

ORIGINAL ARTICLE

Combined use of alcohol hand rub and gloves reduces the incidence of late onset infection in very low birthweight infants

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Objective: To assess the incidence of late onset (> 72 hours) infection and necrotising enterocolitis (NEC) in very low birthweight (VLBW) infants in two 36 month periods using two hand hygiene protocols: conventional handwashing (HW; first 36 month period); an alcohol hand rub and gloves technique (HR; second 36 month period).

Method: VLBW infants admitted to the neonatal intensive care unit during the period December 1993–November 1999 were eligible. A new hand hygiene protocol using alcohol handrub and gloves was introduced in December 1996. Each patient's case record was reviewed retrospectively by two independent investigators using a standard data collection form. The incidence of NEC and systemic infections, including bacterial or fungal septicaemia, meningitis, and peritonitis, in the two periods were compared.

Results: The HW and HR groups contained 161 and 176 VLBW infants respectively. The incidence of late onset systemic infection decreased from 13.5 to 4.8 episodes (including NEC)/1000 patient days after introduction of the HR regimen, representing a 2.8-fold reduction. Similarly, the incidence of Gram positive, Gram negative, and fungal infections decreased 2.5-fold, 2.6-fold, and 7-fold respectively. There was also a significant reduction in the incidence of NEC in the HR group ($p < 0.0001$). Subgroup analysis revealed that the incidence of methicillin resistant *Staphylococcus aureus* (MRSA) septicaemia was significantly decreased in the second 36 month period ($p = 0.048$). The clinical data suggest that infants in the HW group had significantly earlier onset of sepsis ($p < 0.05$) and required oxygen supplementation for longer ($p < 0.05$) than those in the HR group. Significantly more VLBW infants were discharged from the neonatal intensive care unit without ever being infected ($p < 0.0001$), and also significantly fewer infants had more than one episode of infection in the HR group ($p < 0.0001$).

Conclusion: The introduction of the HR protocol was associated with a 2.8-fold reduction in the incidence of late onset systemic infection, and also a significant decrease in the incidence of MRSA septicaemia and NEC in VLBW infants. This decrease in infection rate was maintained throughout the second 36 month period.

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Late onset neonatal infection is a serious complication of prematurity and a significant cause of morbidity and mortality.¹⁻⁴ A recent survey of 15 major neonatal centres in the United States indicated that infants who developed late onset sepsis had a significantly longer hospital stay and higher mortality than patients who were not infected.¹ Therefore efficient and effective interventions are required to prevent this complication. Hand hygiene is often emphasised as being the single most important measure in any infection control programme for preventing cross transmission of microorganisms between patients.⁵⁻⁶ However, compliance with handwashing guidelines has been recognised to be unsatisfactorily low, often being less than 50% in published surveys,⁷⁻⁸ and such observations have been relatively consistent in the past two decades.⁷⁻⁸ Recent reports show encouraging results of the alcohol hand rub in the effectiveness of microorganism killing, skin tolerability, and compliance of healthcare workers in practicing hand hygiene.⁹⁻¹⁵ The alcohol hand rub has been recently recommended as the method of choice for hand hygiene by the Centers for Disease Control and Prevention (CDC) in the United States.¹⁶ There are limited data on the value of routine glove wearing for prevention of infection in intensive care, but a few studies have shown reduced infection rates with barrier protocols which included gloves and gowns.¹⁷⁻¹⁹ This

study reports our clinical experience of changing from a conventional handwashing (HW) programme to an alcohol hand rub and gloves (HR) regimen in a tertiary neonatal intensive care unit (NICU).

METHODS

Patients

Very low birthweight (VLBW) infants admitted to the NICU at the Prince of Wales Hospital between December 1993 and November 1999 were eligible for the study. The HW and HR groups contained 161 and 176 patients respectively. Infants with lethal congenital malformations or chromosomal abnormalities were excluded. Table 1 presents basic and clinical data on these infants.

Hand hygiene policies

The neonatal unit consists of 20 intensive care and 60 special care cots. The intensive care cots are distributed evenly in three cubicles, each containing six cots, plus two other single bedded isolation rooms. Chlorhexidine gluconate 4% (Hibiscrub; Zeneca Ltd, Macclesfield, Cheshire, UK) was the

Abbreviations: BPD, bronchopulmonary dysplasia; MRSA, methicillin resistant *Staphylococcus aureus*; NEC, necrotising enterocolitis; NICU, neonatal intensive care unit; VLBW, very low birthweight

Table 1 Clinical characteristics of the study population

	HW group (n = 161)	HR group (n = 176)
Gestational age (weeks)	28.9 (26.3–30.7)	29.4 (27.3–30.9)
Birth weight (g)	1115 (835–1300)	1163 (935–1340)
Sex (M/F)	79 (49%):82 (51%)	96 (55%):80 (45%)
Inborn/outborn	149 (93%):12 (7%)	166 (94%):10 (6%)
Mechanical ventilation (days)	9 (3–23)	8 (3–25)
Oxygen supplementation (days)	11 (3–38)	6 (1–25)*
Hospital stay (days)	80 (39–118)	76 (48–109)

Results are median (interquartile range) or number (%).

*p < 0.05 compared with HW group.

HW, Conventional handwashing; HR, alcohol hand rub and gloves.

antiseptic cleansing agent used for handwashing. On 1 December 1996, the whole unit switched from a conventional HW policy to the HR protocol. The standard HW policy was as defined in the 1985 CDC guidelines.²⁰ In addition, the hospital infection control team provided monthly lectures and workshops on hand hygiene and contact precautions in the hospital education programme.

Table 2 summarises the HR protocol. Hexol lotion containing 1% chlorhexidine in isopropyl alcohol and ethyl alcohol (Hexol; Sigma Pharmaceuticals Pty, Ltd, Croydon, Victoria, Australia) was the waterless alcoholic antiseptic agent used. The new protocol required the wearing of disposable, clean but non-sterile gloves for routine non-invasive procedures. As non-sterile gloves have been shown to be contaminated with a mean bioburden of approximately 1.8 log colony forming units,²¹ the HR protocol also recommended that the alcohol handrubbing procedure be repeated on the gloves before the incubator was entered. There was, however, no change in the hand hygiene policy for the parents (table 2, step 1) because of the importance of them “feeling and touching” their babies to maintain good bonding.

Case record review and data collection

Each case record was independently reviewed by two investigators (HLW and FL) using a standard data collection form. The purpose of data collection was not initially disclosed to these investigators, and they were asked to

collect information for routine neonatal audit. Details of an infection episode, including age of onset of sepsis, types of organism isolated from various body fluids such as blood, cerebrospinal fluid, and peritoneal fluid, serial C reactive protein concentrations, antibiotic susceptibility profile of the organisms, the requirement for surgical intervention and outcome, were recorded from the case notes. Other important clinical indices such as the duration of oxygen supplementation, duration of mechanical ventilation, and length of hospital stay were also documented. Microbiological, biochemical, and pathological laboratory results were extracted from the hospital computer system, and then cross checked manually with information documented in the case records. A total of 321 case records were systematically reviewed. Eleven and six sets of case notes from the first and second 36 month periods were missing. Their clinical summaries and laboratory data could only be extracted electronically from the NICU and hospital computer systems.

Late onset infection

All VLBW infants with clinical evidence suggestive of systemic infection received a full sepsis screen as previously described.²² In brief, the sepsis screen included cerebrospinal fluid, blood, stool, urine, and endotracheal aspirate (infants on mechanical ventilation) cultures for bacteria and fungi. Central line tips and surgical specimens such as peritoneal fluid, pus, and biopsy specimens were also sent for culture. Chest radiographs were routinely obtained but abdominal radiographs were selectively performed as clinically indicated.²²

Late onset neonatal infection was defined as proven systemic infection that occurred after 72 hours of postnatal age. This category consisted of suspected infective episodes that had positive blood cultures and clinical features of sepsis. Microbiologically confirmed infections other than septicaemia, such as peritonitis, meningitis, systemic fungal infection, and also necrotising enterocolitis (NEC) (stage II or above in Bell’s classification²³) were also included.²² Repeated infection in the same patient was defined as a new systemic infection if at least one negative blood culture set was obtained after the previous infective episode, and there was a time lapse of more than seven days from the previous episode.

Table 2 Alcohol hand rub and glove protocol

1. All healthcare workers (doctors, nurses and allied health workers) **must** wash their hands, up to the elbows, thoroughly according to the 1985 CDC guidelines with an antiseptic cleansing agent (Hibiscrub) at the beginning of each shift.
2. Every time before entering the incubator or heated platform all healthcare workers **must**:
 - (i) rub both hands thoroughly with an alcohol based antiseptic agent (Hexol lotion; 2 plunges = 4 ml) and let it **dry**;
 - (ii) wear a pair of disposable, clean latex gloves after the handrubbing procedure, then, apply the same amount (2 plunges = 4 ml) of alcohol antiseptic agent to the gloves and let it dry before nursing the baby.
3. The alcohol based antiseptic agent (2 plunges = 4 ml) should be reapplied to the gloves after the touching of any equipment or utensils such as pens, monitors, thermometers, observation charts, etc while nursing the same baby.
4. If gloves are visibly soiled, new ones should be used and step 2 (ii) repeated.
Note: working with visibly soiled gloves is strictly prohibited.
5. All healthcare workers must take off their gloves immediately after leaving the incubator and rub their hands with alcohol antiseptic agent.
6. Step 2 should be repeated before re-entering the same incubator or nursing a different baby.
7. All staff should repeat step 1 when leaving the NICU.

Statistical analysis

The clinical characteristics of VLBW infants before and after introduction of the new protocol, and the pattern of late onset infection in the two periods were compared using the Mann-Whitney U test and the χ^2 or Fisher’s exact test as appropriate. All statistical tests were performed by using SPSS for Windows (Release 11; SPSS Inc, Chicago, Illinois, USA). The incidence of late onset infection expressed as the number of infection episodes per 1000 patient days is a descriptive figure. Thus, the reduction in incidence after the change of hand hygiene protocol could not be assessed statistically, and the importance of such a reduction could only be judged clinically.

RESULTS

The rate of admission of VLBW infants to the NICU remained relatively constant throughout the study period (52–60 patients a year). Tables 1 and 3 summarise the clinical characteristics of the study population and the pattern of late onset infections respectively. VLBW infants in the HW group had significantly earlier onset of sepsis (p < 0.05; table 3) and required oxygen supplementation for longer (p < 0.05; table 1). Table 3 lists details of the pathogens isolated from blood cultures and other body fluids. Coagulase negative staphylococci were usually responsible for late onset

infections in both periods (50% and 66% in the HW and HR group respectively). There was no significant change in the pattern of infection, and the proportion of Gram positive, Gram negative, and fungal infections remained relatively constant in the two periods (table 3). Subgroup analysis revealed that there were significantly fewer methicillin resistant *Staphylococcus aureus* (MRSA) infections ($p = 0.048$; table 3) in the HR group. The incidence of NEC in the HR group was also significantly lowered ($p < 0.0001$; table 3).

The incidence of late onset infection decreased from 13.5 to 4.8 episodes (including NEC)/1000 patient days after introduction of the HR regimen, representing a 2.8-fold reduction in infection rate. Table 4 illustrates the change in incidence of different categories of infection and NEC. Figure 1 represents the incidence of late onset infection and NEC (episodes/1000 patient days) in each 12 month period during the study. The results indicate that the incidence of Gram positive, Gram negative, and fungal infections was 2.5-fold, 2.6-fold, and 7-fold respectively lower in the HR period than in the HW period. Similarly, the incidence of NEC decreased 3.8-fold. There was no clustering of cases or major outbreak of a particular type of infection or NEC throughout the study period (fig 1). Although the number of patients with one episode of infection was comparable between the two groups, significantly more infants in the HR group were discharged from NICU without ever being infected ($p < 0.0001$; table 5), and significantly fewer infants in the HR group had more than one episode of infection ($p < 0.0001$; table 5).

DISCUSSION

Our results suggest that the HR regimen decreased the incidence of late onset sepsis, including NEC, by 2.8-fold in a NICU setting. Although the incidence of all types of infection decreased in the later HR period, the most striking phenomenon was the substantial and significant reduction in MRSA septicaemia, which as a proportion of all sepsis

Table 4 Incidence of late onset infection and necrotising enterocolitis (number of infection episodes/1000 patient days) before and after the alcohol hand rub and gloves regimen

Type of infection	HW group (n=161)	HR group (n=176)	Reduction in incidence (fold)
Gram positive	7.5	3.0	2.5
Gram negative	2.3	0.9	2.6
Fungal	0.7	0.1	7
NEC	3.0	0.8	3.8

HW, Conventional handwashing; HR, alcohol hand rub and gloves; NEC, necrotising enterocolitis.

decreased from 14% (20 cases) to 3% (2 cases). The reason for the disproportional decrease in MRSA sepsis has not been fully elucidated although other investigators have described a similar finding.²⁴ There was no concurrent reduction of MRSA sepsis in the hospital during the study period.²⁵ The results also suggest that significantly more VLBW infants in NICU were discharged home without ever being infected, and fewer infants had multiple (two or three) episodes of systemic infection after switching to the HR regimen. The median age of late onset sepsis was deferred for more than one week in the HR period. Nonetheless, the reduction in the infection rate did not translate into improved mortality. This was not unexpected, as the use of early warning diagnostic markers such as interleukin 6 and CD64,^{22, 26} and sophisticated supportive treatments have contributed to early detection and better management of life threatening infections. Pittet *et al*²⁴ reported a significant decrease in incidence of late onset infection and MRSA transmission after their hospital introduced a bedside, alcohol based hand disinfection programme. Parienti and coworkers²⁷ further suggested that the efficacy of hand decontamination by the alcohol hand rub was equivalent to traditional surgical hand scrubbing. We have observed a sustained decrease in the incidence of late onset infection even at 36 months after introduction of the campaign. This finding is in contrast with previous published reports of hand hygiene promotion programmes which have

Table 3 Pattern of late onset infection and necrotising enterocolitis before and after introduction of the alcohol hand rub and gloves regimen

	HW group (n=161)	HR group (n=176)
Postnatal age at onset of sepsis (days)	24 (12-39)	32 (18-54)*
Septicaemic episodes (n)	144	65
Gram positive organisms	103 (71.5%)	49 (75%)
CONS	72 (50%)	43 (66%)
MSSA	3 (2%)	-
MRSA	20 (14%)	2 (3%)*
<i>Enterococcus faecalis</i>	8 (5.5%)	4 (6%)
Gram negative organisms	31 (21.5%)	15 (23%)
<i>Enterobacter (aerogenes, cloacae)</i>	13 (9%)	5 (8%)
<i>Klebsiella pneumoniae</i>	5 (3.5%)	4 (6%)
<i>Escherichia coli</i>	1 (1%)	1 (1.5%)
<i>Acinetobacter spp</i>	2 (1%)	1 (1.5%)
<i>Pseudomonas aeruginosa</i>	3 (2%)	-
<i>Serratia marcescens</i>	6 (4%)	2 (3%)
<i>Salmonella spp</i>	1 (1%)	-
<i>Proteus mirabilis</i>	-	1 (1.5%)
<i>Sphingomonas paucimobilis</i>	-	1 (1.5%)
Fungi	10 (7%)	1 (2%)
<i>Candida spp</i>	10 (7%)	-
<i>Malassezia furfur</i>	-	1 (2%)
NEC	41 (25%)	12 (7%)†
NEC requiring surgery	6 (7%)	5 (9%)
Serum CRP concentration (mg/l)	54 (15-80)	40 (16-69)
Infection related deaths	4 (4.7%)	2 (3.7%)

Results are median (interquartile range) or number (%).
 * $p < 0.05$, † $p < 0.0001$ compared with HW group.
 HW, Conventional handwashing; HR, alcohol hand rub and gloves;
 CONS, coagulase negative staphylococci; MRSA, methicillin resistant *Staphylococcus aureus*; MSSA, methicillin sensitive *Staphylococcus aureus*; NEC, necrotising enterocolitis.

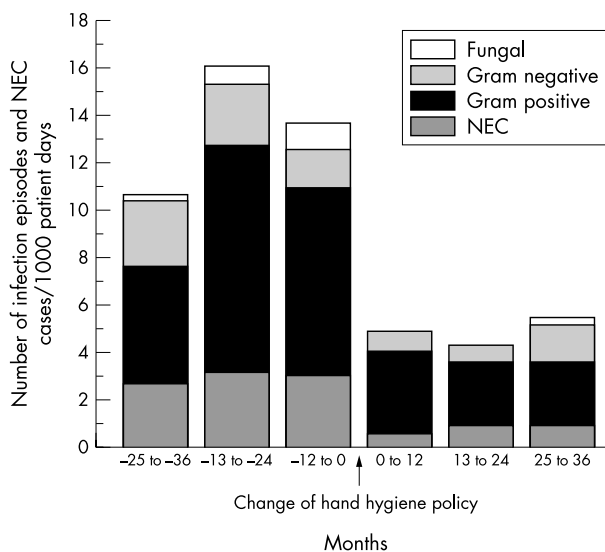


Figure 1 Incidence of necrotising enterocolitis (NEC) and Gram positive, Gram negative, and fungal infections before and after the change of hand hygiene programme. The arrow indicates introduction of the new hand hygiene programme. There was no clustering of cases or major outbreak of NEC or a particular type of infection throughout the study period.

Table 5 Incidence of late onset infection per patient before and after the introduction of alcohol hand rub and gloves protocol

Number of septic episodes per patient	HW group (n = 161)	HR group (n = 176)	Adjusted p values
0	75 (47%)	122 (69%)	<0.0001
1	32 (20%)	38 (22%)	1.0
2	26 (16%)	11 (6%)	<0.0001
≥3	28 (17%)	5 (3%)	

HW, Conventional handwashing; HR, alcohol hand rub and gloves.

shown only transient improvements in compliance and modest reductions in infection rates.²⁸ Ease of access, better skin tolerance, and the simplicity of the protocol may have been significant contributing factors in improving compliance.^{12 14 29} We also speculate that the universal glove wearing policy may play a role in the behavioural modification process, as glove wearing was a conspicuous act that could be easily monitored.

There was also a significant decrease in the duration of oxygen supplementation in infants in the HR group. No significant difference in gestational age and birth weight were observed between the HW and HR group. Infected and non-infected infants had comparable gestations and clinical characteristics. However, infected infants in the HW group required oxygen supplementation for significantly longer than corresponding infants in the HR group (median (interquartile range) 22 (8–60) days *v* 12 (3–37) days; *p* = 0.01). The latter difference was not observed between non-infected infants. There are several plausible explanations. Firstly, more infected patients may have died early in the HR group, but the current data do not support this hypothesis. Secondly, bronchopulmonary dysplasia (BPD) may have increased the risk of infants acquiring late onset infection. Although sick infants with chronic pulmonary diseases are more likely to become infected, it is usually lower respiratory tract infection³⁰ rather than septicaemia or meningitis. Further, it would be most unusual that infants in the HR group, with comparable gestational age and clinical characteristics, were not equally affected. In our opinion, the likeliest scenario is that the HR programme prevented a significant number of life threatening late onset infections and reduced the number of repeated infections in VLBW infants. This would reduce the opportunity for preterm infants to be exposed to high concentration oxygen and the barotrauma of mechanical ventilation during acute resuscitation and immediately after infection. In addition to prematurity, infection has been postulated to be an important factor predisposing to BPD.^{31 32}

There are limitations to this study. Ideally, a randomised, controlled trial should be performed to quantify the outcome of the intervention programme. However, this option was not feasible, as the protocol was introduced into the entire neonatal unit for better protection of staff against blood borne pathogens and also as a measure to reduce endemic systemic infection. Secondly, pneumonia was difficult to define in this age group, as an increase in pulmonary infiltrates on chest radiographs secondary to infection were often indistinguishable from interstitial emphysema and BPD. The small number of "pneumonia-like" episodes (20 and eight cases in the HW and HR periods respectively) were thus not included in the analysis. Thirdly, it is conceivable that inconspicuous new measures or unknown confounding factors may have been inadvertently introduced during the study period and accounted for the improvement in infection rate. This is unlikely as there were no changes in admission criteria and antibiotic policies or introduction of other new infection control measures during the study period. Fourthly, it is not

possible to identify whether alcohol handrubbing alone, glove protection, or the combination of the two procedures resulted in the improvement in infection rate, as the programme was introduced as a single package.

In summary, the HR programme substantially reduced the incidence of late onset systemic infection, MRSA septicaemia, and NEC in VLBW infants. Clinically, fewer preterm infants were infected or had repeated (second or third) infections, and the median age of onset of infection was delayed by eight days. The results also suggest that the protocol produced a sustained improvement in the infection rate. In addition, there is an important association between the HR programme and a reduction in the duration of oxygen supplementation. Whether the use of these measures can effectively decrease the duration of oxygen supplementation or incidence of BPD will require further investigation.

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