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ORIGINAL ARTICLE

Implementation of a ventilator-associated pneumonia prevention bundle in a teaching hospital

Implementação de um bundle de prevenção de pneumonia associada à ventilação mecânica em um hospital universitário

Implementación de un paquete de prevención de neumonía asociada a ventilador en un hospital escuela

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ABSTRACT

Background and objectives: the implementation of ventilator-associated pneumonia (VAP) prevention bundles in Intensive Care Units (ICU) has been recommended due to the considerable increase in hospital costs, length of stay, morbidity and mortality in affected hospitalized patients. However, the results of its effectiveness are still controversial. This study aimed to assess the impact of implementing a VAP prevention bundle in an Adult ICU of a university hospital. **Methods:** a quasi-experimental study, with implementation of a VAP prevention bundle in an Adult ICU and analysis of indicators. This study addressed secondary data from hospital records recommended in the routine of the Hospital Infection Control Commission team and from the medical records of patients undergoing mechanical ventilation, from June 2016 to July 2019, who developed VAP. **Results:** VAP incidence density before the intervention was 4.13 infections, and after the intervention, it was 7.15 infections per thousand patients on ventilation/day. When performing the linear regression test, we showed that VAP density decreased as sedation was reduced, extubation was increased, and when compliance with all bundle elements occurred. **Conclusion:** there was no reduction in VAP incidence after the adoption of preventive measures, perhaps due to an underreporting of cases in the period prior to the bundle and a low team compliance with the bundle components. However, we noticed a decrease in VAP notifications after the eighth month of implementation of bundle of measures.

Keywords: *Ventilator-Associated Pneumonia. Intensive Care Unit. Prevention. Patient Safety.*

RESUMO

Justificativa e objetivos: a implementação de bundles de prevenção de pneumonia associada à ventilação mecânica (PAV) em Unidades de Terapia Intensiva (UTI) tem sido recomendada devido ao aumento considerável dos custos hospitalares, tempo de internação, morbidade e mortalidade em pacientes hospitalizados acometidos. No

entanto, os resultados de sua eficácia ainda são controversos. Este estudo teve como objetivo avaliar o impacto da implantação de um bundle de prevenção de PAV em uma UTI Adulto de um hospital universitário. **Métodos:** estudo quase experimental, com implantação de bundle de prevenção de PAV em UTI Adulto e análise de indicadores. Este estudo abordou dados secundários de prontuários hospitalares recomendados na rotina da equipe da Comissão de Controle de Infecção Hospitalar e dos prontuários de pacientes em ventilação mecânica, no período de junho de 2016 a julho de 2019, que desenvolveram PAV. **Resultados:** A densidade de incidência de PAV antes da intervenção foi de 4,13 infecções e após a intervenção foi de 7,15 infecções por mil pacientes em ventilação/dia. Ao realizar o teste de regressão linear, mostramos que a densidade da PAV diminuiu à medida que a sedação era reduzida, a extubação aumentava e quando ocorria complacência com todos os elementos do feixe. **Conclusão:** não houve redução da incidência de PAV após a adoção de medidas preventivas, talvez pela subnotificação de casos no período anterior ao bundle e baixa adesão da equipe aos componentes do bundle. No entanto, notamos diminuição das notificações de PAV após o oitavo mês de implantação do bundle de medidas.

Palavras-chave: *Pneumonia Associada à Ventilação. Unidade de Tratamento Intensivo. Prevenção. Segurança do paciente.*

RESUMEN

Justificación y objetivos: la implementación de paquetes de prevención de neumonía asociada al ventilador (NAV) en las Unidades de Cuidados Intensivos (UCI) ha sido recomendada debido al aumento considerable de los costos hospitalarios, la estancia hospitalaria, la morbilidad y la mortalidad en los pacientes hospitalizados afectados. Sin embargo, los resultados de su eficacia aún son controvertidos. Este estudio tuvo como objetivo evaluar el impacto de la implementación de un paquete de prevención de NAVM en una UCI de adultos de un hospital universitario. **Métodos:** estudio cuasi-experimental, con implementación de un paquete de prevención de NAVM en una UCI de Adultos y análisis de indicadores. Este estudio abordó datos secundarios de registros hospitalarios recomendados en la rutina del equipo de la Comisión de Control de Infecciones Hospitalarias y de los registros médicos de pacientes en ventilación mecánica, de junio de 2016 a julio de 2019, que desarrollaron NAV. **Resultados:** La densidad de incidencia de NAVM antes de la intervención fue de 4,13 infecciones y después de la intervención fue de 7,15 infecciones por mil pacientes en ventilación/día. Al realizar la prueba de regresión lineal, mostramos que la densidad de VAP disminuyó a medida que se redujo la sedación, se incrementó la extubación y cuando se produjo el cumplimiento de todos los elementos del paquete. **Conclusión:** no hubo reducción en la incidencia de NAVM después de la adopción de las medidas preventivas, quizás debido a un subregistro de casos en el período anterior al paquete y al bajo cumplimiento del equipo con los componentes del paquete. Sin embargo, notamos una disminución en las notificaciones de VAP después del octavo mes de implementación del paquete de medidas.

Palabras clave: *Neumonía asociada a ventilador. Unidad de Cuidados Intensivos. Prevención. Seguridad del paciente.*

INTRODUCTION

Ventilator-associated pneumonia (VAP) is one of the healthcare-associated infections (HAI) that generate considerable increases in hospital costs, length of stay, morbidity and mortality in hospitalized patients.[1,2]

VAP occurs in approximately 10 to 25% of patients who require invasive mechanical ventilatory support for more than 24 hours.[3] It is the hospital infection that most commonly affects patients admitted to the Intensive Care Unit (ICU), representing up to 60% of hospital infections,[4,5] depending on patients' comorbidities, clinical status and duration of mechanical ventilation (MV).[6]

According to the Brazilian National Regulatory Health Agency (ANVISA - *Agência Nacional de Vigilância Sanitária*), VAP is characterized by a pulmonary infection occurring after 48 hours of endotracheal MV, associated with one or more chest radiographs with the presence of a new, persistent or progressive infiltrate, fever (> 38°C) or leukocytosis or leukopenia, worsening pulmonary secretions or worsening pulmonary function.[7]

There are several risk factors for the development of VAP, which can be classified as modifiable and non-modifiable.[8] Non-modifiable risk factors are age, severity score at the time of admission of patient to ICU and presence of comorbidities.[8] Modifiable factors include length of hospital stay, prolonged intubation time, supine position, surgery, tracheostomy, multiple intubations and use of steroids.[2,5]

Considering the relevant negative impact caused by VAP on critically ill patients, it is essential to adopt preventive care, taking into account the modifiable factors. Several studies suggest bundles of measures for VAP prevention in critically ill patients.[2,6,9] These care bundles have been widely used today, which bring together a small group of interventions that, when implemented together, result in substantial improvements in health care[9]. In turn, these bundles vary greatly from one institution to another, according to the specificity of hospitalized patients.[10]

According to the literature, the effectiveness of bundles for VAP prevention is still controversial. Some studies point to a reduction in VAP incidence,[6,9,11-14] while others failed to observe such an improvement.[2,15,16]

Faced with the need to adopt preventive measures in the ICU of a teaching hospital that is a reference for

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the city and 26 municipalities of Minas Gerais, and, in this scenario of uncertainty regarding the efficiency of bundles, we understand the need to know the effectiveness of bundle implementation for VAP prevention in the population assisted in our service.

Therefore, the aim of this study was to assess the impact of implementing a bundle for VAP prevention in an Adult ICU of a university hospital.

METHODS

This is a quasi-experimental study conducted in an Adult ICU of a teaching hospital in Minas Gerais.

The implementation of VAP prevention bundle in the aforementioned ICU began in January 2018, with the institution of the Ministry of Health's "Improving Patient Safety on a Large Scale in Brazil" (*Melhorando a Segurança do Paciente em Larga Escala no Brasil*) program. Initially, the care teams were trained to carry out the measures proposed by the bundle and record the actions performed in patients' medical records. The records were monitored daily by the Hospital Infection Control Commission (HICC) and collected to evidence the team compliance rate with the bundle elements.

This study addressed secondary data from hospital records, recommended in the routine of the HICC team and assisted patients' medical records. All HICC data records related to VAP density, from June 2016 to July 2019, from the aforementioned ICU and the medical records of all patients over 18 years of age diagnosed with VAP after admission to the ICU in the same period. In order to compare patients' profile, medical records of patients who underwent MV for more than 48 hours in the same study period and who did not develop VAP were also included. Medical records of patients under 18 years of age, patients on MV for a period of less than 48 hours and patients diagnosed with VAP prior to ICU admission were excluded.

In the reports, indicators related to VAP incidence in the ICU were analyzed in the months prior to bundle implementation (June 2016 to December 2017) as well as after its implementation (January 2018 to July 2019). In this last period, data related to team compliance with the bundles were collected.

Data were extracted regarding VAP incidence density (number of VAP cases in the month divided by the number of patients on MV/day in the month, multiplied by 1,000), mortality rate, ICU stay rate, length of stay on MV and MV utilization rate. Team compliance with the bundle elements was also verified: keeping the headboard elevated, maintaining adequate cuff pressure, performing sedation reduction, performing oral hygiene with chlorhexidine (0.12%) twice a day, verifying the possibility of extubation and maintaining a MV system, according to the recommendations in force in the country.

In the analysis of medical records, data from patients' sociodemographic and clinical profile were analyzed, such as age, sex, diagnosis of ICU admission, comorbidities and type of device used for MV at the time of infection (nasotracheal, orotracheal or tracheostomy tube), type of treatment to which patients underwent (clinical or surgical), Apache II severity score, type of VAP and outcome (discharge or death).

Descriptive exploratory analysis of the variables was performed, with numerical variables measured by central tendency and dispersion. To apply the statistical tests, it was necessary to verify the population's distribution and normality; for this, the Shapiro-Wilk test was performed. To test the hypothesis that two variables presented in the patient table are associated, Fisher's test was performed comparing the elements presented in the table. A statistical significance was established at * = p< 0,05. Data with non-normal distribution were found, and the Mann-Whitney test was used to assess whether there was a difference in VAP density before and after bundle application. To predict associated factors based on the correlation between VAP density and each element of the bundle, a linear regression and Spearman correlation analysis were performed, in which Spearman's r values and p-value were found, in addition to R^2 value. The Odds Ratio for the development of VAP was calculated with a 95% confidence interval. A statistical significance was established at * = p< 0,05.

For statistical analyses, GraphPad Instat and GraphPad Prism, version 8.02, were used. According to distribution (Shapiro-Wilk test), the results with non-normal distributions were expressed as medians (minimum and maximum values), with a significance level lower than 0.05.

Data collection to determine compliance with preventive measures was carried out between January 2018 and July 2019. At least 20 monthly observations of each bundle element were performed. Compliance with these measures was measured through observations of compliance with each bundle element, separately and together.

In order to know the monthly team compliance with thee bundle elements, the number of items in compliance was divided by the total number of items assessed, arriving at the value in percentage of compliance with each element and with all elements together. From these results, the average value of compliance with the bundle elements was calculated, which will be presented as the median of the percentage of compliance.

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national, if applicable) and with the Declaration of Helsinki of 1975, as revised in 2000. The study was approved by the institution's Research Ethics Committee, under CAAE (*Certificado de Apresentação para Apreciação Ética* - Certificate of Presentation for Ethical Consideration) 04794918.9.0000.8667 and Opinion 3,257,340.

RESULTS

This study involved 64 patients: 30 (46.9%) patients before bundle application and 34 (53.1%) after bundle application, with 15 patients diagnosed with VAP before bundle application and 15 patients without VAP in this pe-

riod, 17 patients with VAP after bundle implementation and 17 patients without a diagnosis of VAP in the same period.

VAP incidence density value of 4.13 was found before the bundle and 7.15 infections per thousand patients on MV/day after the institution of prevention measures (Figure 1).

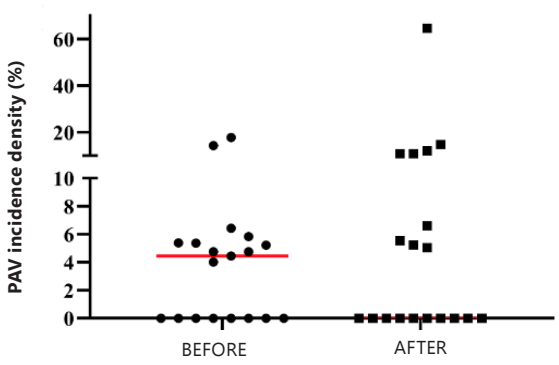

Figure 1. Assessment of VAP density comparing the period before and after bundle application. Mann-Whitney test, p= 0.8966.

The median (minimum-maximum value) of patients' age before the bundle was 54.5 (18-87), and 53.5 (20-87) for patients after the bundle. For the Apache II variable, it was 22 (9-31) for patients before the bundle, and 23 (14-32) for patients after the bundle. The length of hospital stay (in days) was 20.5 (2-123) for patients before the bundle, and 18 (3-123) for patients after the bundle. Regarding MV duration (days), the median was 16 (3-120) for patients before the bundle, and 13.5 (3-102) for patients after the bundle.

Regarding overall mortality, there was no difference between the period before the bundle (30.4%; 13.6-50) and after the bundle was implemented (31.4%; 17.9-39.4).

Most patients were male (66.7% before the bundle and 58.8% after the bundle), with a predominant diagnosis of external causes (e.g., traumatic brain injury, multiple traumas, gunshot wounds, among others) (33.3%) before and (41.2%) after the bundle. They had comorbidities (46.7%) in the pre-bundle and (55.9%) post-bundle periods. They received surgical treatment (60%) pre-bundle and (55.9%) post-intervention

The predominant type of VAP before and after the bundle was late (86.6%), which, after the institution of preventive measures, showed a slight reduction to 82.35%, with no statistically significant difference.

Table 1 shows the detailed characterization of the sample used in the study.

The medians (minimum-maximum value) of the percentage of compliance with the bundle by the team were oral hygiene (100%; 30-100), elevated headboard (95%; 65-100), reduced sedation (95 %; 0-100), verifica-

Table 1. Characteristics of patients admitted to an Adult ICU of a teaching hospital. From June 2016 to July 2019.

	Before the intervention					After the intervention				
	With VAP		Without VAP			With VAP		Without VAP		
	n (%)	Median (min-max)	n (%)	Median (min-max)	p-value*	n (%)	Median (min-max)	n (%)	Median (min-max)	p-value*
Age										
< 60 years	10 (66.7)	51 (18-85)	9 (66.7)	57 (33-87)	1.000	8 (47.1)	62 (22-87)	13 (76.5)	45 (20-77)	0.157
>= 60 years	5 (33.3)		6 (40.0)			9 (52.9)		4 (23.5)		
Sex										
Male	9 (66.7)	-	11 (73.3)	-	0.700	9 (52.9)	-	11 (64.7)	-	0.728
Female	6 (40.0)		4 (26.7)			8 (47.1)		6 (35.3)		
Comorbidities										
Yes	6 (40.0)	-	8 (53.3)	-	0.715	12 (70.6)	-	7 (41.2)	-	0.1663
No	9 (66.7)		7 (46.7)			5 (29.4)		10 (58.8)		
Treatment										
Surgical	11 (73.3)	-	7 (46.7)	-	0.264	11 (64.7)	-	8 (47.1)	-	0.4905
Clinical	4 (26.7)		8 (53.3)			6 (35.3)		9 (52.9)		
Outcome										
Hospital discharge	9 (66.7)	-	8 (53.3)	-	1.000	8 (47.1)	-	6 (35.3)	-	0.4905
Death	6 (40.0)		7 (46.7)			9 (52.9)		11 (64.7)		
Apache										
>= 20	9 (66.7)	20 (9-30)	12 (80.0)	24 (17-31)	0.427	15 (88.2)	25 (14-30)	12 (70.6)	21 (15-32)	0.3983
<20	6 (40.0)		3 (20.0)			2 (11.8)		5 (29.4)		
Length of stay										
>= 30	6 (40.0)	24 (4-123)	2 (13.3)	12 (2-119)	0.215	7 (41.2)	24 (9-123)	2 (11.8)	14 (3-35)	0.1175
< 30	9 (66.7)		13 (86.7)			10 (58.8)		15 (88.2)		
MV time										
>= 10 days	14 (93.3)	17 (5-102)	7 (46.7)	8 (3-120)	0.014*	16 (94.1)	17 (9-102)	6 (35.3)	9 (3-38)	0.0008*
< 10 days	1 (6.7)		8 (53.3)			1 (5.9)		11 (64.7)		
Total	15 (100)		15 (100)			17 (100)		17 (100)		

*VAP - ventilator-associated pneumonia; Fisher's test; *p<0.05.*

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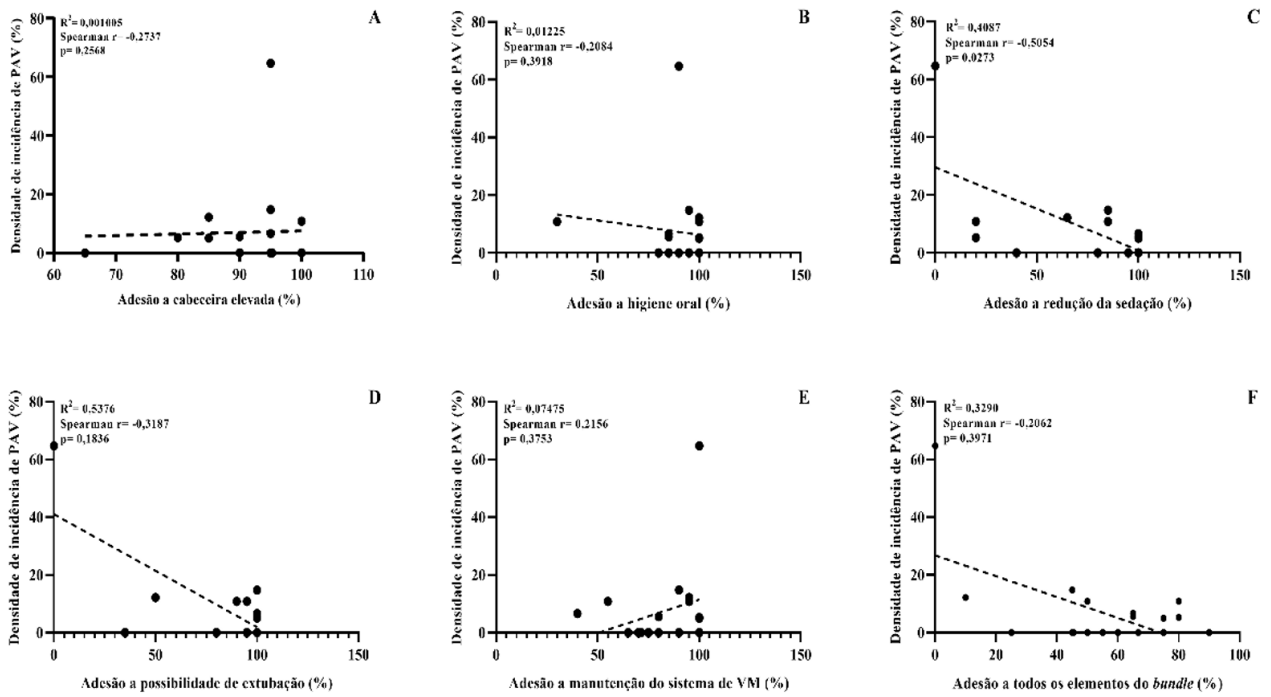

Figure 2. Linear regression and correlation of VAP incidence density related to bundle elements during the intervention period (January 18 to July 19), correlating the incidence in the month with the percentage of compliance with bundle indicators: (A) compliance with elevated headboard; (B) compliance with oral hygiene; (C) compliance with sedation reduction; (D) compliance with possibility of extubation; (E) compliance with MV system maintenance; and (F) compliance with all bundle elements. Linear regression was performed, presenting the R^2 value. For the assessment of correlation, Spearman's test was performed and the correlation of each of the bundle elements was presented, as well as compliance with all elements. Spearman's r value and p-value of the test were presented, being statistically significant when $p<0.05$.

Table 2. Analysis of risk factors for the development of VAP in an Adult ICU. From June 2016 to July 2019.

Risk factors	With VAP n= 32	Without VAP n= 32	(95% CI) OR	p-value*
Age				
>= 60 years	14	10	1.711 (0.6150 - 4.761)	0.4390
< 60 years	18	22		
Sex				
Female	14	10	0.5844 (0.2100 - 1.626)	0.4390
Male	18	22		
Comorbidities				
Yes	18	15	1.457 (0.5441 - 3.902)	0.6173
No	14	17		
Treatment				
Surgical	22	15	2.493 (0.8987 - 6.918)	0.1282
Clinical	10	17		
Apache				
>= 20	24	24	1.000 (0.3224 - 3.101)	1.000
< 20	8	8		
Length of stay				
>= 30	13	4	4.789 (1.354 - 16.94)	0.0219*
<30	19	28		
MV time				
>= 10	30	21	7.857 (1.575 - 39.19)	0.0109*
< 10	2	11		
Outcome				
Hospital discharge	17	19	0.7754 (0.2881 - 2.087)	0.8013
Death	15	13		

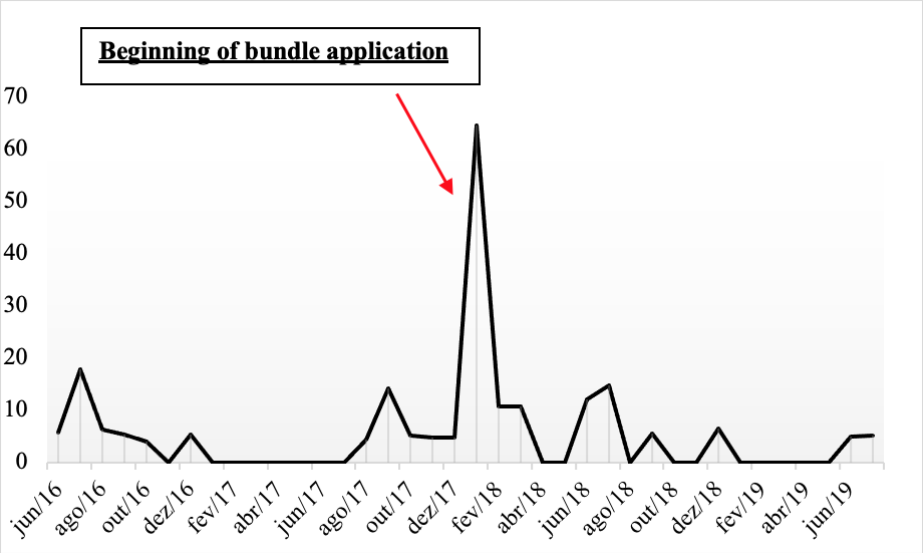

Figure 3. Incidence of numbers of VAP cases during the study period in an Adult ICU.

tion of extubation possibility (100%; 0-100), maintenance of cuff pressure (85%; 55-100), maintenance of ventilator circuits (80%; 40-100) and compliance with all elements (55%; 0-90). We did not see a sustained improvement in team compliance over the months. We had months with an improvement in the performance of a measure, but, on the other hand, a worsening in other elements.

When performing the linear regression test to predict behavior based on the association between VAP density and each bundle element, VAP density decreased as sedation was reduced [(R^2=0.4087; p= 0.0032) (Figure 2)], as well as VAP density decreased as extubation increased [(R^2=0.5376; p= 0.0003) (Figure 2)], and compliance with all bundle elements managed to decrease VAP density [(R^2=0.329; p= 0.0102) (Figure 2).

When assessing the Odds Ratio and the confidence interval of some variables on VAP density, length of hospital stay (4.789; 95%CI: 1,354 - 16.94) and MV time (7.857; 95%CI: 1,575 - 39.19) showed to be a risk factor for the development of VAP (Table 2)

Figure 3 demonstrates the incidence of pneumonia during the study period, June 2016 to July 2019, in an Adult ICU. There was a significant increase in the notification of VAP cases in January 2018, when bundle implementation to prevent VAP in the ICU began.

DISCUSSION

In the present study, VAP incidence density before the intervention was 4.13 infections, and, after the intervention, it was 7.15 infections per thousand patients on MV/day, demonstrating an increase in infections after the introduction of VAP prevention bundle. Although most studies show a reduction in VAP after the adoption of preventive measures,[9,11-14] some studies like this also did not show improvements after the implementation of bundles.[15,16] These results may be due to several factors. First, the diagnostic bias of VAP is one of the factors that affect its incidence; the clinical definitions of VAP are quite subjective and unspecific; and the subjectivity and inconsistencies of VAP diagnostic criteria allow manipulating its real incidence, which can result in underreporting of this infection.[17-19] Moreover, in the period prior to bundle implementation, attention was not focused on the diagnosis of VAP. On the other hand, in the bundle post-implementation period, a multidisciplinary team, composed of physicians, nurses and physiotherapists from the ICU, was assigned to monitor and daily discuss the cases of hospitalized patients, therefore, attention was redoubled in the tracking of suspected cases until the diagnosis is confirmed.

Another point that suggests the underreporting of cases in the pre-bundle period is the data from several studies, which describe VAP prevalence in ICU, ranging from 7 to 40 infections per 1,000 patients on MV/day, values higher than those found in this study. [11,15,16]

We should also highlight the team compliance with the bundle elements. This compliance with recommendations has been recognized as the main factor associated with the reduction in VAP rates.[20] In the literature, we found several sets of measures to prevent VAP. [19] In general, these are simple precautions that, when used together in a systematic way, can prove to be effective.[9] This study was presented in accordance with the Ministry of Health's "Improving Patient Safety on a Large Scale in Brazil" program, with the adoption of 6 preventive measures: headboard elevation between 30 and 45°; oral hygiene with chlorhexidine twice a day; verification of possibility of extubation, reduction of sedation, maintenance of cuff pressure and maintenance of ventilation circuits, in accordance with the recommendations in force in the country. Compliance with these measures was measured through observations of compliance with each

bundle element, separately and together. Most bundle studies have only analyzed complete bundles rather than testing the contributions of each bundle component. According to Klompas, this analysis of the components in isolation is important, because the data that support each component are variable.[19]

In this study, we observed a general compliance with all bundle elements of 55%, which is lower than that recommended in the literature, which should reach 95%.[11,21] Overall compliance rates were 71.8% in a study in 6 university hospitals in South Korea,[21] 74.16% in ICU in Belgium [14] and 77% in a teaching hospital of large size in Brazil,[11] in which reductions in VAP incidence density rates were evidenced. Thus, we can infer that low compliance can also justify the data found in our study. On the other hand, when we analyzed the incidence of VAP and compliance with the bundle elements, we evidenced a trend towards VAP reduction, as was the case of compliance with sedation reduction, verification of possibility of extubation and compliance with all bundle elements in set. Klompas found positive results in VAP prevention, with spontaneous breathing tests and reduced sedation, which corroborates our results.[19] However, it also found a reduction in VAP with an elevated headboard, which was not evidenced in our research. Differently from what was found here, oral hygiene was reported as an impact factor in VAP reduction in some studies.[21,22] However, Klompas showed that, despite reducing VAP, oral hygiene with chlorhexidine was potentially harmful and may be associated with higher mortality rates.[10,19]

VAP reduction, associated with the components reduction of sedation and verification of possibility of extubation, is in line with the significant risk factor in our study for the development of VAP, which was MV duration and length of hospital stay. The earlier sedation is withdrawn and extubation is performed, the less time patients are susceptible to the development of VAP. Therefore, implementing a bundle based on minimizing sedation and spontaneous breathing tests seems to effectively contribute to VAP prevention. Measures that can contribute to reduce long-term mortality, since VAP has been repeatedly associated with prolonged MV, length of hospital stay and increased mortality.[19,23] In our study, the overall mortality rate remained stable (30.4%) pre- and (31.4%) post-bundle, and was not related to a higher prevalence of VAP.

When we compared the groups with and without VAP in relation to the Apache II severity score, sex, age, presence of comorbidities and treatment, we did not find significant differences, suggesting that the population characteristics remained similar. Only in relation to MV duration there was a significant difference, confirming this data as a risk factor for VAP.

Late VAP, which occurs after the fourth day of intubation, was predominant in patients before the bundle. Unlike early VAP, which is caused by antibiotic-sensitive microorganisms, late VAP is related to multidrug-resistant pathogens and therefore more difficult to treat.[5] In a multicenter study in Spain, the authors showed that bundle measures had a greater impact on late-onset VAP;[23] however, in our study, it was not possible to observe such improvements.

Despite the lack of improvement in VAP incidence in the post-bundle period, we noticed, after the eighth month of implementation, a tendency towards a decrease in VAP incidence density, suggesting that the measures adopted can, in the long term, be effective and therefore should be continued and monitored to ensure patient safety, as we believe that the sustained bundle application can increase its clinical impact.

A limiting factor in the present study is due to the number of patients included, due to the low incidence of VAP, which may not reflect reality. Prospective studies with extended periods of time should be carried out, in an attempt to reach more expressive samples.

In the present study, we did not find a reduction in VAP incidence after preventive care implementation, perhaps due to an underreporting of cases in the period prior to the adoption of measures and a low team compliance with the bundle elements. However, we noticed a decrease in VAP notifications after the eighth month of bundle implementation, which may suggest that the measures adopted may, in the long term, be effective and, therefore, should be continued and monitored to ensure patient safety. In any case, we understand that studies with larger samples are necessary to determine whether this bundle is efficient in preventing VAP in the population studied.

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Taciane Cristina Santana and **Luciana Paiva** contributed to study conception, design, analysis and writing;

Taciane Cristina Santana, Luciana Paiva and **Cristina da Cunha Hueb Barata de Oliveira** contributed to article planning and design, review and final approval;

All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.