioned, the characteristics of this ICU have probably contributed to this finding, since the presence of one or more chronic diseases is higher in older male individuals [21]. Conversely, in Brazil, women present a higher prevalence of findings related to chronic diseases compared to men [22].

Concerning intubation, a study [23] observed the same primary causes found in this research: respiratory failure, overall lowering of consciousness, and hemodynamic instability. It is important to mention that the proportion of these findings was similar between all groups.

The MV time is a risk factor that is known and solidly related to VAP development. The risk is greater in the first week [15]. The subjects of the VAP group also remained hospitalized in the ICU for a considerably longer period compared to the free_VAP group. In this study, the MV average time until VAP diagnosis was 11.18±8.11 days and the average total MV time was higher in the VAP group. Similar data was found in the literature. Therefore, it is possible to infer that MV time was also a possibly triggering factor for VAP. Likewise, a VAP may also have extended MV time because it compromised respiratory bronchioles and alveolus which, filled by inflammatory exudate, and this situation would complicate gas exchanges and require a longer time for expert assistance [24].

The average length of stay in the hospital ward did not differ considerably between groups. However, 31.42% of the subjects of the VAP group required hospital transfer after leaving ICU compared to the group without VAP. Thus, the greater prevalence of hospital transfers and the lower incidence of hospital discharges suggest a possible interference of VAP on the clinical outcome of these subjects. These findings are compatible with other studies [25, 26].

Also, at the moment of extubation, the chance of success in weaning from mechanical ventilation is associated to how high the Glasgow coma scale is [27]. Therefore, it is believed that the higher extubation failure in the VAP group may be a result of the lower degree on the Glasgow coma scale [13]. In the VAP group, 54.79% of subjects necessitated tracheostomy. Such situation can be explained since the extended MV time in association with neurological lowering are risk factors for the development of VAP and the necessity of this type of intervention [28, 29]. Another risk factor for VAP is reintubation [30]. According to Consensus [31], about 13 to 19% of the extubated subjects necessitate reintubation. An increased prevalence of extubation failure was observed in the VAP group compared to the free_VAP group. The factors "unconsciousness" and "possible subglottic dysfunction" (not analyzed in this recent research) may as well be other reasons for the development of VAP in the subjects examined in this study. As expected, the necessity of tracheostomy, indicated in case of bad prognosis and MV dependence, was also high in the VAP group.

The prognosis of in-hospital mortality determined by APACHE II for both groups was approximately 30%. A score equal or higher than 18 is an independent

risk factor for the development of VAP [20]. Also, it is known that subjects admitted with APACHE II higher than 25 points evolve into a bad prognosis in more than 50% of the cases [32, 33]. According to the literature [20], respiratory, cardiovascular, and neurological dysfunctions are the ones that mostly cause hospitalizations in the ICU [23, 34].

Respiratory and neurological dysfunctions are related to a higher score in APACHE II and a longer length of stay in ICU. This allows us to infer, considering the factors "unconsciousness" and "MV time", that these dysfunctions could have been associated with the development of VAP in the subjects of this study [33]. Specifically, the Chronic Obstructive Pulmonary Disease and the presence of septic shock are independently associated with a lower survival rate, in other words, a higher mortality rate [35].

The total number of deaths during the hospitalization period was verified to be similar between the free_VAP (66.66%) and with VAP groups (65.75%). Study [15] suggests that the mortality attributed to VAP is around 30%. A possible explanation for the high percentage of deaths may be the severity of the pathological condition of subjects, analyzed by using APACHE II [6, 7]. Other study that monitored 673 patients for 12 months identified that 74 patients developed VAP. From them, 12 (21.41%) died and were contaminated with multi-resistant pathogens [11]. In another research, from 40 patients with acute respiratory distress syndrome, with a median of 10 days of MV and 10.7 days of hospitalization, 20% developed VAP and 24 (60%) died [16]. In the same year and with similar rates, Ranjan et al. [36] verified that the total mortality associated to VAP was of 48.33%. Another fact to be considered is the decision of the medical team to limit the care to patients with poor prognosis because there is no remedy and this leads to death, regardless of the place of hospitalization, intensive care unit or hospital ward.

The more preventive measures the intensive care unit has, such as the position of the bed, decontamination of the digestive tract, control of cuff pressure, oral care, endotracheal suctioning, and appropriate antibiotic therapy, lower the chances of developing PAV and other problems related to it. Apart from that, the risk factors for pneumonia change during the period of intubation and to prevent pneumonia requires a combination of approaches [8].

Above all, new information, research, and methods of evaluation and treatment are indispensable for relieving these situations. Some aspects must receive particular attention on the prevention of VAP [1]: the position of the patient during MV (head of bed elevation between 30 - 45°), the use of strategies of weaning that decrease MV time, as well as the maintenance of the cuff pressure equal or higher than 20 cmH_2O [7, 37 – 40].

This research intended to reinforce the magnitude of the problem, identify some possible clinical factors that may compromise the therapy, and use these findings to highlight the necessity of teamwork to approach a severe patient to avoid complications and irreversible outcomes.

Limitations of the study

The study is retrospective; thus the results were interpreted as a causal association; also, the lack of complete data hindered us from doing more associations and incrementing the initial characterization of samples.

Conclusion

VAP is a determining factor in the time of mechanical ventilation and the length of stay in ICU. However, it did not interfere in the length of stay in the ward. The incidence of VAP resulted in a higher number of deaths from the 16° to the 20° day of hospitalization in ICU.

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