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REVIEW

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Are central line bundles and ventilator bundles effective in critically ill neonates and children?

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Abstract Central line-associated bloodstream infections (CLABSI) and ventilator-associated pneumonia (VAP) are common problems in adult, pediatric (PICU) and neonatal (NICU) intensive care unit patients. Care bundles have been developed to prevent these hospital-acquired infections and to provide best possible care. Studies in adults have proven that care bundles contribute to a decrease in CLABSI and VAP rates. The purpose of this literature review was to critically appraise the known evidence of the effectiveness of central line bundles and ventilator bundles in PICU and NICU patients. The number of publications of central line bundles and ventilator bundles in PICU and NICU patients is limited compared to adults. Ten studies in PICU patients demonstrated a significant decrease in the CLABSI or VAP rate after implementation of the bundle. Two studies in neonates demonstrated a reduction in the CLABSI rate after implementation of the central line bundle. No studies on the effectiveness of the ventilator bundle in neonates were found. Bundle elements differed between studies, and their scientific basis was not as robust as in adults. Monitoring of compliance to bundle elements seems required for optimal reduction of CLABSI and VAP. Bundle components that focus on maintenance of a central line probably are important to prevent CLABSI in children.

Keywords Central line-associated bloodstream infections · Ventilator-associated pneumonia · Care bundles · Neonatal intensive care unit · Pediatric intensive care unit · Quality improvement

Abbreviations

CLABSI	Central line-associated bloodstream infection
VAP	Ventilator-associated pneumonia
PICU	Pediatric intensive care unit
NICU	Neonatal intensive care unit
HAI	Hospital-acquired infection
NHSN	National healthcare safety network

Introduction

Hospital-acquired infections (HAIs) are common in adult, pediatric and neonatal intensive care patients and are associated with an increased risk of complications. Between 5 and 10 % of adult patients admitted to acute care hospitals acquire one or more HAIs [1]. In the pediatric intensive care unit (PICU), the prevalence of HAIs has been reported to be as high as 12 % [2]. The most common HAI in PICU and neonatal intensive care unit (NICU) patients is a central line-associated bloodstream infection (CLABSI) [3, 4]. A CLABSI is a bloodstream infection occurring in a patient with a central line or within 48 h after removal of that line and where no other source of infection is detected [5]. Pneumonia is the second most common HAI and accounts for 23 % of HAIs in the PICU [1]. Mechanical ventilation increases the risk for the development of a hospital-acquired bacterial pneumonia 6- to 21-fold [6, 7] and is therefore often referred to specifically as ventilator-associated pneumonia (VAP). Traditionally, it has been defined as an acquired pneumonia that develops 48 h or more after the initiation of mechanical ventilation. To prevent delayed diagnosis and treatment, the most recent guidelines of the Center for Disease Control indicate there is no minimum period of time that the ventilator must be in place [8, 9]. The gold standard to diagnose VAP requires direct examination of lung tissue obtained by biopsy, which is rarely done in children. What remains are clinical, microbiologic and radiologic criteria, but these often lack specificity and make it difficult to adequately diagnose VAP in children [8].

CLABSI and VAP are associated with increased morbidity, mortality and costs [3, 10–15]. Prevention is therefore urgently needed [2]. The Institute for Healthcare Improvement developed "care bundles" to improve patient safety and to prevent HAIs in collaboration with other organizations. According to the Institute of Healthcare Improvement, the definition of a bundle is "a small, straightforward set of evidence-based practices—generally three to five—that, when performed collectively and reliably, have been proven to improve patient outcomes" [16]. By combining the elements into a single compound process, the potential for them all to be performed is increased. The principle of an all-or-none measure of the bundle is central to its success [17, 18].

The purpose of a bundle is to provide best possible care for patients undergoing particular treatments with inherent risks [19]. Care bundles are a popular topic and their effects have been evaluated in several studies, focusing almost exclusively on adult patients. The use of central line bundles and ventilator bundles has proven to reduce the rate of CLABSI [20–24] and VAP [17, 25, 26] in adult patients. To our knowledge, however, the information about the application of care bundles in NICU and PICU patients is limited compared to adults [18, 27, 28]. Results in these patients may well be different compared to adults: there are obvious differences among these 3 populations in anatomy and physiology, in underlying illnesses they have, and in interventions and procedures they undergo [18, 27].

Our objective with this literature review was to establish evidence of the effectiveness of central line bundles and ventilator bundles in critically ill neonates and children in the recent 10 years.

Methods

A comprehensive literature search was performed in PubMed and Cochrane Central Register of Controlled Trials. Combinations of the following search terms were used for CLABSI: (1) catheter-related sepsis, catheter-related bloodstream infection(s), central line-associated bloodstream infection(s); (2) bundle(s), care bundle(s), sepsis bundle(s), guideline(s), reduction; (3) adolescent(s), child(ren), infant(s), p(a)ediatric intensive care unit and NICU. These search terms were used in titles and abstracts of published articles to identify all eligible studies. Combinations of the following search terms were used for VAP: (1) VAP; (2) bundle(s), care bundle(s), ventilator bundle(s), guideline(s), reduction; (3) adolescent(s), child(ren), infant(s), p(a)ediatric intensive care unit and NICU.

Inclusion criteria were: (1) use of bundles to prevent CLABSI or VAP; (2) species: humans; (3) language: English; (4) published between 2002 and 2011; (5) limit: all children (0–18 years). The last search was done on 23 January 2012. Two reviewers independently reviewed the titles, abstracts and references for relevance for this review. One reviewer read the full text of the included studies.

Bundles

In our review, two bundles were evaluated: the central line bundle and the ventilator bundle. These bundles focus on the prevention of CLABSI and VAP. The central line bundle originally developed by the Institute for Healthcare Improvement consists of five care steps: hand hygiene; maximal barrier precautions upon insertion; chlorhexidine skin antisepsis; optimal catheter site selection with avoidance of the femoral vein for central venous access in adult patients; daily review of line necessity with prompt removal of unnecessary lines [16]. The ventilator bundle originally developed by the Institute for Healthcare Improvement consists of four care steps: elevation of the head of the bed 30°–40°; peptic ulcer disease prophylaxis; deep venous thrombosis prophylaxis; daily assessment of readiness to extubate [16]. These two bundles were developed in adult care. The scientific evidence for the bundle components in children and neonates is not as robust, which may contribute to more diversity in specific elements in bundles for NICU and PICU patients. For our review, all central line bundles and ventilator bundles were included; the exact interventions in the bundle to prevent CLABSI or VAP could vary between included studies.

Results

The searches revealed a total of 191 articles: 54 articles for CLABSI and 137 articles for VAP. A total of 144 articles performed only in adults were excluded. The remaining 47 articles were scanned for titles and abstracts if they met the inclusion criteria. Most common causes for exclusion were: (1) no involvement of bundles, (2) no involvement of PICU or NICU, (3) no CLABSI or VAP, (4) not answering the research question and (5) a review. For CLABSI, this strategy yielded: three articles for NICU patients and ten articles for PICU patients; for VAP: one article for NICU patients and four articles for PICU patients. The full text of these 18 articles was read. Another 6 articles were then excluded because they did not answer the research question; therefore, 12 articles remained. These 12 articles all were found in PubMed. The references of these 12 articles were reviewed; this yielded no further studies. No articles for VAP in NICU patients were found. No randomized controlled trials were found.

In Table 1 the two included articles of a central line bundle in NICU are summarized. The CLABSI rates before implementation of the central line bundle were 6.4 and 8.4 CLABSIs per 1,000 catheter days. After implementation of the bundle a significant decrease was demonstrated in the CLABSI rate to 1.7 and 2.1 respectively.

In Table 2 the seven included articles on a central line bundle in PICU patients are summarized. The CLABSI rates before implementation ranged from 3.0 to 7.8 CLABSIs per 1,000 catheter days. A summary of the elements of the bundles is reported in Table 2. With the exception of McKee et al. [33], a significant decrease in the CLABSI rate was demonstrated in all articles after implementation of the central line bundle. The CLABSI rates after implementation ranged from <1 to 4.3 per 1,000 catheter days. Jeffries et al. [32] reported a decrease of costs after implementing the bundle.

Table 3 summarizes the three included articles on a ventilator bundle in PICU. The VAP rate before implementation of the bundle varied from 5.6 to 7.8 per 1,000 ventilator days. The VAP rate after implementing the

Table 1 Studies of central line bundles in NICU patients

Author and study years	Setting, no. of patients	Bundle elements	Results[a,b]	Details
Bizzarro [29] 2005–2009	NICU, $N = 576$	Annual lectures Hand hygiene Antisepsis with iodine with 70 % alcohol Dressing only changed when dressing is soiled or when readjusting of catheter is needed Daily discussion for catheter need Surveillance conducted	CLABSI rate decreased from 8.4 to 1.7	Quasi-experimental study, meaning: data collection, implementation of bundle, post intervention data collected
Schulman [30] 2007–2009	18 NICUs, $N =$ not known	Central line kit or cart containing all necessary items for insertion Hand hygiene Maximal barrier precautions Antiseptic chlorhexidine skin preparation Sterile transparent semipermeable dressing or sterile gauze Daily evaluation of catheter insertion site Aseptic skin disinfection Aseptic technique when changing intravenous tubing Daily discussion for catheter need	CLABSI rate decreased from 6.4 to 2.1 Use of maintenance checklists is associated with lower CLABSI rate	Prospective cohort study Number of patients unknown, but more than 55,000 central line days

N number of patients with a central line, *NICU* neonatal intensive care unit

[a] Rate of CLABSI/1,000 catheter days

[b] $p < 0.05$ unless noted otherwise

Table 2 Studies of central line bundles in PICU patients

Author and study years	Setting, no. of patients	Bundle elements	Results[a,b]	Details
Costello [31] 2004–2009	Pediatric CICU, $N = 936$	Evaluate central line necessity before placing Insertion checklist Clean gloves, hub disinfection when accessing line Change end caps when removed to access line Central line not routinely replaced Central line dressing change kit to change transparent semipermeable dressing Skin antisepsis, chlorhexidine disk after insertion, transparent dressing	CLABSI rate decreased from 7.8 to 2.3	Retrospective interventional study
Jeffries [32] 2004–2005	26 PICUs and CICUs, $N = 1{,}013$	Hand hygiene Transparent semipermeable dressings Maximum sterile barrier Aseptic gloves Antiseptic chlorhexidine skin preparation Replace dressing if necessary	CLABSI rate decreased from 6.3 to 4.3 Total cost avoidance of $2.9 million	Observational study
McKee [33] 2001–2006	PICU, $N =$ not known	Staff education Hand hygiene Maximum barrier precautions Chlorhexidine at insertion Sterile drape at insertion Central catheter procedure cart Immediate sterile dressing Insertion checklist Stop procedure if guidelines were not followed	CLABSI rate decreased from 5.0 to 3.0 ($p = 0.07$)	Prospective interventional cohort study Number of patients unknown
Miller [34] 2004–2009	29 PICUs, $N =$ not known	Hand hygiene Chlorhexidine at insertion, no iodine Insertion checklist Full sterile barrier Insertion training Daily discussion for catheter need Catheter site care: chlorhexidine scrub, change gauze and dressing, prepackaged dressing change kit Catheter hub/cap/tubing care	CLABSI rate decreased from 5.2 to 2.3	2004–2006: control data. 2006–2009: multi-institutional interrupted time series design (bundle implementation, assessing CLABSI rate and bundle compliance)
Miller-Hoover [35] 2008–2009	PICU, $N = 291$	Skin antisepsis Maximum barrier precautions Hand hygiene Daily discussion for catheter need Bundle compliance check by nurse Maintaining closed system Scrub the hub Regular change of dressing	CLABSI rate decreased from 4.9 to 1.5	Retrospective observational study
Morgan [36] 2005–2006	28 PICUs, $N =$ not known	Hand hygiene Maximum barrier precautions Sterile gloves Chlorhexidine skin antisepsis Optimal catheter site selection Insertion checklist No blood cultures from arterial lines	CLABSI rate decreased from 5.2 to 3.0	Multicenter trial Number of patients unknown
Wheeler [37] 2006–2010	Children's hospital, $N =$ not known	Hand hygiene Maximum barrier precautions Chlorhexidine skin scrub at insertion Insertion checklist Catheter site care: chlorhexidine scrub, change gauze and dressing, no iodine, prepackaged dressing change kit Catheter hub/cap/tubing care Daily discussion for catheter need	CLABSI rate decreased from 3 to <1[a]	Retrospective observational study Children's hospital: PICU, NICU, CICU and all other wards are included Number of patients unknown

N number of patients with a central line, *PICU* pediatric intensive care unit, *CICU* cardiac intensive care unit

[a] Rate of CLABSI/1,000 catheter days

[b] $p < 0.05$ unless noted otherwise

Table 3 Studies of ventilator bundles in PICU patients

Author and study years	Setting, no. of patients	Bundle elements	Results[a,b]	Details
Bigham [38] 2004–2007	PICU, $N = 1{,}782$	Hand hygiene Head of bed elevation Scheduled mouth care Change ventilator circuits and in-line suction catheters when visibly soiled Heated-wire ventilator circuits	VAP rate decreased from 5.6 to 0.3	Cohort study
Brierley [39] 2008	PICU, $N = 730$	Head of bed elevation Mouth care with oral antiseptic 4 hourly or 12 hourly toothbrush Clean suctioning Peptic ulcer disease prophylaxis Documentation to be completed 4 hourly Compliance monitoring	VAP rate decreased from 5.6 to 0	Following implementation of bundle
Brilli et al. [40] 2005–2007	PICU, $N = 26$	Head of bed elevation Daily sedation vacations and assessment of readiness to extubate Peptic ulcer disease prophylaxis Daily oral care with chlorhexidine	VAP rate decreased from 7.8 to 0.5 Length of stay decreased by 400 days $2.4 million decrease in hospital costs	Retrospective case-control study

N number of intubated patients, *PICU* pediatric intensive care unit
[a] Rate of CLABSI/1,000 ventilator days
[b] $p < 0.05$ unless noted otherwise

bundle varied from 0 to 0.5, respectively. A decrease in the length of stay and hospital costs was reported by Brilli et al. [40].

Discussion

In this study we examined the known evidence of the effectiveness of central line bundles and ventilator bundles in critically ill neonates and children. Our main finding was the limited number of publications compared to adults. The publications that were available all demonstrated a clear decrease in the number of CLABSI or VAP after the implementation of the bundles.

Care bundles are considered to be a key element in quality improvement in health care [25]. Besides promising results in studies of implementing bundles, there are still some general comments and constraints. First, according to the Institute for Healthcare Improvement, elements in bundles have to consist of evidence-based practices. This may be true for bundles in adults, but in NICU and PICU patients this is far less obvious. There is even discussion in the literature about the specificity of the diagnosis of VAP in these populations [8]. Collection of blood for cultures in NICU and PICU patients is often not performed by venipuncture, but by drawing blood from the arterial and central venous line, which also makes the diagnosis of CLABSI less specific [28]. Not only the definition of VAP or CLABSI, but also the scientific evidence for the bundle elements in NICU and PICU patients is by far not as robust as it is in adults. For example, the use of peptic ulcer disease prophylaxis is controversial in pediatric patients [39]. Elevation of the head of the bed may be difficult in neonates and young infants and may impose unintended harms [18]. The weaker scientific foundation for bundle elements is reflected in the variation of bundle elements that is found among the 12 included studies (Tables 1, 2, 3). Second, it can be questioned which exact bundle elements are causing the effect and whether some elements are more effective than others. One might draw the conclusion from several studies in adults that extreme vigilance with insertion hygiene and sterility is the most effective measure to reduce CLABSI rates [41]. It is claimed that bundles are more effective when all elements are performed together and that compliance to all bundle elements is important [42]. This sounds appealing and logical, but there are no hard data to support it. Third, the elements of a bundle have to be easy to perform: the strength of a bundle is in its simplicity, consistency and evidence behind each component [16]. There is a risk of adding additional components to existing adult bundles for NICU and PICU patients. Although well intentioned, this may result in lower rates of adherence and thus may worsen outcome [41]. In daily clinical practice, it has been shown that only by having a bundle policy, monitoring compliance with it, *and* a 95 % or greater compliance led to decreased CLABSI rates [23].

Despite the variation of bundle elements in included studies in NICU and PICU patients, they all showed a positive effect on the occurrence of CLABSI or VAP. It could therefore be argued that the mere implementation of the bundle resulted in a decrease in the number of infections, comparable to the Hawthorne effect. It cannot be excluded that other measures have reduced the reported rate of CLABSI or VAP over time, such as, for example, changes in definitions of CLABSI or VAP, changes in thrombosis prevention, anti-infective catheters or antimicrobial lock solutions [41]. Where bundles in adults are focused on insertion of a central line, there is evidence that attention to the maintenance of a central line is important to prevent CLABSIs in children [43]. Only McKee et al. [33] did not implement a procedure for maintenance of the central line, and this was the only study that did not report a significant decrease in CLABSI rate. Schulman et al. [30] reported an inter-institutional variation in their results among the NICUs included in their study, which was partly explained by differences in the use of maintenance checklists. Furuya et al. [23] noted that in adults monitoring of implementation and monitoring of compliance are important to reduce the incidence of HAIs.

There are some limitations to the conclusions we can draw in this study. First, there is variation among the studies we reviewed. There is a difference in the study design, setting, bundle elements and compliance of these elements. Second, only few studies for ventilator bundles were found, and these were only performed in PICU patients and not in NICU patients. There were more publications found for central line bundles, but this number was also limited in NICU patients. Third, there were no randomized controlled trials available. Despite of these limitations the effects of bundles are promising. It is important to always keep evaluating and looking for improvement of quality of care, because the medical care system is changing continuously [44].

Conclusion

In conclusion, CLABSI and VAP are a common problem in PICU and NICU patients. Central line bundles and VAP bundles seem to be effective in PICU patients. The central line bundle seems to be effective in critically ill neonates too, although the number of studies performed in neonates is limited. No studies on VAP bundles in neonates were found. The scientific basis for bundle elements in NICU and PICU patients is by far not as robust as it is in adults, resulting in heterogeneity of bundle elements. Continuous compliance and monitoring of compliance to bundle elements seems required for optimal reduction of CLABSI and VAP.

Conflicts of interest The authors indicate no potential conflicts of interests.

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