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IMPROVEMENT OF PREVENTIVE MEASURES AND PATIENT OUTCOMES IN MULTI-ORGAN FAILURE CAUSED BY SEPSIS IN VENTILATOR-ASSOCIATED PNEUMONIA

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Abstract: Critical care management in Hong Kong has changed dramatically since the construction of the first intensive care unit (ICU) in 1967. Ventilator-associated pneumonia (VAP) remains a major concern in ICUs, frequently resulting in multi-organ failure (MOF) and increased mortality rates. Despite sparse data, recent research indicates a significant frequency of VAP in Hong Kong, emphasizing the necessity of prevention strategies. This research investigates the historical development of critical care in Hong Kong and how it affects VAP outcomes. The paper evaluates the effectiveness of preventive measures such as the ventilator bundle, which includes semi-recumbent positioning, daily oral care with chlorhexidine, and daily sedation interruption (DSI) with spontaneous breathing trials (SBTs), in lowering VAP rates and improving patient outcomes. The findings highlight the crucial importance of critical care in influencing VAP preventive methods and, ultimately, improving patient care in Hong Kong's ICUs.

Keywords: critical care, coronary care units, ventilator-associated pneumonia, Multi-organ failure, sepsis, prevention of VAP, retrospective cohort study, Hong Kong, Epidemiology, Mortality rate, Intensive care unit (ICU),Preventive measures, Ventilator bundle, Semi-recumbent posture, Oral care with chlorhexidine, Sedation interruption, Spontaneous breathing trials, Multi centre randomized controlled trial (RCT),Meta-analysis, Patient outcomes, Healthcare system, Ventilator free days.

INTRODUCTION :

1. Critical care development in Hong Kong

The concept of critical care management was initially developed in 1952 in Copenhagen during the polio epidemic (Kelly et al., 2014), and subsequently, it spread worldwide. Before the establishment of the intensive care units (ICUs) in Hong Kong (HK), patients requiring intensive care were exclusively treated in general wards with additional management (Hong Kong Academy of Medicine et al., 2014).

After the establishment of the first ICU in 1967 (Hong Kong Society of Critical Care Medicine, 2012), critically ill patients in ICU were managed with enhanced surveillance and nursing care. However, these ICU patients were attended to by their admitting medical doctors during their regular patient rounds without receiving exclusive medical attention. Junior doctors were tasked with addressing calls from the ICU regardless of the severity of incident (Hong Kong Academy of Medicine et al., 2014). Prior to the establishment of dedicated coronary care units (CCUs), many hospitals in HK relied on their ICUs to attend to patients with coronary heart disease until the development of the first independent ICU in 1986 (Hong Kong Society of Critical Care Medicine, 2012). Since 1984, specific doctors from the Department of Anaesthesia have been overseeing the hospital's intensive care resources, empowering anaesthetists to provide care and management for ICU patients.(Hong Kong Academy of Medicine et al., 2014). In 1996, a

hospital in HK founded the initial independent Department of Intensive Care, offering specialised care to patients through dedicated ICU doctors and nurses (Hong Kong Academy of Medicine et al., 2014).

2. Multi-organ failure due to sepsis in ventilator-associated pneumonia in Hong Kong

2.1. Summary of multi-organ failure due to sepsis in ventilator-associated pneumonia

Multi-organ failure (MOF) is the primary cause of illness and death among ICU patients (Sakr et al., 2012). Sepsis is the primary contributing factor to MOF, with other causes including trauma, burns, pancreatitis, etc (Brealey and Singer, 2000). Ventilator-associated pneumonia (VAP) is common in mechanically ventilated patients, leading to sepsis and causing MOF, which accounts for nearly one-third of nosocomial infections (Papazian et al., 2020). VAP is characterised by lung tissue infection in patients receiving invasive mechanical ventilation for more than 48 hours (Kohbodi et al., 2018). When microbial pathogens causing VAP enter the bloodstream, they can induce a systemic infection and lead to a dysregulated systemic inflammatory response syndrome (SIRS). SIRS triggers an inflammatory cytokine storm, resulting in cell damage that causes MOF (Gotts and Matthay, 2016). VAP accounts for approximately a 10% mortality rate in the ICU (Papazian et al., 2020). In the subsequent sections, I will delve into the background of VAP in HK, examine the evolution of these outcomes over time, and describe how critical care influences the modification of VAP outcomes.

2.2 Background of VAP in Hong Kong

As government departments in HK, including the Hospital Authority, the Centre for Health Protection (CHP), and the Department of Health, have not released data related to VAP in hospitals to the public, there is no national data available for the epidemiology of VAP in HK. The following information associated with VAP is based on the most recent studies conducted in HK. HK is a slow starter in critical care development, therefore, the rate of VAP is slightly higher when compared to Western countries. According to the cohort study published by Kwan et al., 2012, the VAP rate in HK was around 22%, or nearly 48 per 1000 ventilator days. This was associated with a prolonged mechanical ventilation duration, an extended length of stay in ICU, and an ICU mortality rate of 16.7% (Kwan et al., 2012). In this cohort study, the baseline characteristics of patients with VAP leaned towards an older population, with a mean age of 64.6. Moreover, males exhibited a higher prevalence compared to females. Additionally, patients with difficulty swallowing or those with chronic conditions including chronic renal failure, diabetes mellitus, or chronic heart failure had a higher likelihood of developing VAP (Kwan et al., 2012).

2.3 Evolution of critical care in changing outcomes for patients with VAP

Not only does VAP cause an increase in the mortality rate, but it also imposes a significant financial strain on the healthcare system on the healthcare system. The cost of treating VAP patients is approximately 1.4 times higher than that of non-VAP ventilated patients (Luckraz et al., 2018). Therefore, VAP has become an important healthcare issue that critical care focuses on, and the development of critical care has enhanced outcomes for patients. Although VAP can cause sepsis and MOF, accounting for one-sixth of ICU mortality (Kwan et al., 2012), it is a preventable disease. Critical care plays an important role in evolving VAP prevention methods and enhancing patient outcomes. As critical care is highly evidence-based, the guidelines will be updated according to the latest studies. In the following paragraphs, I will explain how the preventive measures evolved in critical care for managing VAP based on evidence.

2.3.1 Ventilator bundle

For the preventive measures, the Institute for Healthcare Improvement (IHI) developed the ventilator bundle for the prevention of VAP and venous thromboembolism in 2001. Initially, it includes four items and one more item was added in 2010. Among the five items, three are for VAP prevention: (1) adjust the bed to semi-recumbent position, (2) daily oral care with chlorhexidine, and (3) perform daily sedation interruption (DSI) and daily assessment for extubation readiness. (Institute for Healthcare Improvement, 2012). The ventilator bundle has been adopted globally and modified in response to updated evidence.

2.3.1.1 Semi-recumbent posture

The practice of positioning patients in a semi-recumbent posture was suggested before the introduction of the ventilator bundle, as it has been proven to decrease the chance of aspiration (Kollef, 1999). IHI included the semi-recumbent position in the bundle based on another study demonstrating its association with a lower frequency and risk of VAP compared to supine position in ventilated patients (Drakulovic et al., 1999).

The study (Drakulovic et al., 1999) was an unblinded and single-centre randomised controlled trial (RCT) with clearly stated PICO criteria. RCT is an appropriate methodology for this study since it represents the gold standard for assessing intervention effectiveness and has the capability to establish a causal relationship between the intervention and the outcome (Hariton and Locascio, 2018). The study utilised intention-to-treat analysis, reflecting real-life clinical scenarios and minimising the biases in interventions (Gupta, 2011).

The study required 182 patients to detect a 50% reduction of VAP risk with an alpha value of 0.05 and a power of 80%. However, the study was terminated after an interim analysis with 86 recruited patients, showing a P value of 0·003 in the primary outcome. The limited sample size might impede the identification of additional independent risk factors. The study may not be directly applicable to the current critical care environment, given that the level of care and knowledge has advanced since the time of the study. Despite its outdated single-centre design and small sample size, which limit its applicability, subsequent meta-analyses of RCTs comparing the supine position with the semi-recumbent posture in VAP prevention consistently show that the semi-recumbent posture can reduce the VAP rate. (Pozuelo-Carrascosa et al., 2022, Wang et al., 2016). Therefore, raising the head of the bed can effectively reduce the risk of VAP and enhance patient outcomes, supported by studies from the past to present. This practice is adopted in HK since the development of ventilator bundle and become a general practice in ICUs (Centre for Health Protection, 2018).

2.3.1.2 Daily oral care with chlorhexidine

Similar to the adoption of the semi-recumbent posture, daily oral care with chlorhexidine for preventing VAP was recommended before the development of the ventilator bundle. This practice has been proven to prevent bacterial colonisation in the circuit of ventilator and reduce the risk of pneumonia (Kollef, 1999, Rumbak and Cancio, 1995). In 2010, the IHI added this element into the ventilator bundle, relying on a meta-analysis study that indicated a reduced risk of VAP with oral decontamination using chlorhexidine in mechanically ventilated patients (Institute for Healthcare Improvement, 2012, Chan et al., 2007). Since then, daily chlorhexidine oral care has become a standard practice in ICUs adopted globally. However, two recent retrospective cohort studies indicated that the application of chlorhexidine for oral care was linked to a higher mortality rate. (Klompas et al., 2016, Deschepper et al., 2018). The findings from these studies led to a change in the practice of oral care for ICU mechanically ventilated patients. I will critically appraise the study by Klompas et al., 2016, as the study specifically focused on patients with mechanical ventilator. This was a single-centre, retrospective cohort study that assessed the connection between each component of the ventilator bundle and the results of ventilated patients. The study showed a correlation between oral care using chlorhexidine and an elevated mortality rate in mechanically ventilated patients, with a p-value of 0.006. Cohort design is suitable for the study because there is substantial evidence supporting the association between individual ventilator bundle elements and outcome of ventilated patients. Although RCTs are considered the gold standard for establishing a causative relationship, cohort studies offer the advantage of comparing all ventilator bundle elements within a single study. The study had a well-defined research question, clearly identifying both the population of the study and the desired outcomes. The research included 5539 patients who were ventilated for at least three days between 2009 and 2013 in a single US hospital. Although the single centre design may limit the generalisability or external validity of the findings, the large sample size compensated for this limitation. A larger sample size can enhance the robustness of the analysis, providing greater precision in establishing the association relationship. Therefore, increasing the generalisability of the study. The study precisely reported all results, including odds ratios, p-values, and the range of confidence intervals. The data were presented in tables, categorised according to each specific ventilator bundle and its corresponding outcomes. For generalisability, it can be applied to my workplace as it was a large cohort study, and my workplace has implemented the ventilator bundle for VAP prevention.

In addition to the two observational studies mentioned previously, two meta-analyses have reported that the use of oral chlorhexidine may be associated with an increased risk of mortality (Price et al., 2014, Klompas et al., 2014). Considering the mortality risk associated with oral care using chlorhexidine in mechanically

ventilated patients, the CHP in HK revised the guideline, recommending the use of normal saline instead. (Centre for Health Protection, 2010, Centre for Health Protection, 2018).

2.3.1.3 Daily sedation interruption and daily assessment for extubation readiness

In contrast to the two ventilator bundles mentioned earlier, DSI was introduced during the development of the ventilator bundle in 2001 (Institute for Healthcare Improvement, 2012). The rationale of DSI is that it can markedly reduce the time of mechanical ventilation, consequently reducing the VAP risk (Kress et al., 2000). Moreover, a new RCT demonstrated improved outcomes for mechanically ventilated patients in ICU when DSI was combined with spontaneous breathing trials (SBTs) (Girard et al., 2008). In the upcoming paragraphs, I will critically appraise the study by Girard et al. (2008) as it offers an improved practice for preventing VAP. The study was an unblinded, multi-centre RCT conducted across four hospital ICUs. This trial compared DSI with SBTs (intervention group) to usual care with SBTs (comparison group), focusing on ventilated adult patients exceeding 12 hours of ventilation. The primary outcome was ventilator-free days, and the results indicated that patients in the intervention group had more ventilator-free days than those in the comparison group. The study was conducted at multiple centres, which increased the heterogeneity of patients and critical care environments, improving the generalisability and applicability of the findings. However, the study's multi-centre design and lack of blinding made it susceptible to performance bias due to the variations in practices between ICUs. Therefore, the authors introduced a standardised protocol as a guideline for healthcare professionals to minimise the impact of performance bias. The study aimed to enroll 334 patients to detect a 25% increase in ventilator-free days with a 80% power and a 0.05 alpha value. Sufficient patients were enrolled for the subsequent data analysis. The baseline characteristics data between the groups were similar, promoting comparability and facilitating the comparison of the interventions.

The findings were objectively reported through written descriptions and presented with tables and graphs. All outcome-related data were comprehensively reported, and there were no missing or incomplete data. The p-value for the primary outcome was 0.02. Despite its being an aged study, the study can be applicable to my workplace, as it was conducted across multiple ICUs, and the medications and protocols used in the study were similar to my workplace. Considering the benefits of DSI with SBTs indicated in the study, the CHP in HK revised the guideline from DSI to DSI with SBTs (Centre for Health Protection, 2010, Centre for Health Protection, 2018).

2.3.2 Summary and role of critical care on patient outcomes

The three examples above illustrate how the preventive measures were evolved according to evidence-based studies. In addition, the nature of critical care enables close patient monitoring, facilitating prompt diagnosis and interventions to prevent the progression of the disease. Moreover, critical care emphasises on multidisciplinary collaboration. Engaging in teamwork with healthcare professionals from various disciplines can enhance the quality of patient care.

2.4 How outcomes have changed over time

Due to a limited number of researchers and non-transparent data in HK, only one study related to the prevalence of VAP have been found in the region. An additional set of official data concerning VAP prevalence that has been found is the VAP rate in one of the ICUs in HK spanning from April 2010 to August 2013. According to an unpublished study, the rate of VAP in HK was 10.6 per 1000 ventilator days in 2004 to 2005 (Chawla, 2008). Conversely, according to the official data, the VAP rate ranged from 30 to 70 per 1000 ventilator days before the publication of the first VAP prevention guideline in 2010 (Dr. Hang Mui, 2019). Following the implementation of the VAP prevention bundle in hospitals, the VAP rate significantly dropped to less than 10 per 1000 ventilator days (Dr. Hang Mui, 2019). The data presented above indicates the significant role of the ventilator bundle in preventing VAP, leading to significant improvement in the outcome of critical care patients.

CONCLUSION :

Hong Kong's critical care development, evolving since 1967, has significantly improved patient outcomes. VAP is a preventable disease that can cause sepsis and MOF, accounting for one-sixth of ICU mortality. The characteristic of critical care catalysed the development and evolution of the ventilator bundle, which plays an important role in reducing VAP rates and enhancing patient outcomes.

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