

Short report

A combined education and skin antiseptics intervention effectively reduced persistently high blood culture contamination rates in neonatal intensive care.

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Running title: Effective and safe skin antiseptics in NICU using chlorhexidine and alcohol

Keywords

Intervention, Neonatal, Blood Culture, Bacteria, Contamination, Chlorhexidine

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Summary

Contaminated blood cultures represent challenges impacting diagnosis, duration of hospitalisation, antimicrobial use, pharmacy and laboratory costs. Facing problematic neonatal blood culture contamination (3.8%), we instigated a successful intervention combining skin antisepsis using sterile applicators with 2% chlorhexidine gluconate in 70% isopropanol prior to phlebotomy (replacing 70% isopropanol) and staff education. In the 6-months prior to intervention, 364 neonatal peripheral blood samples were collected. 14 (3.8%) were contaminated. In the post-intervention 6-months, 314 samples were collected. 3 (0.96%) were contaminated, representing significant improvement (Fisher's exact test $P = 0.0259$). No dermatological sequelae were observed. The improvement has been sustained.

(98 words)

Background

Use of blood cultures as a basis for diagnostic testing during hospitalisation is ubiquitous. Unfortunately, contamination of blood cultures (i.e., growth of bacteria in blood samples that were not present in patients' blood during the process of sample collection) with commensal skin microorganisms is relatively common (1) and, due to associated uncertainty regarding "false positive" tests, can cause initiation of empirical antimicrobial treatment, further laboratory testing and lengthened duration of hospital stay (2). The American Society for Microbiology and The Clinical and Laboratory Standards Institute recommend that an acceptable rate of blood culture contamination should not exceed 3%. There has, therefore, been considerable focus on interventions to reduce contamination of blood cultures, including dedicated education and training (3), establishing of dedicated phlebotomy teams, use of preprepared customised blood culture kits and varying skin antiseptics agents, with generally (but not universally) successful outcomes (4). With respect to the latter approach, meta-analysis (5) have demonstrated that alcohol-based approaches were more effective than non-alcoholic, while chlorhexidine plus alcohol performed better than iodine plus alcohol combinations. In 2013, Washer *et al* (6) reported a clinical trial of three antiseptic interventions (70% isopropanol followed by 10% povidone iodine, 70% isopropanol followed by 2% iodine tincture, and 2% chlorhexidine gluconate combined with 70% alcohol) in almost 13,000 blood cultures demonstrating no significant difference in contamination rates and recommending that decisions regarding choice of antiseptics be based on cost or preference.

However, those studies focused on adult patients with relatively little emphasis placed

on paediatric, and specifically neonatal, patients due to concerns regarding, for example, risk of adverse effects on thin, incompletely keratinised skin or potential anaphylaxis (7).

Indeed, when assessments of products such as chlorhexidine have been reported, the described approaches to antiseptics use lower concentration products (e.g., 1% or lower) (8) rather than the 2% chlorhexidine in 70% alcohol combination that has shown efficacy in adults. A notable exception to this is a 2010 report by Marlowe (9) that determined significantly greater efficacy of a 70% alcohol with 3% chlorhexidine gluconate combination versus povidone-iodine alone in reducing blood culture contamination in a pediatric emergency department setting. However, that study did not assess chlorhexidine in children under 2 months.

Here, we describe what we believe is the first successful combined intervention, involving both adoption of 2% chlorhexidine in 70% alcohol use and staff education, in a neonatal intensive care unit (including premature and very low-birth-weight newborns (VLBW, <1500g) babies) with persistently high blood contamination rates.

Methods

Setting

This intervention was performed at the Neonatal Intensive Care Unit (NICU) with 19 cots in the University Maternity Hospital Limerick, Ireland (UMHL). For context, in 2012, there were 909 NICU admissions (from a cohort of 4905 live births). This intervention was instigated by an audit of NICU records showing blood culture contamination rates of 3.4% in 2009, 3.1% in 2010 and 3.2% in 2011) (unpublished data). In the immediate pre-intervention period (January to July 2012), a total of 364 peripheral blood cultures resulted in 17 positive cultures were detected from 14 patients (10 male and 4 female). Three were considered significant clinical isolates; two *Escherichia coli* and one *Streptococcus bovis*.

A blood culture was considered to be contaminated if at least one of the following organisms (considered representative of skin microflora and most commonly reported contaminants) (10) was identified in at least one of a series of blood cultures: coagulase-negative *Staphylococcus* spp., *Corynebacterium* spp., alpha- or beta-haemolytic streptococci, *Micrococcus* spp., *Bacillus* spp. and *Propionibacterium* spp. in the context of correlated clinical findings (e.g. fever, leukocytosis, blood biochemistry), and time to positivity. Thereby, the remaining 14 blood cultures were considered “false positives”, containing coagulase negative *Staphylococcus* (CoNS, 13 specimens), and mixed CoNS and Diptheroids (1 specimen). This represents a contamination rate of 3.8% (14/364).

Intervention

We introduced skin antisepsis using 2% chlorhexidine gluconate in 70% isopropyl sterile applicators (ChloroPrep®) (replacing 70% isopropyl alcohol swabs) prior to phlebotomy for all neonates. The antimicrobial efficacy of the chlorhexidine preparation was validated separately in our hospital. Our protocol required that the antisepsis combination remain post-blood collection (leveraging residual chlorhexidine antimicrobial activity). Therefore, in the context of avoiding adverse events for our neonatal patients with potentially fragile skin (particularly premature children), we focused specifically on emergence of any adverse events potentially associated with chlorhexidine use.

A concomitant educational programme was provided to NICU staff (consultant neonatologists/paediatricians, doctors in training including registrars and senior house officers, as well as neonatal nursing and midwifery staff) emphasising the importance and opportunities for hand hygiene, detailing the intervention procedures and use of the sterile applicators. This training occurred between July and December 2012 while the introduction of ChloroPrep® use began in January 2013.

The intervention was approved by the Ethics Board of the Mid-West Teaching Hospitals (Ireland). Informed consent for participation was obtained from parents of all children.

Results and Discussion

We describe the first successful intervention to improve persistently high blood culture contamination rates in a neonatology setting using a combination of 2% chlorhexidine and 70% isopropanol complemented with education of NICU staff. Attendance at the 30 minute training sessions achieved 100% compliance and the intervention was well received. All found the sterile applicator to be user-friendly, did not require unusual storage or handling and with a drying time (an important consideration for NICU staff) of 15-30 seconds being no different to the 70% alcohol swabs previously employed.

In the immediate post-intervention period (January to July 2013), 314 peripheral blood cultures (from children aged less than one day to more than 3 weeks) resulted in 3 contaminated blood cultures (from 3 separate patients), each involving CoNS (a rate of 0.96%; Fisher's exact test $P = 0.0259$). Although CoNS may cause sepsis in neonates, sepsis was not present. We attribute that improvement to the introduction of 2% chlorhexidine, the applicator system allowing gentle contact with delicate neonate skin, and a greater emphasis on aseptic technique brought about through the provided education programme. We noted no evidence of adverse effects during or following use of the antiseptics combination, thereby providing evidence to support judicious use of chlorhexidine in the neonate setting.

During that period, there were no changes in NICU staffing levels, and no reduction in bed numbers within the unit. Additionally, there were no changes implemented regarding antimicrobial use and no other changes in practice introduced that could have been confounding factors. However, within our NICU, there is increased awareness among staff regarding the procedural skills and expertise necessary for

maintaining a sterile field to prevent contamination during taking of blood samples, increased practical phlebotomy training for new staff entering the unit, increased knowledge of the consequences of false positive blood cultures, and a heightened awareness of international best practice guidelines in striving to remain below the recommended rate of <3% blood culture contamination.

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Conclusions

The introduction of staff education and sterile applicators containing 2% chlorhexidine in 70% isopropanol for neonatal skin antisepsis has significantly reduced blood culture contamination, from 3.8% pre-intervention to 0.96% post-intervention. Staff welcomed the training, accepted use of the applicators, neonatal care was not compromised, and no dermatological adverse events were observed. We are unable to determine which element of our intervention was most influential, however, we believe that replication of our combined intervention in larger cohorts or through randomised, controlled trials would have merit. That said, due to our results, we plan to introduce this product for skin antisepsis throughout the University of Limerick Group of Hospitals for medical, surgical and obstetric patients.

Acknowledgements

We thank the staff of the University Hospital Limerick microbiology laboratory and the NICU for their continued enthusiasm and commitment to the intervention described here.

Conflict of interest

The authors declare that they have no competing interests.

Funding sources

None

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