IMPACT OF BUNDLES IMPLEMENTATION IN THE PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Ventilator-associated pneumonia is an infection caused by the orotracheal tube in mechanically ventilated patients. Bundles are a small group of interventions evidence-based which, when implemented together, improve the quality of patient care. This systematic review aims to analyze the impact of bundles implementation on the prevention of ventilator-associated pneumonia.

Methods: A database research (EBSCO and PUBMED) was performed using keywords such as: ventilator-associated pneumonia, prevention and bundle, and using the Boolean operator AND. 88 studies were obtained and, after a careful selection and evaluation of their methodological quality, we included 6 of them in this review.

Results: The most common measures used in these bundles are oral hygiene with chlorhexidine, 30º head-of-bed elevation and daily sedation interruption. The bundles adherence results in lower ventilator-associated pneumonia rates. The bundles adherence tends to increase when strategies are implemented. The implementation of different bundles led to a decrease of ventilator-associated pneumonia incidence rate, between 3.8% and 62.8%.

Discussion: In addition to the decrease of ventilator-associated pneumonia rate, the implementation of these bundles also led to a reduction in the length of hospital stay and mechanical ventilation days, antibiotic use, mortality and associated costs. Different definitions and ways to diagnose VAP can influence the results and their incidence rate. The fact that different measures are used to create bundles, makes it difficult to determine which ones are responsible for the obtained results.

Keywords: Ventilator-associated pneumonia; disease prevention; bundle; health-care bundles; systematic review.

INTRODUCTION

Ventilation Associated Pneumonia (PAV) is still nowadays an infection with a high prevalence in the Intensive Care Units (ICU), which has consequences such as the increase of the mechanical ventilation period, in the length of hospital stay, use of antimicrobials and mortality(1).

PAV is defined as an infection process that develops 48 hours following the invasive mechanical ventilation or in patients who have been extubated for less than 48 hours(2). In practice, the diagnosis of VAP is based on the association of clinical, radiological and mi-
crobiological features such as the presence of fever, purulent secretions, leukocytosis, accompanied by onset or progression of infiltrate\textsuperscript{[3]}. 

In Portugal, the incidence of VAP has decreased from 11.2 to 7.1 per 1,000 days of intubation between 2008 and 2014\textsuperscript{[4]}. Given the importance and complexity of this issue, strategies have been adopted to prevent VAP. Currently, care bundles are used, which are no more than a small set of evidence-based interventions that, when implemented together, result in improved care if they are performed at all times in clinical practice\textsuperscript{[5]}.

Both the World Health Organization and the European Commission emphasize that health must be based on the best research data\textsuperscript{[6]}. Thus, the use of scientific evidence in care decisions is crucial because although clinical experience is recognized as necessary, it is not sufficient to provide the best possible care\textsuperscript{[7]}.

Since PAV is a theme present in the ICU, where our daily practice has influence, it is necessary to develop care based on scientific assumptions so as to have an improvement in quality.

**METHODOLOGY**

It was decided for a systematic review of the bibliography, which is an accurate and reliable method, allowing to synthesize a set of information with relevance and scientific evidence\textsuperscript{[8]}. The research question was based on the PICOS strategy, Population, Intervention, Control, Outcomes and Study design, this being: is there scientific evidence that the use of bundles contributes to the prevention of VAP in the adult patient?

For the identification of the bibliography we used the databases EBSCO and PUBMED, using the search terms: ventilator associated pneumonia, prevention and bundle and using the Boolean operator AND.

The selection of the studies was carried out in two distinct stages, the screening and the assessment of its methodological quality. The following inclusion criteria were defined for screening: (1) target population over 18 years; (2) studies using bundles; (3) approach to the prevention of VAP; (4) quantitative primary studies; (5) time period between 2011-2016; (6) studies in English and finally (7) access to the full text. After the adopted research strategy, 88 studies were identified. Of these, 25 were automatically eliminated by repeated publication, 7 were excluded because they did not include the target population, 37 canceled through the title, 9 deleted after reading the abstract, and 3 excluded
after the complete review of the article, as shown in Figure 1. One of the studies was excluded because it is a systematic review, however, in the discussion phase of this article will be made a comparison with the results that were obtained in it.

Thus, 7 studies (6 cohort and 1 quasi-experimental) were included in this review, and an assessment of the methodological quality was made through the critical appraisal tools of the Joanna Briggs Institute\(^9\). This evaluation eliminated one of the studies (quasi-experimental) that did not fulfill most of the required criteria. This procedure was carried out by two appraisers.

![Flow diagram describing the systematic review process.](image)

**Figure 1** – Flow diagram describing the systematic review process.
RESULTS

A detailed characterization of the six studies included in the systematic review can be found in Table 1.
### Table 1 – Summary of the general characteristics of the studies included in the systematic review.

<table>
<thead>
<tr>
<th>Study Identification</th>
<th>Authors (Date)</th>
<th>Study Type/Levels of Evidence Joanna Briggs Institute(^ {10} ) (2013)</th>
<th>Study Objective</th>
<th>Number and type of participants</th>
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<tr>
<td>Use of Ventilator Bundle and Staff Education to Decrease Ventilator-Associated Pneumonia in Intensive Care Patients.</td>
<td>Parisi et al. (2016)</td>
<td>Cohort (prospective) Level 3.c</td>
<td>- Evaluate the incidence of VAP in an ICU;</td>
<td>1,097 patients evaluated: 362 met the inclusion criteria.</td>
<td>- The baseline PAV rate was 21.6 per 1,000 days of ventilation. In the post-intervention period, it decreased to 11.6 per 1,000 days of ventilation; The length of ICU stay decreased from 36 to 27 days and the mechanical ventilation period decreased from 26 to 21 days.</td>
<td>- The incidence of VAP was high in the general ICU of a Greek hospital. However, the bundles implementation and the team education reduced both the incidence of VAP and the length of ICU stay.</td>
</tr>
<tr>
<td>The effectiveness of a bundle in the prevention of ventilator-associated pneumonia.</td>
<td>Ferreira et al. (2016)</td>
<td>Cohort Level 3.c</td>
<td>- Evaluate the FAST HUG bundle impact on the PAV;</td>
<td>Including 188 patients: 115 in the pre-bundle period; 73 in the post-bundle period.</td>
<td>- After FAST HUG implantation there was a decrease in the incidence of VAP in 16.5%, as well as a reduction in the mortality rate. In addition, the intervention resulted in a significant reduction of hospital costs in the ICU.</td>
<td>- The FAST HUG implementation reduced the number of cases of VAP; Reducing costs, reducing mortality rates and the length of hospital stay resulted in an improvement in the overall quality of care.</td>
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Impact of bundles implementation in the prevention of ventilator-associated pneumonia...

- 125 patients fulfilled the inclusion criteria:
  - 48 in the pre-bundle period;
  - 77 in the post-bundle period.

- The bundle implementation significantly reduced the rates of VAP, particularly those caused by MRSA;
- There was a reduction in the mechanical ventilation period as well as in the length of ICU stay;
- The mortality rate did not change significantly with the bundle implementation.

- The bundle use was associated with a reduction in the incidence of VAP from 42 cases per 1,000 days of ventilation in the pre-intervention group for 19 cases per 1,000 days of ventilation in the post-intervention group;
- The MRSA acquisition rate was significantly different in the pre-intervention group (27%) and in the post-intervention group (3.9%);
- With the bundle implementation there was a significant reduction in the period of mechanical ventilation and the length of ICU stay.

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<td>Reduced incidence of methicillin-resistant Staphylococcus aureus (MRSA) ventilator-associated pneumonia in trauma patients: A new insight into the efficacy of the ventilator care bundle.</td>
<td>Mukhtar et al. (2014)</td>
<td>Cohort (prospective)</td>
<td>Determine the effect of bundle implementation on the incidence of VAP caused by MRSA.</td>
<td>-125 patients fulfilled the inclusion criteria: • 48 in the pre-bundle period; • 77 in the post-bundle period.</td>
<td>- The bundle use was associated with a reduction in the incidence of VAP from 42 cases per 1,000 days of ventilation in the pre-intervention group for 19 cases per 1,000 days of ventilation in the post-intervention group; - The MRSA acquisition rate was significantly different in the pre-intervention group (27%) and in the post-intervention group (3.9%); - With the bundle implementation there was a significant reduction in the period of mechanical ventilation and the length of ICU stay.</td>
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Impact of four sequential measures on the prevention of ventilator-associated pneumonia in cardiac surgery patients.

Pérez-Granda et al. (2014)  
Cohort (prospective)  
Level 3.c  
- To assess the impact of implementing a bundle to prevent VAP in a major heart surgery at ICU.  
- 1,935 Patients underwent major heart surgery;  
  • 401 in the pre-bundle period;  
  • 1534 during bundle implementation.  
- With the bundle implementation, the VAP rate (per 1,000 days of ventilation) decreased from 23.9 to 13.5; the number of days of ventilation (per 1000 days of hospital stay) decreased from 507 to 375; the costs of antibiotics (for 1,000 days of hospital stay) decreased from 70,612 € to 52,775 €; the mortality rate fell from 13% to 10.2%.  

Temporal trends of ventilator-associated pneumonia incidence and the effect of implementing health-care bundles in a suburban community.

Ding et al. (2013)  
Cohort (retrospective)  
Level 3.c  
- To compare the VAP incidence before and after the bundle implementation.  
- Including 350 patients:  
  • 213 in the pre-bundle period;  
  • 137 post-bundle period.  
- The annual estimates of VAP incidence vary between 7.1 and 10.4 cases per 1,000 days of ventilation. In the pre-bundle period, the VAP incidence was 9.0 cases per 1,000 days of ventilation and in the post-bundle period it was 10.1 cases per 1,000 days of ventilation;  
  - The standardized hospital mortality rate for critically ill patients at high risk for developing VAP declined significantly from 7.1 to 0.7.  

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| Impact of four sequential measures on the prevention of ventilator-associated pneumonia in cardiac surgery patients. | Pérez-Granda et al. (2014)          | Cohort (prospective) Level 3.c                                | - To assess the impact of implementing a bundle to prevent VAP in a major heart surgery at ICU. | - 1,935 Patients underwent major heart surgery;  
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| Temporal trends of ventilator-associated pneumonia incidence and the effect of implementing health-care bundles in a suburban community. | Ding et al. (2013)                 | Cohort (retrospective) Level 3.c                              | - To compare the VAP incidence before and after the bundle implementation. | - Including 350 patients:  
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  • 137 post-bundle period. | - The annual estimates of VAP incidence vary between 7.1 and 10.4 cases per 1,000 days of ventilation. In the pre-bundle period, the VAP incidence was 9.0 cases per 1,000 days of ventilation and in the post-bundle period it was 10.1 cases per 1,000 days of ventilation;  
  - The standardized hospital mortality rate for critically ill patients at high risk for developing VAP declined significantly from 7.1 to 0.7. | - The VAP incidence, the length of hospital stay and the mechanical ventilation period did not change with the bundle implementation.  
  - Changes in hospital mortality are unlikely to be associated with the bundle alone. |
A care bundle approach for prevention of ventilator-associated pneumonia.

Rello et al. (2013)

Cohort (prospective) Level 3.c

- To determine the impact of a 5 measures bundle implementation in the prevention of VAP, on the mechanical ventilation period and the length of hospital stay;
- To determine the impact of each individual measure on the risk of developing VAP.

- Including 1,034 patients:
  - 149 at baseline;
  - 885 in the post-bundle period.

- Of the 885 patients studied after the bundle implementation, the 5 measures were applied to only 264 of them. However, when this occurred, the incidence of VAP decreased from 15.5% to 11.7%, the mechanical ventilation period decreased from 8 to 4 and the length of hospital stay average decreased from 10 to 6 days;
- Most cases of VAP occur before the seventh day of mechanical ventilation;
- Hand hygiene prior to airway manipulation, cuff pressure control and oral hygiene with chlorhexidine are the measures that most contribute to reducing the risk of developing VAP;
- Of the 5 measures that constitute the bundle, 4 contributed to the prevention of VAP while, the lack of respiratory circuit change did not reveal a significant impact in this reduction.

- High adherence to the implementation of preventive bundles of VAP can lead to a significant improvement in results;
- Efforts should be concentrated to promote continuing education of health professionals to maintain high levels of adherence.

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- To determine the impact of each individual measure on the risk of developing VAP. | - Including 1,034 patients:
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- Efforts should be concentrated to promote continuing education of health professionals to maintain high levels of adherence. |
**Bundles Elements**

The bundles for VAP prevention, implemented in the different studies, do not consist of the same measures. The most common measures are oral hygiene with chlorhexidine, 30º head-of-bed elevation and daily sedation interruption. Prophylaxis of peptic ulcer and deep vein thrombosis, cuff pressure control, and the subglottic secretions drainage are also measures that often make up the bundles. The non-change of respiratory circuit is a measure that has no impact on the decrease of the prevalence rate of VAP\(^\text{[11]}\). The bundles belonging to the different studies were composed of 4 to 9 interventions. Ding et al.\(^\text{[12]}\) do not state the measures that constitute the bundle that incorporated their study.

**Bundles Adherence**

The bundles adherence rate is an extremely important factor since it influences the results obtained. Most studies have shown that increased bundle compliance results in a decrease in the VAP rate. In parallel to this, Ding et al.\(^\text{[12]}\) concluded that even with a high bundle adherence rate, the VAP prevalence rate did not decrease.

In the study conducted by Rello et al.\(^\text{[11]}\) it was observed a lower rate of bundle adherence, which was lower than 30%. In this study, only 264 of the 885 patients included were subject to the five measures that constituted the bundle. In this same study, the measure with lower adherence was oral hygiene with chlorhexidine with 16.4%.

There were measures with a higher adherence rate, such as the daily sedation interruption in the study of Mukhtar et al.\(^\text{[13]}\), which had an adherence of almost 100%, followed by oral hygiene with chlorhexidine with a 70-80% adherence. Pérez-Granda et al.\(^\text{[14]}\) found that adherence to the education program, the subglottic secretions drainage and oral hygiene with chlorhexidine was of 100%. On the other hand, the measure with the lowest adherence was the implementation of the 30º head-of-bed elevation, that no strategy was adopted to increase this adherence.

**Strategies implemented in Bundles Adherence**

In the analyzed studies, several strategies were used to increase bundle adherence. For example, in the study conducted by Rello et al.\(^\text{[11]}\) leaflets/cards were used with the measurements of the bundle and the results obtained were presented at meetings and through posters, in order to maintain high adherence rates. The most commonly used strategy was team education\(^\text{[11,13,15]}\). As a strategy, the use of the FAST HUG mnemonic to help health professionals to establish the health care interventions should be highlighted\(^\text{[16]}\).
Bundle adherence was found to have improved after the implementation of strategies\(^{(15)}\).

**Results of bundle implementation**

The results of the bundle implementation were evaluated through the VAP prevalence rate, mechanical ventilation period, length of hospital stay, mortality rate and costs.

As we can see in Graph 1, in five of the six studies analyzed, the implementation of the different bundles led to a decrease in the VAP incidence rate. In one study only, the application of the bundle did not lead to a reduction of the VAP, there was actually an increase up to 3\(^{(12)}\). It is also possible to verify that the largest reduction in the VAP rate was 62.8\(^{(13)}\) and the lowest was 3.8\(^{(11)}\).

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**Graphic 1 – PAV reduction after bundle.**
The influence of bundle implementation on mechanical ventilation period was analyzed in five of the reviewed studies\textsuperscript{(11-15)}, only one did not dissect this aspect\textsuperscript{(16)}. Parisi et al.\textsuperscript{(15)} reported that, with the bundle implementation, the mechanical ventilation period decreased from 26 to 21 days. Mukhtar et al.\textsuperscript{(13)} reported a decrease (from 8 to 6 days of mechanical ventilation), whereas Rello et al.\textsuperscript{(11)} found that this decrease was more significant (from 8 to 4 days of mechanical ventilation). The number of days of ventilation per 1,000 days of hospital stay decreased from 507 to 375 in the study by Pérez-Granda et al.\textsuperscript{(14)}. Ding et al.\textsuperscript{(12)} were the only investigators who did not observe changes in the mechanical ventilation period after the bundle implementation.

The variation in the length of hospital stay caused by the application of bundles was studied in four of the six studies undergoing revision. Of these four studies, three concluded that the bundles implementation contributed to the reduction of the length of hospital stay\textsuperscript{(11,13,15)}. This reduction ranged from 411 to 9 days\textsuperscript{(15)}. In the study conducted by Ding et al.\textsuperscript{(12)}, there was no decrease in the length of hospital stay with the introduction of the bundle.

Only two studies did not analyze the effects of bundle implementation on the mortality rate\textsuperscript{(11,15)}. The decline in the highest mortality rate was observed in the study conducted by Ding et al.\textsuperscript{(12)} in which the standardized hospital mortality index for critically ill patients at high risk of developing VAP decreased from 7.1 to 0.7. However, these researchers claim that this significant decline should not be associated with the bundle alone. Ferreira et al.\textsuperscript{(14)} found a decrease in the mortality rate from 60% to 30%, while Pérez-Granda et al.\textsuperscript{(14)} observed a decrease from 13.2% to 10.2%. Mukhtar et al.\textsuperscript{(13)} did not show significant changes in the mortality rate after the introduction of the bundle.

Cost analysis was done only in two of the six studies. In one of them it was found that the introduction of the bundle led to a significant reduction of hospital costs\textsuperscript{(14)}. In the other, the cost of the necessary antibiotic treatment in VAP cases was evaluated and it was concluded that these expenses, for 1,000 days of hospital stay, decreased from € 70,612 to € 52,775.14\textsuperscript{(14)}.

**Criticism**

Only Rello et al.\textsuperscript{(11)} involved more than one ICU in the data collection process, encompassing five ICUs in their study.

All studies identify the sample size. The study by Pérez-Granda et al.\textsuperscript{(14)} is the one with the largest population sample, with 1935 patients. Parallel to this, Mukhtar et al.\textsuperscript{(13)} present the smallest sample of the six studies analyzed, involving only 125 patients in their investigation.
Four of the studies involved in this review process specify the way in which the constituent measures of bundles were implemented\(^{[11,13,15,16]}\). There is uniformity in the way this evaluation was done since in all the concerned studies there was a record sheet with the list of different measures and each of them was evaluated with the yes/no dichotomy. In the particular case of the study by Rello et al.\(^{[11]}\), these data were later recorded in computer system by a previously selected collaborator.

**DISCUSSION**

All the studies reviewed are cohort, with a pre and post implementation analysis of the bundles and all have a control group, which is great because it facilitates the analysis of the impact of this implementation. The main objective of this review was to find primary studies that evaluated the effect of bundle use in the prevention of VAP.

The concern about this subject is clear, which results in the accomplishment of several studies to obtain conclusions that lead to the reduction in the prevalence rate of VAP in the ICUs. In 5 of the 6 studies analyzed, positive results were obtained in the prevention of VAP, when adopting bundles\(^{[11,13-16]}\). In addition to the decrease in the VAP rates for 1,000 days of ventilation, benefits were observed in other dimensions, that is, a decrease was also observed in the length of ICU stay, the mechanical ventilation period, the use of antibiotic therapy, as well as mortality and associated costs. Only one study did not reveal positive post-bundle outcomes\(^{[12]}\). The researchers attempted to explain what happened because the definitions of VAP were subjective and non-specific. Also, the occurrence of non-payment by social health programs in the case of hospital infections was a factor that triggered this result, since many of the observers minimized the VAP rates through the application of subjective criteria.

Despite the convergence of results, the interventions that make up the bundles are not the same, so it is difficult to make a comparison. However, it is possible to affirm that the bundle consisting of 30° head-of-bed elevation, daily sedation interruption, daily assessment of possibility of orotracheal extubation, prophylaxis of peptic ulcer and deep vein thrombosis and oral hygiene with chlorhexidine was the one that had a better outcome in reducing VAP with a 62.8% decrease\(^{[13]}\). Only one study mentions which bundle interventions most contributed to the reduction of the risk of developing VAP\(^{[13]}\). It should also be noted that all measures which constitute each bundle are evidence-based.
In most of the studies under analysis it is possible to notice that there is a relation between the adherence to the bundles and the VAP incidence rate, that is to say, a greater bundles adherence leads to a decrease of the VAP. Applying strategies to increase bundle adherence was an important factor for the end result.

It should also be noted that the fact that different definitions and ways of diagnosing VAP are used in the various studies may in some way influence the results regarding their incidence rate.

As previously mentioned, a systematic review of this subject was found in the survey conducted in the present study[17]. The results obtained in that study are in line with those obtained in this analysis. As an example, there is a strong relationship between the bundles use and the VAP reduction, the importance of auditing bundle adherence rates and the fact that strategies to increase this rate of adherence are an aspect that influences in a positive way the obtained result. This systematic review of 2011, as also found in this analysis, states that the use of different measures in the constitution of bundles, made it difficult to determine which measures are responsible for the obtained results.

**CONCLUSION**

In conclusion, and after analysis of the different studies, it is possible to confirm that bundles implementation contributes to the prevention of VAP in the adult patient, noting that this has not happened in only one of the studies. VAP incidence rate was not the only variable that changed after the adoption of bundles, since differences were also observed in the days of mechanical ventilation, length of hospital stay, mortality and costs.

From the analysis, the notion that it is important to implement strategies to increase and maintain high levels of bundle adherence has also emerged.

It is also necessary to reinforce the idea that further studies in this area should be carried out in order to define the most effective interventions to incorporate bundles. At the same time, it is important to clarify the best strategies that motivate a behavior change of healthcare professionals and consequently to better clinical results.

*Declaration of conflicting interests*

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
REFERENCES


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