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Research article

Application of a ventilator associated pneumonia prevention guideline and outcomes: A quasi-experimental study

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ABSTRACT

Objective: Ventilator associated pneumonia is the most frequent health-care-associated infection in Intensive Care Units, causing increased antibiotic consumption and resistance, length of stay, plus multiple health and economic costs. The aim of the study was to assess whether a customised guideline implementation would improve ventilator-associated pneumonia incidence and associated intensive care outcomes.
Design: This was a quasi-experimental, before-after study consisting of pre-intervention, intervention and post-intervention periods.
Setting: Three intensive care units at a well-known Portuguese hospital centre.
Intervention: A set of eight recommendations was implemented after a guideline adaptation process.
Patients: Adult patients admitted to the intensive care units over the study periods, aged 18 years or older and under invasive ventilation through an endotracheal tube or tracheostomy cannula.
Measurements and main results: Data related to patient characterisation, guideline compliance and health outcomes were analysed. From a population of 1970 patients, a study sample of 828 was studied. Compliance with the recommendations was high. We identified a significant reduction in the incidence of ventilator-associated pneumonia in two of the units ($p = 0.020$ and $p = 0.001$) and a reduction in duration of invasive ventilation, intensive care unit length of stay and mortality in all the three units. We found associations between some recommendations and the implementation of the set of recommendations and intensive care unit length of stay, duration of invasive ventilation and mortality.
Conclusion: The implementation of an evidence-based, locally customised guideline may improve ventilator associated pneumonia incidence and several outcomes.

Implications for clinical practice

- Guideline compliance is associated with a significant reduction in the incidence of ventilator associated pneumonia.
- Compliance with cuff pressure maintenance, ventilator weaning and all guideline recommendations simultaneously are associated with better intensive care unit outcomes.
- The implementation of an evidence-based guideline, locally customised guideline may improve ventilator associated pneumonia incidence and several intensive care unit outcomes.

Introduction

Health care associated infections (HCAI) represent one of the main complications of hospitalisation. Ventilator associated pneumonia (VAP) is the HCAI with the highest incidence rate in

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intensive care units (ICUs) and it is defined as "a pneumonia where the patient is on mechanical ventilation for >2 calendar days on the date of event, with day of ventilator placement being Day 1 and the ventilator was in place on the date of event or the day before" (CDC, 2015).

VAP is associated with an increase in antibiotic consumption and antimicrobial resistance, days of invasive ventilation, length of stay (LOS), as well as an estimated cost of $40,000 USD in the USA per episode (Kollef et al., 2012) and an estimate cost of £10,000 in Europe (Wyncoll and Camporota, 2012). Although in recent years a decreasing tendency of incidence density has been observed, it is still a very high value, entailing significant economic and health implications.

The implementation of Clinical Practice Guidelines is advocated by some authors as the solution for the adoption of safe clinical practices (Vaz Carneiro et al., 2007; McKinlay et al., 2001). Using the best evidence to support clinical decision-making, health care professionals are able to achieve better outcomes. Although theoretically guideline implementation generates positive changes, in practice some studies have revealed different success rates (NZGG, 2001). A recent study from Sachetti et al. (2014) found no significant changes in VAP rate after implementing a prevention guideline and compliance varied from 34,5% to 77,8%. Different results were obtained from Bird et al. (2010) in which VAP decreased from 10.2 cases/1000 ventilator days to 3.4 cases/1000 ventilator days and compliance increased 91% and 81% respectively in each ICU. This variability in the results can be explained by differing compliance rates in the studies. Several experts recommend the development of an implementation and dissemination plan when implementing a guideline (McKinlay et al., 2001). Oliveira et al. (2014) emphasise the need to incorporate the most recent findings regarding VAP prevention recommendations in guidelines and to carry out studies which assess their impact when applied jointly. The aim of this study is to evaluate the impact of a VAP prevention guideline in VAP rate, duration of invasive ventilation, mortality and ICU LOS. Our study question was "Does the implementation of a VAP prevention guideline influence health outcomes?" In this article we will focus on the discussion of the health outcomes after application of the guideline and not on the detailed development and implementation process, which will be addressed in future publications.

Methods

Study design

This was a quasi-experimental, before-after study that aimed to determine if a customised guideline implementation would improve ventilator-associated pneumonia incidence and associated ICU outcomes. The Guideline was developed according to the ADAPTE® methodology, following a sequence of steps that included: a search for guidelines and other relevant documents; quality selection and assessment of currency, acceptability and applicability; presentation of recommendations and production of the final document. The guideline was tested using a before-after methodology that consisted of a pre-intervention period of six months, an intervention period of six months and a post-intervention intervention period of three months. The implementation took place in three ICUs, two general and one neurocritical, of a central university hospital in the north of Portugal. In all ICUs, the basic infection control measures recommended by the World Health Organisation had been adopted. Compliance with the recommendations was assured by the Infection Control Commission, who regularly conducted audits and provided feedback to the health care team. VAP was diagnosed according to CDC (2015) and HELICS criteria, namely: the presence of newly developed or progressive infiltrates on chest radiographs plus at least two other signs of respiratory tract infection: temperature >38 °C, purulent sputum, leukocytosis (WBC >10 × 103/mm3) or leukopenia (WBC <4 × 103/mm3), signs of inflammation during auscultation, cough and/or respiratory insufficiency with a PaO2/FiO2 ratio of ≤300 mmHg. The guideline was implemented after a multifaceted dissemination and implementation teaching period. Compliance was evaluated by observation and documentation query. Three groups were then compared: the pre-intervention group (between October 2015 and March 2016), the intervention group (between July and December 2016), and the post-intervention group (from January to March 2017, during which teaching to encourage compliance on all strategies was suspended). The choice of a six month period for duration of the intervention was made based on the number of a representative sample needed for a quantitative study, according to the number of patients in ICU in previous periods.

The first two months of the intervention period were devoted to education, in which the guideline was presented to its users and disseminated in the ICUs, so compliance data was not assessed. We opted for this two-month period to ensure all of the professionals would be able to receive adequate and necessary information and training. Fig. 1 describes the investigation process. The population consisted of all patients admitted in the ICUs in the considered periods. Inclusion criteria for the three groups were adult patients aged 18 years or older and under invasive ventilation through an endotracheal tube or tracheostomy cannula. Exclusion criteria were discontinuation of mechanical ventilation within 48 hours of initiation and readmissions to the ICU<48 hours after discharge.

Guideline recommendations were:

- Avoid endotracheal ventilator if possible (Klompas et al., 2014)
- Perform daily sedation assessment and reduction to a minimum level (Klompas et al., 2014; National Guideline, C., 2011; Paiva et al., 2015)
- Perform daily weaning and/or extubation discussion (Klompas et al., 2014; National Guideline, C., 2011; Paiva et al., 2015)
- Change ventilator circuit only when visibly soiled or damaged (Klompas et al., 2014; National Guideline, C., 2011; Paiva et al., 2015)
- Maintain head of bed elevation at an angle of 30-45°, avoiding periods of supine position (Klompas et al., 2014; National Guideline, C., 2011; Paiva et al., 2015)
- Promote early exercise and patient mobility (Klompas et al., 2014)
- Evaluate and maintain endotracheal tube (ETT) cuff pressure between 20 and 30cmH2O (Klompas et al., 2014; National Guideline, C., 2011; Paiva et al., 2015)
- Perform oral hygiene care with chlorhexidine 0.12% or 0.2% according to the following sequence of events: aspiration of oral and nasal secretions above the ETT cuff; tooth and gum cleaning with sponge or gauze and irrigation with 15 ml of chlorhexidine solution 0.12% or 0.2% for 30 seconds 2–4 times a day followed by aspiration. All three guidelines included in this study recommend oral care with chlorhexidine (Klompas et al., 2014; National Guideline, C., 2011; Paiva et al., 2015). The use of this solution, however, is not recommended by all researchers. A systematic review and *meta*-Analysis by Klompas et al. (2014) found an association between the increased concentration of chlorhexidine and a greater mortality rate. Therefore, these researchers recommend low concentrations (0.12%), as well as undertaking new studies that reveal the relationship of the concentration of the chlorhexidine with the incidence of "acute respiratory distress syndrome" (ARDS).

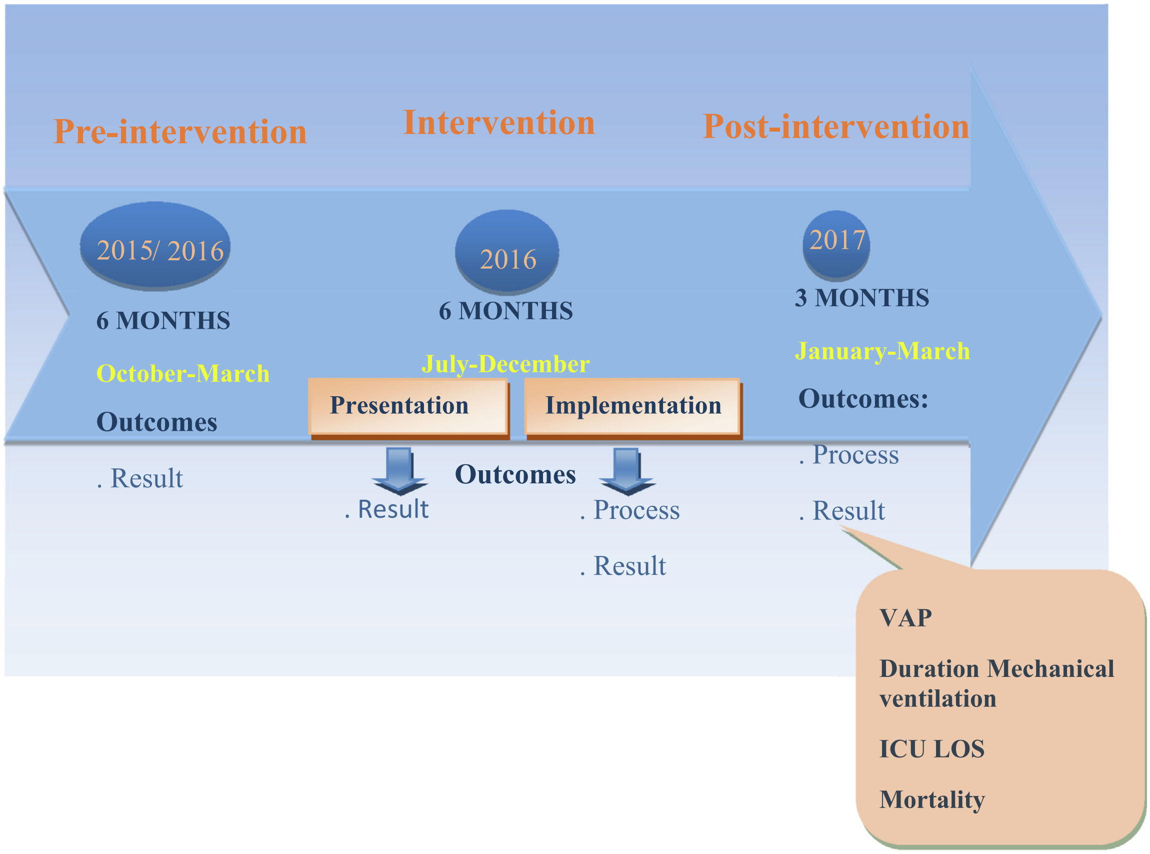

Fig. 1. Investigation Process Diagram.

In order to establish the optimum chlorhexidine application, frequency, quantity to be applied and technique, MEDLINE and B-on databases were searched on December 28, 2015, to answer these questions. A *meta*-analysis by the Cochrane collaboration concluded that the use of chlorhexidine solution or gel decreases the incidence of VAP, with or without brushing, but with no effect on other outcomes such as mortality rate, duration of mechanical ventilation and hospital LOS (Shi et al., 2013).

Paiva et al., (2015) recommend the completion of oral hygiene with chlorine gluconate-chlorhexidine at 0.2%, at least three times a day, in all patients aged over two months, which predictably remain in the ICU more than 48 hours. The *meta*-analyses carried out by Klompas et al. (2014) and Pileggi et al. (2011) and the literature review by Kornusky and Schub (2015) recommend a frequency of application of chlorhexidine between 2 and 4 times per day. Therefore, we consider this to be the appropriate frequency of application of this antiseptic.

In relation to the amount of chlorhexidine that should be applied in the oral cavity, only Shi et al. (2013) specify irrigation with 15 ml during seconds followed by an aspiration or application of the gel solution. Shi et al. (2013), in a *meta*-analysis that sought to characterise oral hygiene in ventilated patients, identified three main components of oral hygiene care: suction of secretions, cleaning of teeth and gums with sponge or gauze and washing with chlorhexidine solution. Table 1 summarises guideline recommendations.

Analyses were conducted using the Statistical Package for the Social Sciences (IBM® SPSS® Statistics 24) system. To answer the question: "Does the implementation of a VAP prevention guideline influence health outcomes?", we compared the period of the study with the variables: VAP rate; duration of invasive ventilation; mortality and ICU LOS. Furthermore, because the implementation of a guideline is conditional on compliance with all its requirements, the association between compliance and each recommendation, individually and simultaneously and VAP rate, duration of invasive ventilation, mortality and ICU LOS was studied.

All the calculations were made considering the independent character of the samples, testing bilaterally and considering as statistically significant a $p < 0.05$. The mean values are represented as mean ± standard deviation. The relationship between VAP, duration of invasive ventilation, ICU LOS and study period was studied using the One-Way ANOVA test and the relationship between mortality and study period was studied using the Chi-square test.

Ethics

This study was conducted in accordance with the amended Declaration of Helsinki. The study was approved by the Hospital Health Ethics Committee, the Intensive Care Unit Directorate and the Hospital Center Board of Directors. Written informed consent was obtained from the patients or their guardians (70-16). The proposal was made by the principal investigator who explained potential benefits and damages of the study, as well all patient and family rights according to the Helsinki Declaration. Written information about study aims and interventions was given to patients' guardians.

Results

During the time period under study, 1970 patients were admitted in the ICUs. According to the established criteria, 1130 patients were excluded due to duration of ventilation being inferior to

Table 1
Guideline recommendations.

Guideline recommendations
Avoid endotracheal ventilator if possible;
Perform daily sedation assessment and reduction to a minimum level;
Perform daily weaning and/or extubation discussion;
Change ventilator circuit only when visibly soiled or damaged;
Maintain head of bed elevation at an angle of 30–45°, avoiding moments of supine position;
Promote early exercise and patient mobilization;
Evaluate and maintain endotracheal tube (ETT) cuff pressure between 20 and 30cmH2O;
Perform oral hygiene care with chlorhexidine 0.12% or 0.2% according to the following sequence of events: aspiration of oral and nasal secretions above the ETT cuff; tooth and gum cleaning with sponge or gauze and irrigation with 15 ml of chlorhexidine solution 0.12% or 0.2% for 30 seconds 2–4 times a day followed by aspiration.

48 hours, six patients due to age, being minors under the age of 18, and six due to being ICU readmissions within less than 48 hours. After applying the inclusion and exclusion criteria, the sample consisted of 828 patients, aged between 18 and 95 years, with a mean age of 61.85 ± 15.8 years. Groups are described in Table 2. All of the patients who met inclusion criteria, or their legal guardians, gave their consent to be involved in the study.

There were no significant differences between the pre-intervention, intervention and post-intervention groups regarding age, Simplified Acute Physiology Score II (SAPS) and type of admission, so we can consider the samples similar and comparable.

Guideline compliance

Guideline compliance was measured for each intervention individually and for all interventions simultaneously. Compliance for each intervention individually ranged from 94,7% to 99,8%. The mean compliance rate for all interventions simultaneously was 88.6%.

ICU LOS was significantly reduced by higher compliance with the maintenance of cuff pressure ($p < 0.001$) and by compliance with all the recommendations simultaneously ($p = 0.004$). Duration of invasive ventilation was significantly reduced by higher compliance with ventilator weaning, ($p = 0.016$), cuff pressure maintenance ($p < 0.001$) and with the application of all interventions simultaneously ($p = 0.005$).

Considering mortality rate, we found a significant reduction by higher compliance with ventilator weaning ($p = 0.008$) and cuff pressure maintenance ($p = 0.002$). We did not find any significant association between compliance and VAP rate, though.

Number of days under invasive ventilation

The mean number of days under invasive ventilation decreased in the intervention period (12.4 ± 10.1 days) compared to the pre-intervention period (12.8 ± 10.5 days) and increased slightly in the post-intervention period (12.7 ± 11.1 days).

Comparing data referring to duration of invasive ventilation versus VAP rate over the study periods, we found a significant decrease in the mean duration of invasive ventilation among individuals who did not exhibit VAP (<0.001 in the pre-intervention, 0.004 in the intervention, and <0.001 in the post-intervention period). Normality of the data was studied using the Shapiro-Wilk test (Table 3).

Table 2
Study groups description.

Study Phase Variable	Pre-Intervention	Intervention	Post-Intervention	F	χ2	*p*
Age	62.0 (±15.2)	61.3 8 ± 15.6)	61.0 (±16.3)	0.256	–	0.774
95% Confidence Intervals	(60.2; 63.8)	(59.7; 63.0)	(58.6; 63.5)			
Masculine gender	202 (63.7%	214 (63.9%)	105 (60.3%)	–	0.707	0.702
SAPS II	50.5 (±16.8)	49.9 (±17.5)	52.9 (± 17.1)	1.371	–	0.178
95% Confidence Intervals	(48.6; 52.4)	(48.1; 51.8)	(50.3; 55.4)			
Type of Admission					6.334	0.610
Surgical schedule	24 (7.6%)	15 (4.5%)	8 (4.6%)			
Surgical urgent	79 (24.9%)	76 (22.6%)	44 (25.3%)			
Coronary	18 (5.7%)	16 (4.7%)	7 (4.0%)			
Medical	146 (46.1%)	170 (50.4%)	90 (51.7%)			
Trauma	50 (15.8%)	60 (17.8%)	25 (14.4%)			
Mean days under invasive ventilation	12.8 (±10.5)	12.4 (±10.1)	12.7 (±11.1)	0.146	–	0.864
95% Confidence Intervals	(11.6; 14.0)	(11.3; 13.4)	(11.0; 14.3)			

p: Significance. χ2: Chi-squar test statistic. F: One-Way ANOVA test statistic.

Table 3
Duration of invasive ventilation per study period according to the incidence of VAP.

	Study Period	VAP	Mean	95% CI (difference of means)	Statistic test	p value
Number of days under invasive ventilation	Pre-intervention	Negative	83.1	(−15.5; −7.1)	MW = 1142.0	<0.001*
		Positive	130.8			
	Intervention	Negative	13.2	(−15.5; −3.6)	t(28.268) = −3.094	0.004*
		Positive	22.5			
	Post-intervention	Negative	11.5	(−22.3; −10.7)	t(99) = −5.646	<0.001*
		Positive	28.0			

* Significant test. p: Significance. t: Student's *t* test statistics. MW: Mann-Whitney test statistics. Mean position expressed in days under invasive ventilation.

VAP incidence

During this study, we observed a decrease in the incidence rate of VAP, between the pre-intervention period (7.89/1000 intubation days) and the intervention period (6.24/1000 intubation days), which corresponds to a reduction of approximately 21% (p = 0.552). In the post-intervention period, we observed a slight non-significant rise (6.81/1000 intubation days, p = 0.552).

When assessing the evolution of VAP incidence rate in each ICU, we found a significant decrease in two ICUs (p = 0.020 and p = 0.001) (Table 4). In ICU A we observed an increase in VAP rate between the pre-intervention period (4%) and the intervention period (4.7%) and a decrease in the post-intervention period (1.4%, p = 0.539), with 54% of cases identified between July and August 2016, which corresponded to the guideline teaching phase of the intervention period. When we extended this analysis to the three ICUs, we found that 50% of the cases of VAP occurred between July and August.

ICU length of stay

A reduction in the mean values of ICU LOS was registered between the pre-intervention period, [26.4 (±14.9) days] and the intervention period [23.3 (±14.0) days] (table 5). In the post-intervention period we observed an increase [30.0 (±13.7) days]. Analysing the ICU LOS between the group with VAP and the group with no VAP, within each study phase, we verified that there were significant differences. We studied the normality of the data using the Shapiro-Wilk test.

Mortality rate

ICU mortality declined significantly over the study period, with 31.9% in the pre-intervention period, 31.2% in the intervention period and 29.3% in the post-intervention period (p = 0.037), corresponding to a reduction of 8%.

In Fig. 2 we can see the evolutionary trend of the health outcomes VAP, ICU LOS, duration of invasive ventilation and mortality rate in the pre-intervention, intervention and post-intervention periods.

Discussion

We identified a significant reduction in duration of invasive ventilation, ICU LOS and mortality rate in the three ICUs during the intervention phase. The incidence of VAP was significantly reduced in two ICUs. Compliance with the recommendations was high and was associated with ICU LOS, duration of invasive ventilation and mortality.

Outcome variation

Regarding duration of invasive ventilation and ICU LOS in the three study periods, we found that both groups of patients, VAP and no VAP, had a significant reduction in both outcomes. Nevertheless, the VAP group experienced higher duration of invasive ventilation. This data may lead us to conclude that longer time under invasive ventilation increases the risk of acquiring VAP, but also acquiring VAP increases the duration of invasive ventilation and consequently ICU LOS. This relationship is also described by Alp and Voss (2006), Karatas et al. (2016) and Miguel-Díez et al. (2017).

A relatively low baseline incidence of VAP and high bundle compliance may contribute to the fact that a statistically significant reduction was not obtained in the study periods, despite the reduction of this rate from 7.89 to 6.24 episodes/1000 days of ventilator. The variability in the results of similar studies is considerable, reporting reductions in this outcome ranging from 0% to 100% (DeLuca et al., 2017; Ferreira et al., 2016, Khan et al., 2016; Klompas et al., 2016; Marini et al, 2016; Okgun Alcan et al., 2016; Parisi et al., 2016). One of the possible explanations for this phenomenon may be different rates of compliance with recommendations, not reported in all of the studies found.

Table 4
Evolution of VAP incidence by ICU.

ICU			Groups			Total		
			Pre-intervention	Intervention	Post-intervention		Statistic test	P value
ICU C	VAP	Negative	34.7%	37.6%	11.8%	84.1%	$X^2(2) = 7.39$	0.020*
		Positive	7.1%	3.5%	5.3%	15.9%		
	Total		41.8%	41.2%	17.1%	100.0%		
ICU B	VAP	Negative	35.2%	38.6%	21.3%	95%	$X^2(2) = 14.256$	0.001*
		Positive	2.4%	2.1%	0.5%	5%		
	Total		32.1%	32.1%	35.7%	100.0%		
ICU A	VAP	Negative	33.0%	35.9%	21.0%	89.9%	$X^2(2) = 1.236$	0.539
		Positive	4.0%	4.7%	1.4%	10.1%		
	Total		37.0%	40.6%	22.5%	100.0%		

* Significant test. $\chi 2$: Chi-square test statistic. p: Significance. Incidence of VAP expressed as a percentage. VAP positive: patients who acquired VAP. VAP negative: patients who do not acquired this infection.

Table 5
Evolution of ICU LOS according to the incidence of VAP.

	Study period	VAP	Mean	95% CI (difference of means)	Statistic test	P value
ICU LOS	Pre-intervention	Negative	83.5	(−16.0: −7.1)	MW = 1198.5	<0.001*
		Positive	129.1			
	Intervention	Negative	91.0	(−13.0; −2.5)	MW = 1319.5	0.002*
		Positive	127.8			
	Post-intervention	Negative	13.3	(−22.8; −10.6)	t(93) = −5.420	<0.001*
		Positive	30.0			

* Significant test. p: Significance. t: Statistic of student T test. MW: Mann-Whitney test statistics. Mean position expressed in days ICU LOS. VAP positive: patients who acquired VAP. VAP negative: patients who do not acquired this infection.

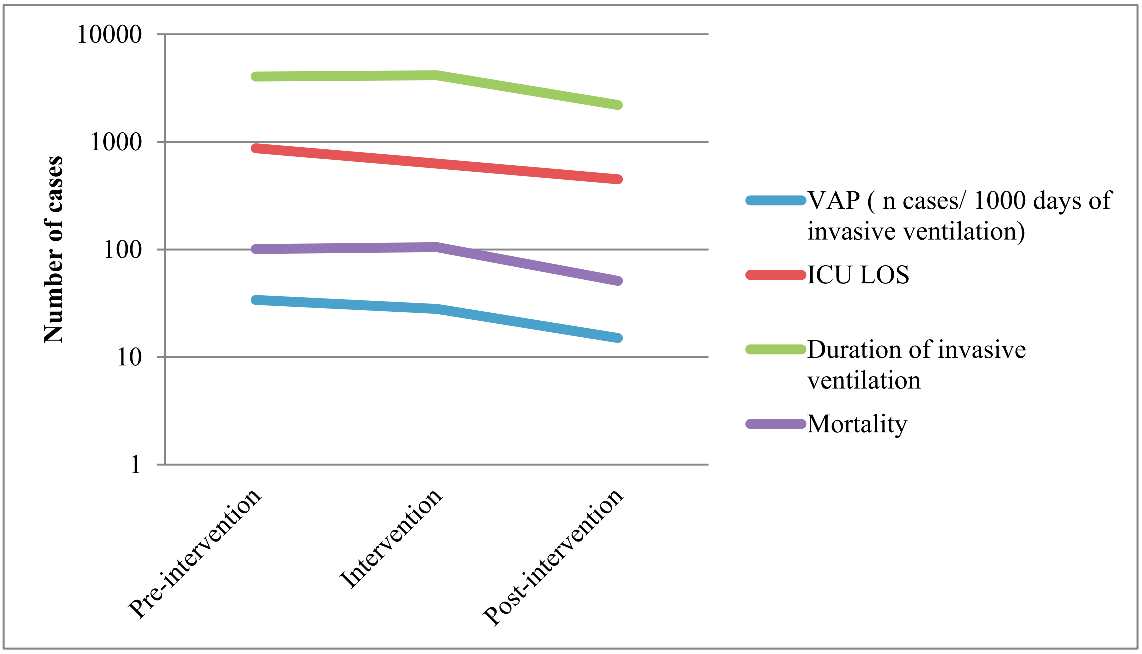

Fig. 2. Evolution of VAP indicators, days of hospitalisation in ICU, days of invasive ventilation and mortality by study period.

The lack of specificity in VAP diagnostic criteria, especially in the interpretation of the radiological exams and in the bacteriological analysis, whose positive results are neither sensitive nor specific to VAP, contribute as bias factors in the interpretation of the results. (Klompas, 2017). On the other hand, focusing the outcomes only on the VAP incidence rates for quality accreditation reasons, led to the application of more restricted diagnostic criteria, which in practice led to a decrease in VAP incidence rate with no changes in other important health outcomes, such as duration of invasive ventilation, ICU LOS and mortality rate, as reported by Klompas (2017) and Munro and Ruggiero (2014). Another explanation for the lack of significance in VAP reduction may be the fact that in ICU C more than half of the VAP cases identified in the intervention period occurred between July and August 2016, a time that corresponded to the guideline teaching phase and during which all professionals were not as yet familiar with the recommendations.

Mortality rate had a statistically significance reduction between the pre- and post- implementation period of 8% ($p = 0.037$). Comparing these data with other similar studies, we found that most of the recent studies did not report changes in the mortality rate (Bird et al., 2010; Lim et al., 2015; Mohamed., 2014; Samra et al., 2017). However, Hampton et al. (2005) reported a 50% reduction in mortality rate and Crunden et al. (2005) a reduction of 9%.

Guideline compliance and outcomes

Guideline compliance was high and ranged from 94.7% to 99.8%. When comparing this data with other pre- and post-intervention studies, the compliance rate was found to be similar, although we did not find studies describing compliance with all interventions simultaneously. Bird et al., (2010) report a compliance of 91% and 81%, Lim et al. (2015) and Samra et al. (2017) between 80% and 100%.

Results comparing compliance with outcomes allow us to conclude that lower rates of ICU LOS, duration of invasive ventilation and mortality occurred when there was higher compliance to cuff pressure maintenance. Also, lower rates of ICU LOS and duration of invasive ventilation were identified when compliance rates to ventilator weaning and to all the recommendations simultaneously were higher.

The effect of cuff pressure evaluation and maintenance in reducing the duration of invasive ventilation and ICU LOS has been proven by several studies, individually (Rello et al., 1996), or as part of a set of recommendations, which agrees with the findings in this study (Bouadma et al., 2010; Samra et al., 2017; Lim et al., 2015; Rello et al., 2013). Despite these findings, we cannot assume a cause-effect relation between compliance and LOS, as a greater LOS can also decrease compliance to cuff pressure evaluation.

Multiple studies have associated sedation reduction and ventilator weaning with lower duration of mechanical ventilation and lower mortality rate as part of a set of recommendations (Klompas et al., 2016; Lim et al., 2015; Rello et al., 2013). A recent quasi-experimental study found a relationship between reduction of sedation and shorter duration of invasive ventilation ($p < 0.001$). Ventilator weaning was also associated with a shorter time of invasive ventilation ($p < 0.001$) and lower mortality rate ($p = 0.001$) (Klompas et al., 2016).

Compliance with all Guideline recommendations is advocated by several researchers as the key to success in preventing VAP, including Berwick (2014), Horner and Bellamy (2012), and Institute for Healthcare Improvement (2017).

Limitations

Due to the lack of control of all variables in the application of a quasi-experimental study, we cannot establish a full cause-effect relation, as other individual and external patient factors may influence the results, therefore we suggest other similar studies be undertaken in other locations. One possible cause of bias is the difficulty of VAP diagnosis, as some of the criteria are subjective. To minimise this risk, though, the diagnosis was double-checked by two different doctors.

Conclusion

This study showed that the improvement of health outcomes regarding VAP is possible through the development of an evidence-based guideline, adapted to local conditions, coupled with an implementation process to guarantee its effectiveness. We identified a significant reduction in the incidence of VAP in two of the ICUs, which likewise showed significant levels of guideline compliance. We also identified a significant reduction in duration of invasive ventilation, ICU LOS and mortality rate, in all three ICUs.

These results give strength to the idea that the essence of health management lies, as Warren G. Bennis (1985) said, not only in "doing the right things" but in "doing the right things right."

Acknowledgments

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