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State of the Science Review

Methods for microbial needleless connector decontamination: A systematic review and meta-analysis

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Key Words:
Bloodstream infection
CABSI
CLABSI
Vascular access device

Background: The objective of this review was to compare the effectiveness of connector decontamination with 70% alcohol wipes, alcoholic chlorhexidine gluconate wipes, or alcohol impregnated caps to prevent catheter-associated bloodstream infection (CABSI).

Methods: A systematic search was conducted in CINAHL, Cochrane Central Register of Controlled Trials, Medline, and PubMed. The primary outcome was CABSI, with randomized and observational studies included. The inclusion criteria were: English language, any age group, no date limitations, and reporting connector decontamination interventions to prevent CABSI. The exclusion criteria were: multimodal interventions, letters, and conference abstracts. Quality assessment with the Newcastle-Ottawa Scale, a narrative synthesis, and meta-analysis were conducted. Pooled data used a random effects model for pair-wise comparisons, due to clinical heterogeneity. Statistical heterogeneity was investigated by visual model inspection, χ^2, and I^2 statistics.

Results: Ten studies compared 70% alcohol wipes with 70% alcohol-impregnated caps, and 2 studies (n = 1,216) tested an alcoholic chlorhexidine gluconate wipe. Alcoholic chlorhexidine gluconate wipes were associated with significantly less CABSI than 70% alcohol wipes (risk ratio, 0.28; 95% confidence interval, 0.20-0.39). Alcohol-impregnated caps were associated with significantly less CABSI than 70% alcohol wipes (risk ratio, 0.43; 95% confidence interval, 0.28-0.65). Studies were of low to moderate quality.

Conclusions: Alcohol impregnated caps and alcoholic chlorhexidine gluconate wipes were associated with significantly less CABSI than 70% alcohol wipes. This requires confirmation in randomized controlled trials.

Since the 1990s, needleless connectors (NCs) have been used with vascular access devices to administer intravenous fluids, medications, blood products, and specialized treatments such as chemotherapy. Although NCs were introduced to reduce the risk of health care workers to needlestick injuries,[1] some designs increase the risk of catheter-associated bloodstream infection (CABSI), as microorganisms can collect on the external surface of the NC.[2] Therefore, effective NC decontamination presents a significant, ongoing challenge.

The incidence of CABSI can be up to 5.2%,[3] with increased mortality in vulnerable populations.[4] The most common and preventable microorganisms associated with CABSI are coagulase-negative staphylococci,[5-7] *Staphylococcus aureus,* and *S epidermidis.*

Currently, products for NC decontamination include wipes that contain either chlorhexidine gluconate (CHG) in 70% isopropyl alcohol (IPA) or 70% IPA alone.[8,9] These are considered *active* decontamination, as they require a scrubbing mechanism during application. Alternatively, *passive* decontamination can be achieved with 70% IPA-impregnated caps,[10] which are applied directly onto the NC, inertly decontaminating the surface of the NC until the cap is removed and discarded prior to medication administration. To ensure decontamination, it is recommended that these products be applied for a minimum of 2-5 minutes, with a maximum use of 7 days.[11,12]

There is little agreement in practice or clinical guidelines regarding the optimal decontamination type (*active* vs *passive*; IPA vs CHG). For example, United Kingdom guidelines (Epic3) recommend 2% CHG

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in IPA wipes,[8] whereas some Australian guidelines recommend 70% IPA wipes.[13] The Centers for Disease Control and Prevention guidelines suggest disinfection with a wipe, IPA, CHG in alcohol, or povidone iodine.[9] In addition to these solutions, the Infusion Therapy Standards of Practice also recommends passive disinfection caps be considered.[14]

With multiple decontaminant approaches recommended in guidelines, it is unclear which is the most effective. A recent systematic review[15] highlighted the low quality of evidence for some products but did not directly compare all products available. An in vitro study[16] highlighted the varying efficacy of a 70% IPA wipe, a 2% CHG in IPA wipe, and a 70% IPA-impregnated cap. In that study, 2% CHG and 70% IPA wipes (*active* decontamination) resulted in the greatest reduction of NC contamination. This laboratory study is not directly generalizable to the clinical setting. To our knowledge, to date, there has not been a direct comparison of all 3 products in the same clinical study or via meta-analysis. This has resulted in the uncertainty about the most clinical and cost-effective approach and underpins the considerable inconsistency in guidelines regarding the most effective approach to NC decontamination.

AIM AND RESEARCH QUESTION

The aim of this review was to evaluate the effectiveness of NC decontamination products to prevent CABSI, addressing the following research question:

When comparing NC decontamination type (*active*; [eg, wipe] vs *passive* [eg, impregnated cap]) and solution (70% IPA vs CHG), which method is the most effective to prevent CABSI?

METHODS

Design

A systematic review and meta-analysis were undertaken, based primarily on Cochrane Collaboration systematic review methodology, incorporating quality assessment using the Newcastle Ottawa Scale (NOS).[17] The review was prospectively registered on PROSPERO (CRD42018026597).

Inclusion criteria

The review included interventional clinical research, published in peer-reviewed journals, with data available in English, with no date limitations, that compared NC decontamination products using either *active* (eg, wipe) or *passive* (eg, impregnated cap) decontamination type, on any vascular access device type (peripheral and central) to prevent CABSI. The populations were any age group in any clinical setting. Only articles published in English were included. The aim was to search for randomized controlled trials (RCTs); however, in the absence of RCTs, observational studies were included.

Exclusion criteria

Studies that included a multimodal approach to reducing CABSI, such as the implementation of a bundle, were excluded because of the inability to determine the impact of the co-interventions. Letters to the editor and conference abstracts were also excluded, because of the lack of peer review.

Primary outcome

The outcome for this review was any type of CABSI. This was pragmatically chosen a priori because of the variety in CABSI definitions reported in the literature. Studies were included that had a primary outcome of CABSI, including catheter-related bloodstream infection. Results were reported as CABSI events per 1,000 catheter days where available. If results were reported per 100 catheter days, this was converted to 1,000 catheter days for consistency.

Search strategy

A systematic literature search was conducted on August 9, 2018, using CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane Central Register of Controlled Trials, Medline, and PubMed. The search was developed in consultation with a health librarian using medical subject headings wherever possible involving: ([disinfect* OR decontaminat*] AND [vascular access device OR hub OR connector]). The references of included studies were hand searched.

Data extraction

Screening of titles and abstracts, and data extraction were performed by 2 reviewers independently (J.F. and E.L.). A third reviewer (S.K.) was consulted to resolve any disparities. Data extracted were standardized via a Microsoft Word data extraction tool and included patient population, setting, control, and interventions used (70% IPA wipe, CHG wipe, and a 70% IPA-impregnated cap), and results for CABSI (including rate per 1,000 catheter days). For studies with missing data, the corresponding authors were requested to supply additional data via e-mail. However, no authors responded.

Determining the quality of the studies

The quality of nonrandomized studies was assessed using the NOS[17] by 2 study authors independently (J.F. and E.L.), with a third author (S.K.) consulted for consensus. The range is from a low to a high quality score. The NOS evaluates 3 domains of study methodology: the selection of study groups, the comparability of study groups, and the quality of determining the outcomes of interest.[17] The 3 domains include 9 questions: 1 = Representativeness of the exposed cohort; 2 = Selection of the non-exposed cohort; 3 = Ascertainment of exposure; 4 = Demonstration that outcome of interest was not present at start of study; 5A and 5B = Comparability of cohorts on the basis of the design or analysis; 6 = Assessment of outcome; 7 = Was follow-up long enough for outcomes to occur; and 8 = Adequacy of follow up of cohorts.

Data synthesis

We initially conducted a narrative review of the included studies according to NC decontamination product and entered quantitative data into RevMan (Review Manager 5.3; The Cochrane Collaboration, Copenhagen, Denmark). Eligible data were pooled for meta-analysis, and we used a random effects model for pair-wise comparisons, due to clinical heterogeneity.[18] The degree of statistical heterogeneity was investigated by a combination of methods that involved visual inspection of the meta-analytic model and interpretation of the χ^2 and I^2 statistics that examine the total variance across studies due to heterogeneity rather than chance.[18] This test examines the percentage of total variations across studies caused by heterogeneity: categorized as low (0%-40%), moderate (30%-60%), high (50%-90%), or very high (75%-100%).[18] A sensitivity analysis was then performed including studies of moderate to high quality and studies with at least 100 participants. Forest plots were used to display the data, and dichotomous outcomes were presented as risk ratio (RR) with a 95% confidence interval (CI). A rate per event analysis was planned; however, this could not be conducted because of issues with data availability.

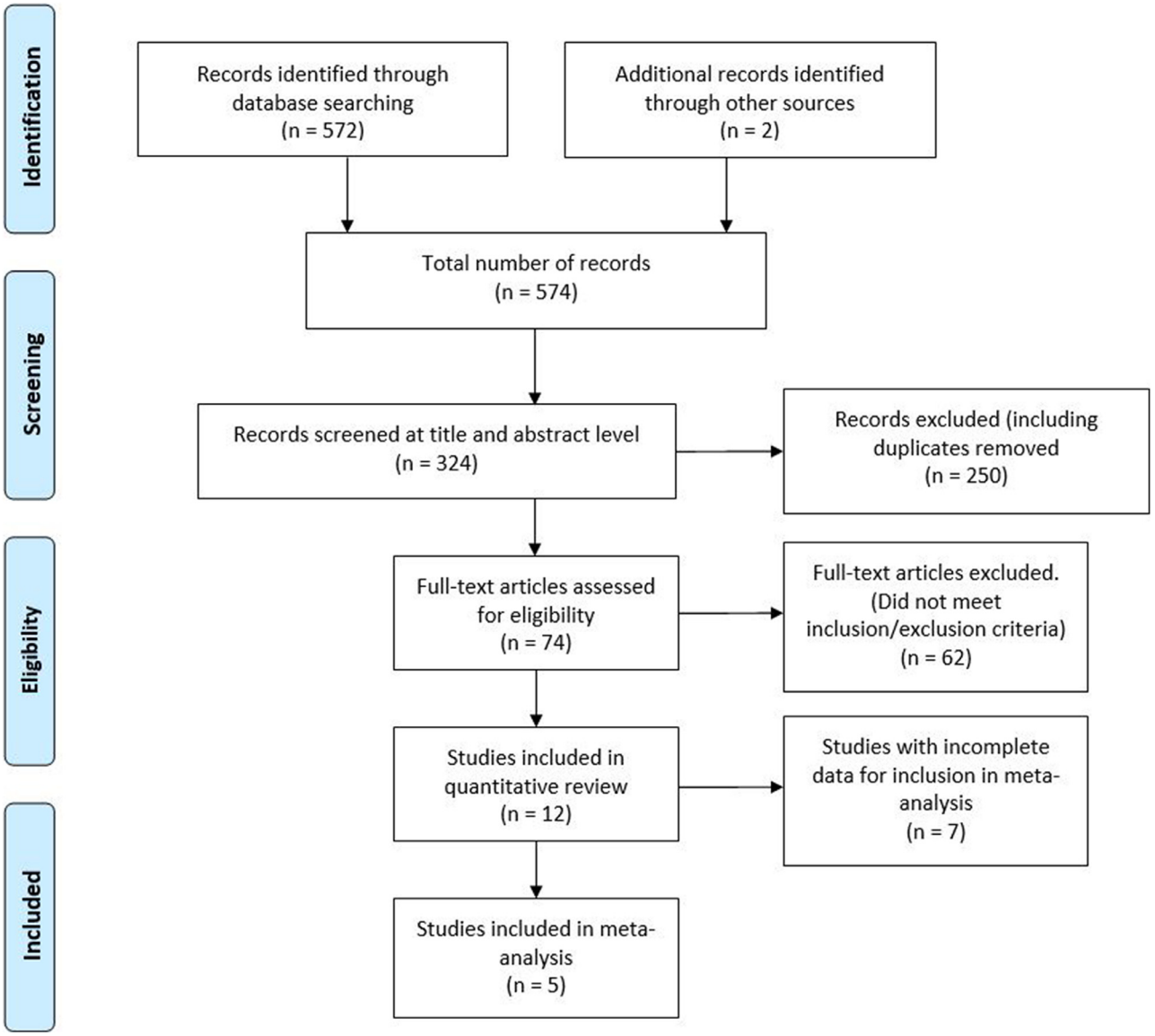

Fig 1. PRISMA flow diagram.

Publication bias

We intended to use a funnel plot to identify small-study effects and to assess for publication bias, but there was an insufficient number of studies to allow this.

RESULTS

Search strategy

The database searches revealed 572 (PubMed, n = 233; Medline EBSCO, n = 185; CINAHL EBSCO, n = 112; and Cochrane, n = 42) articles that were retrieved for title and abstract review, as shown in the PRISMA flow in Figure 1. Two additional articles were located from other sources. After review and removal of duplicates, 33 studies were obtained for full-text review. Twenty-one articles did not meet the inclusion or exclusion criteria. No RCTs were identified. Twelve pre-test/post-test observational studies were included in this review.

Study characteristics

As described in Table 1, the majority of included studies compared *active* decontamination using 70% IPA wipes with *passive* decontamination using 70% IPA impregnated caps,[10-12,19-25] although the control was unclear in 1 article.[20] The remaining 2 studies[26,27] compared CHG in 70% IPA wipes versus 70% IPA wipes, both using *active* decontamination. Most studies reported data from 2 time points only (single-measure pre-post intervention), with the exception of Wright et al,[10] Martino et al[24] (3 time points), and Kamboj et al[12] (4 time points). Reporting of CABSI varied; however, most studies reported rates per 1,000 catheter days. Most of the studies were conducted in the United States (n = 9), with the remaining studies conducted in the United Kingdom (n = 3). Ages ranged from neonates[20] to the elderly[11], with all studies focused on central venous access devices, except for 2 studies, which also included PIVCs.[11,19] Industry support was declared by 6 authors,[11,12,19,22,25,26] not stated by 5 authors,[10,20,21,23,27] with 1 author stating that no industry funding was received.[24]

Table 1
Characteristics of included studies

Author, year, and country	Setting	Sample size	Control	Intervention	CABSI type*	CABSI rates†
Cameron-Watson et al, 2016[11], UK	Various patient populations with a PIVC, CVAD, or arterial catheter	Control: ND Intervention: n = 1,094	70% IPA wipe	70% IPA cap	CRBSI‡	Combined rates: Control: 26/ND Intervention: 8/1,000 (0.82%)
DeVries et al, 2014[19], USA	Adult ICU patients with a CVAD or PIVC	Control: 185,950 patient days Intervention: 187,444 patient days	70% IPA wipe	70% IPA cap	BSI in CVADs and PIVCs‡	Control: 0.0075/1,000 Intervention: 0.0038/1,000
Kamboj et al, 2015[12], USA	High-risk units; and general oncology with a CVAD	Control: 84,427 catheter days Intervention: 83,659 catheter days	70% IPA wipe	70% IPA cap	CABSI	Phase 1: 2.84/1,000 (control)§ Phase 2: 2.46/1,000 (control)§ Phase 3; 2.40/1,000 (intervention)§ Phase 4: 1.75/1,000 (intervention)§
Martino et al, 2017[24], USA	Burn patients with a CVAD	Control: n = 107 Time 1: n = 153 Time 2: n = 136 Time 3: n = 287	70% IPA wipe	70% IPA cap	CABSI‡	Control: 7.43/1,000 Time 1: 2.36/1,000 (intervention) Time 2: 9.0/1,000 (intervention) Time 3: 3.04/1,000 (intervention)
Merrill et al, 2014[20], USA	Newborns and adults with a CVAD	Control: ND Intervention: ND	Unclear as not s pecifically stated	70% IPA cap	CABSI	Control: 1.5±0.37/1,000 Intervention: 0.88±0.62/1,000
Pavia and Mazza, 2016[25], USA	Pediatric patients with short bowel syndrome with a CVAD	Control: n = 20-25 Intervention: n = 20-25	70% IPA wipe	70% IPA cap	CABSI‡	Control: 8.59/1,000 Intervention: 3.89/1,000
Pichler et al, 2014[26], UK	Pediatric patients on TPN with a CVAD	Control: n = 42 Intervention: n = 50	70% IPA wipe	2% CHG in 70% IPA wipe	CRBSI	Control: 3.1/1,000 Intervention: 0.4/1,000
Ramirez et al, 2012[21], USA	Adult ICU patients with a CVAD	ND	70% IPA wipe	70% IPA cap	CABSI	Control: 1.9/1,000 Intervention: 0.5/1,000
Soothill et al, 2009[27], UK	Pediatric HSCT patients and non-HSCT patients with a CVAD	Control: n = 553 Intervention: n = 571	70% IPA wipe	2% CHG in 70% IPA wipe	CRBSI	Control: 10-12/1,000 Intervention: 3/1,000
Stango et al, 2014[22], USA	Unidentified number of patients with a CVAD	Unknown	70% IPA wipe	70% IPA cap	CABSI‡	Control: 1.52/1,000 Intervention: 0.83/1,000
Sweet et al, 2012[23], USA	Adult oncology patients with a CVAD	Control: n = 472 Intervention: n = 282	70% IPA wipe	70% IPA cap	CABSI	Control: 2.3/1,000 Intervention: 0.3/1,000
Wright et al, 2013[10], USA	Adult ICU patients with a CVAD	Phase 1: n = 252 Phase 2: n = 364 Phase 3: n = 183	70% IPA wipe: Phase 1 & 3	70% IPA cap: Phase 2	CABSI	Control P1: 1.45/1,000 Intervention P2: 0.74/1,000 Control P3: 1.31/1,000

BSI, bloodstream infection; *CABSI*, catheter-associated BSI; *CHG*, chlorhexidine gluconate; *CRBSI*, catheter-related BSI; *CVAD*, central venous access device; *HSCT*, hemopoietic stem cell transplant; *ICU*, intensive care unit; *IPA*, isopropyl alcohol; *ND*, no data supplied; *PIVC*, peripheral intravenous access device; *TPN*, total parenteral nutrition.
*CABSI unless otherwise stated, such as CRBSI.
†CABSI rate per 1,000 catheter days unless these data were not supplied, in which case CABSI rate per patient was used.
‡Definition not supplied in Methods.
§Hospital-wide results.

Quality assessment

Overall, the studies were of medium quality, with the majority of studies[11,12,20,21,23,26,27] receiving 4-5 stars (Table 2).

Selection

The participants from most studies included a specific population such as infants;[25] however, 2 studies included a wider population, with 1 study[11] examining oncology, acute care of the elderly, critical care, and a surgical ward. All studies examined a similar population in the nonexposed and exposed cohort. Most studies[10,12,20,21,23,24,26,27] could demonstrate that the outcome of interest was not present at the commencement of the study.

Comparability

All studies were pre-posttest in design. However, it was difficult to compare studies because of the lack of reported data. Four studies[23,24,26,27] reported participant demographics.

Outcome

Assessment of outcome was varied. All but 1 study[22] described the assessment of outcome by record linkage or independent blind assessment. However, only 2 studies indicated the follow-up period of participants, with no studies describing whether all participants were accounted for from the commencement of the study to completion of the follow-up time period.

Decontamination product: 70% IPA wipe versus 2% CHG in 70% IPA wipe

Only 2 studies[26,27] compared a 70% IPA wipe to 2% CHG in 70% IPA wipe using *active* decontamination (n = 1,216). All studied populations were pediatric and neonatal patients.

As displayed in Figure 2, 2% CHG in IPA wipes were associated in the meta-analysis with significantly less CABSI, in comparison to IPA wipes (RR, 0.28; 95% CI, 0.20-0.39). There was low heterogeneity evident ($\chi^2 = 0.03$; $I^2 = 0\%$), as reflective of the study population.

CABSI rate per 1,000 catheter days

The CABSI rate ranged from 3.1-12.0 per 1,000 catheter days in the IPA wipe group and 0.4-3.0 in the CHG in IPA wipe group. Whereas CABSI per 1,000 catheter days was reported for both studies in this group, only 1 study[27] reported the total number of catheter days per group. Therefore, we were unable to carry out meta-analysis of CLABSI per 1,000 catheter days.

Table 2
Newcastle-Ottawa Scale quality assessment

Author, year, and country	1	2	3	4	5A	5B	6	7	8	Quality
Cameron-Watson et al, 2016[11], UK	✶	✶	✶	—	—	—	✶	—	—	Moderate
DeVries et al, 2014[19], USA	✶	✶	—	—	—	—	✶	—	—	Low
Kamboj et al, 2015[12], USA	✶	✶	—	✶	—	—	✶	—	—	Moderate
Martino et al, 2017[24], USA	—	✶	✶	✶	✶	✶	✶	—	—	Moderate
Merrill et al, 2014[20], USA	✶	✶	✶	✶	—	—	✶	—	—	Moderate
Pavia and Mazza, 2016[25], USA	—	—	—	—	—	—	✶	—	—	Low
Pichler et al, 2014[26], UK	—	✶	—	✶	✶	✶	✶			Moderate
Ramirez et al, 2012[21], USA	—	✶	✶	✶	—	—	✶	—	—	Moderate
Soothill et al, 2009[27], UK	✶	✶	—	✶	—	✶	✶	—	—	Moderate
Stango et al, 2014[22], USA	✶	✶	—	—	—	—	—	—	—	Low
Sweet et al, 2012[23], USA	✶	✶	—	✶	✶	✶	✶	—	—	Moderate
Wright et al, 2013[10], USA	✶	—	—	✶	—	—	✶	—	—	Low

1, representativeness of the exposed cohort; *2*, selection of the non-exposed cohort; *3*, ascertainment of exposure; *4*, demonstration that outcome of interest was not present at start of study; *5A*, comparability of cohorts on the basis of the design or analysis; *5B*, comparability of cohorts on the basis of the design or analysis; *6*, assessment of outcome; *7*, was follow-up long enough for outcomes to occur; *8*, adequacy of follow-up of cohorts.

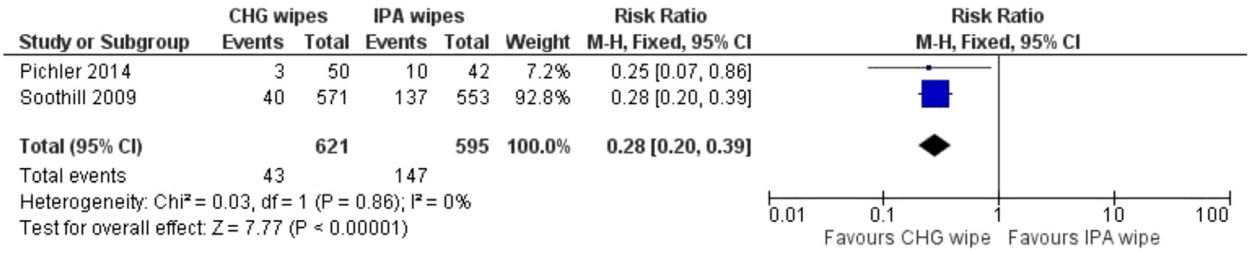

Fig 2. Forest plot for comparison of CHG in IPA wipe to IPA wipe for CABSI. *CABSI*, catheter-associated bloodstream infection; *CHG*, chlorhexidine gluconate; *IPA*, isopropyl alcohol.

Decontamination type: active (wipe) versus passive (impregnated cap)

Of the 10 studies that compared an IPA wipe with an IPA-impregnated cap, only 3 had sufficient patient-level data to be included in the meta-analysis.[10,23,24] All 3 studies reported data as CABSI. As displayed in Figure 3, the IPA cap was associated with significantly less CABSI, in comparison to IPA wipes (RR, 0.43; 95% CI, 0.28-0.65). There was moderate statistical heterogeneity ($\chi^2 = 3.44$; $I^2 = 42\%$).

CABSI rate per 1,000 catheter days

For the 3 studies reported in the meta-analysis, CABSI ranged from 1.31-7.43 per 1,000 catheter days in the IPA wipe group and 0.3-9.0 in the IPA-impregnated cap group. CABSI per 1,000 catheter days was reported for the 3 studies in this meta-analysis; however, most studies did not report the number of catheter days per group. Owing to the lack of available data on total number of catheter days per group, we were unable to carry out meta-analysis per 1,000 catheter days.

Sensitivity analysis

Owing to few remaining studies, a sensitivity analysis was only undertaken for the *passive* decontamination using the IPA-impregnated cap versus the IPA wipes. Of the 5 studies in the primary meta-analysis, 2 were excluded for the sensitivity analyses: 1 because <100 participants were studied (*active* decontamination)[26] and 1 because of a low-quality NOS (*passive* decontamination).[10] The results indicated that IPA caps, in comparison to IPA wipes, were associated with significantly less CABSI, which was consistent with the primary analysis.

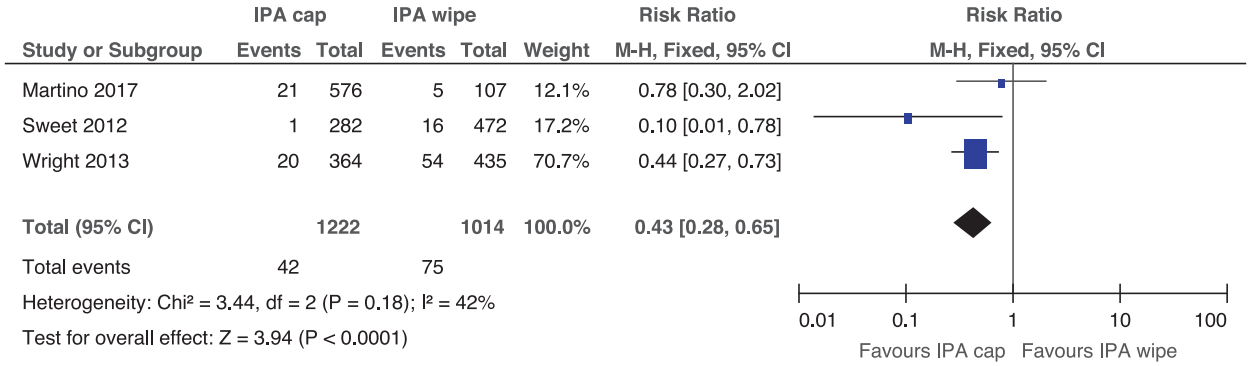

Fig 3. Forest plot for comparison of IPA cap versus IPA wipe for CABSI. *CABSI*, catheter-associated bloodstream infection; *IPA*, isopropyl alcohol.

DISCUSSION

This systematic review and meta-analysis identified that CHG in IPA wipes (*active* decontamination) or IPA-impregnated caps (*passive* decontamination) for NC decontamination were associated with significant lower CABSI risk than IPA wipes. These results suggest that despite widespread use, 70% IPA wipes are likely inadequate for NC decontamination.

Overall, 70% IPA wipes, in comparison to CHG wipes (*active* decontamination) or IPA-impregnated caps (*passive* decontamination), were associated with more CABSI, when used for NC decontamination. CHG in IPA wipes were associated with two-thirds less of a risk of CABSI than IPA wipes, with a highly precise estimate of effect (RR, 0.28; 95% CI, 0.20-0.39). In addition, 70% IPA caps were associated with less than one-half the risk of CABSI, than IPA wipes (RR, 0.43; 95% CI, 0.28-0.65). Therefore, the 70% alcohol wipe may be inadequate for NC decontamination.

Historically, CHG has been used more frequently as a skin antiseptic but is now recommended as an option for NC decontamination.[8,9] Alcohol caps are also recommended, with additional disinfection if multiple vascular access device accesses are required.[14] The practice of NC decontamination before and after every access is currently recommended by some guidelines,[8] with no evidence to support this practice. Given the results of this meta-analysis, this recommendation seems prudent; however, RCTs of adequately large sample size are needed to confirm causality. An RCT comparing 70% IPA wipe, with a CHG wipe, and the 70% IPA-impregnated cap would assist in definitively determining which method of NC decontamination most effectively prevents CABSI.

There have been 2 previous systematic reviews comparing the 70% IPA wipe against the 70% IPA-impregnated cap. The first, highlighted the importance of NC decontamination; however, it did not include a meta-analysis and did not advocate for any 1 product over another.[27] The second review[15] included a meta-analysis of studies comparing an IPA wipe with an IPA-impregnated cap. This review identified that the IPA-impregnated cap was associated with significantly less CABSI, in comparison to IPA wipe (RR, 0.59, 95% [CI 0.45-0.77]). However, the authors also stated that an RCT is needed. Neither review included comparisons involving the CHG wipe, which is increasingly used for NC decontamination. Our findings regarding the superiority of IPA caps over IPA wipes, are consistent with these previous reviews.

We found only 2 studies[26,28] that tested *active* decontamination with a CHG wipe, and the total number of participants included was relatively small (n = 1,216). Both studies reported catheter-related bloodstream infection. This method of NC decontamination is currently being suggested in some clinical guidelines[8,29] with little research to support this. It could be concluded that use of a CHG in alcohol wipe is superior to alcohol alone for infection prevention; however, this has not been well established. It is also noted that CHG has prolonged decontamination activity;[30] however, again, there is insufficient evidence whether this results in less CABSIs.

Ten studies[10-12,19-25] tested *active* decontamination with an alcohol wipe compared to *passive* decontamination using an alcohol-impregnated cap. All studies reported a reduction in bloodstream infection with *passive* decontamination. This method theoretically minimizes the risk for noncompliance when using *active* decontamination; however, this product is not yet widely used, and cost could be 1 explanation. For example, Reynard 70% alcohol wipes cost approximately $0.01 each; and Reynard 2% CHG in 70% alcohol prep pads cost approximately $0.02 each (https://www.pharmacydirect.com.au/), whereas the alcohol-impregnated cap can cost as much as $0.17 each. An acutely ill patient may require >20 NC decontamination products each day leading to a total cost of a minimum of approximately $0.29, $0.43, and $3.33, respectively. Given the significant number of NC decontamination products used, even small differences in product cost can generate significant implications for hospital budgets. However, the costs associated with CABSI management can range from $17,896-$94,879,[31] suggesting that the initial outlay of purchasing the NC decontamination products could be cost effective.

Although not addressed in this review, for *active* decontamination, scrub time, drying time, and scrub technique are important. However, these remain as an unresolved issue in practice and research. The IPA and CHG wipes often contain from 0.6-1.5 mL of solution, making adequate drying time essential to ensure adequate exposure time for microorganism decontamination and that the solution does not inadvertently get infused into the bloodstream.[32] Moreover, a chemical residue can form on the NC with the use of the CHG wipe. It remains unclear if this forms a protective barrier or may attract microorganisms to adhere to the NC.[30] Moving forward, designing and conducting a clinical trial that accommodates and tests NC decontamination solution, method, and timing would be challenging, as this would lead to a potential 3×3 factorial trial, which, although clinically appropriate, may be challenging in practice.

STRENGTHS

This review supports previous reviews into similar NC decontamination products, concluding that the IPA wipe alone is potentially inadequate for NC decontamination. However, these results need to be taken with caution because of the lack of RCT evidence to confirm efficacy. To our knowledge, this review is also the first to include NC decontamination with a CHG in 70% IPA wipe, giving readers a wider understanding of the products available and their effectiveness. This review highlights the need for a suitably large RCT to provide evidence for the best approach for NC decontamination.

LIMITATIONS

The first limitation of the meta-analysis and review was the moderate study heterogeneity for the *active* versus *passive* IPA comparison, meaning the conclusions are more susceptible to change as new studies are conducted. Comparatively, the alcoholic CHG versus IPA wipe studies had low heterogeneity. Second, because of the absence of RCTs, only observational studies were included. RCTs are needed to identify cause and effect relationships and given the design of the included studies the true effect of the interventions may be underestimated or overestimated.[33] Third, a rate-per-time period analysis could not be completed, owing to unavailability of data. This would have been a more sensitive examination of the effectiveness of these interventions. Future trials examining these interventions should report catheter days, to enable such analysis. Fourth, it is unclear if patients may have had >1 vascular access device as this was not reported. We assumed each patient only had 1 device, as no secondary devices were mentioned. Finally, not all studies reported what type of funding, if any, was received. If industry funding was received, this could potentially be a source of bias.

CONCLUSIONS

NC decontamination is an essential component of infection control practices in the health care system, and 70% IPA wipes are likely to be the least-effective approach currently available. Quality postinsertion and maintenance care of the vascular access device is essential to prevent CABSI. Both alcoholic CHG wipes and IPA passive decontamination caps are associated with significantly lower CABSI than IPA wipes in nonrandomized studies. However, there have been no high-quality RCTs undertaken on the impact of NC decontamination for the prevention of introducing microorganisms into this

device. There is a lack of high-quality evidence to confirm the superior decontamination method when accessing and maintaining a vascular access device. With newer methods now available, RCTs are urgently needed to establish the optimal decontamination method to prevent CABSI.

References

1. Hadaway L. Needleless connectors: improving practice, reducing risks. JAVA 2011;16:20-33.
2. Perez E, Williams M, Jacob JT, Reyes MD, Chernetsky Tejedor S, Steinberg JP, et al. Microbial biofilms on needleless connectors for central venous catheters: comparison of standard and silver-coated devices collected from patients in an acute care hospital. J Clin Microbiol 2014;52:823-31.
3. Chopra V, O'horo JC, Rogers Mary AM, Maki DG, Safdar N. The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in adults: a systematic review and meta-analysis. Infect Control Hosp Epidemiol 2013;34:908-18.
4. Ziegler MJ, Pellegrini DC, Safdar N. Attributable mortality of central line associated bloodstream infection: systematic review and meta-analysis. Infection 2015;43:29-36.
5. Weiner LM, Webb AK, Limbago B, Dudeck MA, Patel J, Kallen AJ, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2011-2014. Infect Control Hosp Epidemiol 2016;37:1288-301.
6. Zhang L, Keogh S, Rickard CM. Reducing the risk of infection associated with vascular access devices through nanotechnology: a perspective. Int J Nanomedicine 2013;8:4453-66.
7. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49:1-45.
8. Loveday HP, Wilson JA, Pratt RJ, Golsorkhi M, Tingle A, Bak A, et al. Epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. J Hosp Infect 2014;86(Suppl):1-70.
9. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control 2011;39(Suppl 1):1-34.
10. Wright MO, Tropp J, Schora DM, Dillon-Grant M, Peterson K, Boehm S, et al. Continuous passive disinfection of catheter hubs prevents contamination and bloodstream infection. Am J Infect Control 2013;41:33-8.
11. Cameron-Watson C. Port protectors in clinical practice: an audit. Br J Nurs 2016;25 (Suppl):25-31.
12. Kamboj M, Blair R, Bell N, Son C, Huang Y-T, Dowling M, et al. Use of disinfection cap to reduce central-line–associated bloodstream infection and blood culture contamination among hematology–oncology patients. Infect Control Hosp Epidemiol 2015;36:1401-8.
13. Queensland Government. Tunnelled central venous catheters. Available from: https://www.health.qld.gov.au/publications/clinical-practice/guidelines-procedures/diseases-infection/governance/icare-tcvc-guideline.pdf. Accessed February 7, 2019.
14. Infusion Nurses Society. Infusion therapy standards of practice. J Infus Nurs 2016;39(Suppl):S40.
15. Voor AF, Helder OK, Vos MC, Schafthuizen L, Sülz S, van den Hoogen A, et al. Antiseptic barrier cap effective in reducing central line-associated bloodstream infections: a systematic review and meta-analysis. Int J Nurs Stud 2017;69:34-40.
16. Flynn JM, Rickard CM, Keogh S, Zhang L. Alcohol caps or alcohol swabs with and without chlorhexidine: an in vitro study of 648 episodes of intravenous device needleless connector decontamination. Infect Control Hosp Epidemiol 2017;38:617-9.
17. Wells GA, Shea B, O'connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed February 7, 2019
18. Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. Hoboken (NJ): John Wiley & Sons; 2011.
19. DeVries M, Mancos PS, Valentine MJ. Reducing bloodstream infection risk in central and peripheral intravenous lines: initial data on passive intravenous connector disinfection. JAVA 2014;19:87-93.
20. Merrill KC, Sumner S, Linford L, Taylor C, Macintosh C. Impact of universal disinfectant cap implementation on central line-associated bloodstream infections. Am J Infect Control 2014;42:1274-7.
21. Ramirez C, Lee AM, Welch K. Central venous catheter protective connector caps reduce intraluminal catheter-related infection. JAVA 2012;17:210-3.
22. Stango C, Runyan D, Stern J, Macri I, Vacca M. A successful approach to reducing bloodstream infections based on a disinfection device for intravenous needleless connector hubs. J Infus Nurs 2014;37:462-5.
23. Sweet MA, Cumpston A, Briggs F, Craig M, Hamadani M. Impact of alcohol-impregnated port protectors and needleless neutral pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. Am J Infect Control 2012;40:931-4.
24. Martino A, Thompson L, Mitchell C, Trichel R, Chappell W, Miller J, et al. Efforts of a unit practice council to implement practice change utilizing alcohol impregnated port protectors in a burn ICU. Burns 2017;43:956-64.
25. Pavia M, Mazza M. Adding innovative practices and technology to central line bundle reduces bloodstream infection rate in challenging pediatric population. Am J Infect Control 2016;44:112-4.
26. Pichler J, Soothill J, Hill S. Reduction of blood stream infections in children following a change to chlorhexidine disinfection of parenteral nutrition catheter connectors. Clin Nutr 2014;3:85-9.
27. Moureau NL, Flynn J. Disinfection of needleless connector hubs: clinical evidence systematic review. Nurs Res Pract 2015;2015:796762.
28. Soothill JS, Bravery K, Ho A, Macqueen S, Collins J, Lock P. A fall in bloodstream infections followed a change to 2% chlorhexidine in 70% isopropanol for catheter connection antisepsis: a pediatric single center before/after study on a hemopoietic stem cell transplant ward. Am J Infect Control 2009;37:626-30.
29. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Summary of recommendations: guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52:1087-99.
30. Hong H, et al. Disinfection of needleless connectors with chlorhexidine-alcohol provides long-lasting residual disinfectant activity. Am J Infect Control 2013;41: e77-9.
31. Agency for Healthcare Research and Quality. Reducing hospital acquired conditions. Available from: https://www.ahrq.gov/professionals/quality-patient-safety/pfp/haccost2017-results.html. Accessed February 7, 2019.
32. Slater K, Fullerton F, Cooke M, Snell S, Rickard CM. Needleless connector drying time—how long does it take? Am J Infect Control 2018;46:1080-1.
33. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.