be vaccinated. Although no study shows convincing evidence of benefit overall, Smits *et al* demonstrated statistically significant beneficial effects in children under 6 years of age (crude odds ratio of acute respiratory disease 0.52 (95% CI 0.29 to 0.93, $p = 0.018$)).² Thus young children may be more likely to benefit from vaccination.

CLINICAL BOTTOM LINE

- National guidelines continue to recommend influenza vaccination for all children with asthma receiving inhaled corticosteroids. (Grade D)
- On the basis of the published evidence, there are few data to suggest a benefit of influenza vaccination in children with asthma. (Grade B)
- The need for vaccination in children with asthma should be assessed on a case-by-case basis. Younger children may be more likely to benefit from vaccination. (Grade B)

REFERENCES

- 1 Kramarz P, Destefano F, Gargiullo PM, *et al*. Does influenza vaccination prevent asthma exacerbations in children? *J Pediatr* 2001;**138**:306–10.
- 2 Smits AJ, Hak E, Stalman WAB, *et al*. Clinical effectiveness of conventional influenza vaccination in asthmatic children. *Epidemiol Infect* 2002;**128**:205–11.
- 3 Christy C, Aligne CA, Auinger P, *et al*. Effectiveness of influenza vaccine for the prevention of asthma exacerbations. *Arch Dis Child* 2004;**89**:734–5.
- 4 Bueving HJ, Bernsen RMD, de Jongste JC, *et al*. Influenza vaccination in children with asthma. *Am J Respir Crit Care Med* 2004;**169**:488–93.
- 5 Department of Health. 2005. The influenza immunization programme. <http://www.dh.gov.uk/assetroot/04/11/65/17/04116517.pdf> (accessed 3 April 2007).
- 6 Chung EK, Casey R, Pinto-Martin JA, *et al*. Routine and influenza vaccination rates in children with asthma. *Ann Allergy Asthma Immunol* 1998;**80**:318–22.
- 7 Rickert D, Santoli J, Shefer A, *et al*. Influenza vaccination of high-risk children: what the providers say. *Am J Prev Med* 2006;**30**:111–18.

Safety of anti-infective agents for skin preparation in premature infants

Report by

S Upadhyayula, Rotherham General Hospital, Rotherham, UK; doctorshankar2000@hotmail.com
M Kambalapalli, C J Harrison, Rotherham General Hospital, Rotherham, UK
doi: 10.1136/adc.2007.117002

A baby sustained extensive skin burns after the use of a skin preparation (alcoholic chlorhexidine). Following this event the hospital started using an aqueous preparation of chlorhexidine 0.05%. Was this the right choice and what is the evidence for the use of this or any other skin preparation in preterm infants?

Structured clinical question

In preterm infants of <28 weeks' gestation [patient] what is the choice of skin preparation prior to invasive procedures on the unit [intervention] in terms of safety or least complications and prevention of infection [outcome]?

Search strategy and outcome

Primary source: Medline (1956–2005), MeSH terms were used. An advance search was carried out and close matches from mapping were chosen and another search was carried out using

explode and major subheadings. Secondary sources: Cochrane and EMBASE.

Search terms: Premature and anti-infective agents and invasive procedures and safety and complications.

Search outcome: Only four hits matched all our search criteria. We further searched for trials that looked at the safety and efficacy of different antimicrobials with out restricting the age group. We found two hits that specifically answered our question.^{1 2} See table 2.

Commentary

Care of the preterm infant in neonatal units is challenging and involves a lot of support. Placement of central lines is an important aid in delivering this care and it is a common practice to use an alcohol based skin preparation (0.5% chlorhexidine in 70% methanol) prior to this procedure. However, this preparation has the potential to cause skin burns.⁷

Burns in this population of infants may be associated with increased mortality and morbidity. There is also the possible impact of burns (pain and stress) on neuronal migration and hence long-term outlook.⁴

Evidence for the use of an appropriate agent in this population of infants in sparse; this is understandable because of the ethical issues related to carrying out research in these patients. A considerable proportion of the evidence that we found was in the form of case reports.³

A clinical study comparing skin antisepsis and the safety of different skin preparations¹ in adults showed that aqueous chlorhexidine, chlorhexidine in isopropyl alcohol or isopropyl alcohol alone had good immediate antimicrobial activity but that chlorhexidine in alcohol had more persistent activity; all had an excellent safety profile. Unfortunately, we cannot apply adult data to our population as has been highlighted by cases such as ours.

A review article examined analyses comparing the activity and safety of current antiseptics.² Six randomised, controlled, single blind, parallel group clinical trials were assessed to determine the best preoperative skin preparation. The agents examined included chlorhexidine with isopropyl alcohol (chlorhexidine gluconate with 70% isopropyl alcohol, or another combination of the two) 2% chlorhexidine alone, 4% chlorhexidine alone, 70% isopropyl alcohol alone and 10% povidone iodine alone. An antiseptic containing a combination of two antiseptics with different mechanisms of action consistently and significantly demonstrated better antimicrobial activity than a single antiseptic alone. It was also demonstrated that chlorhexidine or povidone iodine alone did not in some studies qualify as a suitable antiseptic agent. Again, all of these trials were on adults and no side effects were noted.

One paper looked at an alternative agent, octenidine, and reported it to be safe.⁵ However, this study examined a small population of infants (24) and on further enquiry we found that the preparation contained arachis oil and hence is not a viable alternative in the UK.

The EPIC project updating the national evidence based guidelines for preventing health care-associated infections in NHS hospitals in England reported that both alcoholic and aqueous preparations of chlorhexidine provide concentrations of chlorhexidine that are higher than the minimal inhibitory concentration for most nosocomial bacteria and yeasts. Both 0.5% and 1% alcoholic solutions and 0.5% and 2% aqueous solutions were examined.⁸ However, there is no mention of its safety in preterm infants.

We also contacted the manufacturer (Seton Health Care Group, Oldham, UK) seeking more information but did not learn anything new. It was evident to us from our search that

Table 2 Details of articles found

Citation	Study group	Study type	Outcome	Key results	Comments
Watkins and Keogh (1992) ³	Case reports of 2 patients who sustained skin burns following the use of alcoholic skin preparation	Case report	None specified	Chemical burns from skin preparation	Extremely low birth weight infants have high skin permeability Major burns are possible after brief exposure to solution Care is needed in the selection of such solutions Great care must be taken to avoid pooling of the cleanser under the infant Saline must be used for cleaning the immature skin
Reynolds <i>et al</i> (2005) ⁴	Case reports of 2 patients who sustained extensive abdominal burns following the use of 0.5% chlorhexidine in 70% methanol	Images in neonatal medicine	None specified	Morbidity from skin burns	The solution does not cause skin damage in the extreme preterm infant Although absorbed by the skin it is extensively metabolised The overall rate of catheter related bacteraemia was low at 0.25%
Buhrer <i>et al</i> (2002) ⁵	24 preterm babies had 2% phenoxylethanol and 0.1% octenidine as antiseptic for skin preparation	Prospective trial	Transient erythematous skin reaction was noted in the 23 week babies	One infant had culture proven sepsis Urinary concentration of 2-phenoxylethanol was 12-fold versus the original compound in boys	Chlorhexidine based preparations are better than iodine based preparations for decreasing catheter colonisation
Garland <i>et al</i> (1995) ⁶	826 infants were exposed to 10% povidone iodine and 0.5% chlorhexidine sequentially over a 6 month period	Prospective non-randomised trial	Chlorhexidine based preparations are better than iodine based preparations for decreasing catheter colonisation	Incidence of catheter colonisation with chlorhexidine was 4.7% (20/418, $p=0.01$) Incidence with povidone iodine was 9.3% (38/408)	Chlorhexidine based preparation are better than iodine based ones
Hibbard <i>et al</i> (2002) ¹	106 subjects were treated with one or two of three antiseptics (chlorhexidine gluconate plus isopropyl alcohol, 70% isopropyl alcohol, 2% chlorhexidine)	Randomised parallel group open labelled clinical trial	Chlorhexidine gluconate in isopropyl alcohol has better persistent antimicrobial activity than isopropyl alcohol or aqueous chlorhexidine alone	Chlorhexidine gluconate plus isopropyl alcohol provided significantly more persistent antimicrobial activity on abdominal sites than isopropyl alcohol ($p=0.03$) or chlorhexidine gluconate ($p=0.028$) at 24 h	All three antiseptics significantly reduced abdominal and inguinal microbial counts from baseline at 10 min, 6 h and 24 h Chlorhexidine plus alcohol provided more persistent antimicrobial activity

the currently used agents have the potential to cause considerable harm to infants. However, no safer alternative is supported by evidence and this reinforces the need to examine this issue more closely. Research must be carried out to find a safe and effective agent if we are to not make things more difficult for an already challenged population.

CLINICAL BOTTOM LINE

- Extremely preterm infants are at risk of burns from the use of alcoholic skin preparations, but no comparative data are available to suggest the best preparation for this group of patients. (Grade C)
- Making sure there is no pooling seems to be the most effective method of avoiding problems related to skin burns in infants. (Grade C)
- Alcohol based preparations have good antibacterial activity in adults and have an excellent safety profile. (Grade C)

REFERENCES

- Hibbard JS, Mulberry KG, Brady AR. A clinical study comparing the skin antiseptics and safety of chloraprep, 70% isopropyl alcohol, and 2% aqueous chlorhexidine. *J Infus Nurs* 2002;4:244–9.
- Hibbard JS. Analyses comparing the antimicrobial activity and safety of current antiseptic agents: a review. *J Infus Nurs* 2005;28:194–207.
- Watkins AM, Keogh EJ. Alcohol burns in the neonate. *J Paediatr Child Health* 1992;28(4):306–8.
- Reynolds PR, Banerjee S, Meek JH. Alcohol burns in the extremely low birth weight infants: still occurring. *Arch Dis Child Fetal Neonatal Ed* 2005;90:F10.
- Buhrer C, Bahr S, Siebert J, *et al*. Use of 2% 2-phenoxylethanol and 0.1% octenidine as antiseptic in premature infants of 23–26 weeks gestation. *J Hosp Infect* 2002;51:305–7.
- Garland JS, Buck RK, Maloney P, *et al*. Comparison of 10% povidone-iodine and 0.5% chlorhexidine gluconate for the prevention of peripheral intravenous catheter colonisation in neonates: a prospective trial. *Pediatr Infect Dis J* 1995;14(6):510–6.

Langer S, Sedigh Salakdeh M, Goertz O, *et al*. The impact of topical antiseptics on skin microcirculation. *Eur J Med Res* 2004;9:449–54.

Pellowe CM, Pratt RJ, Loveday HP. The EPIC project. Updating the evidence-base for national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England: a report with recommendations. *Br J Infect Control* 2004;5:10–16.

Should creatine kinase be checked in all boys presenting with speech delay?

Report by

Claire T Lundy, Department of Paediatric Neurology, Paul Ward, Royal Belfast Hospital for Sick Children, 180 Falls Road, Belfast BT12 6BE, UK;

clairelundy@btopenworld.com

Gary M Doherty, Elaine M Hicks, Royal Belfast Hospital for Sick Children, Belfast, UK

doi: 10.1136/adc.2007.117028

Jack is a 2.5 year old boy. He has been referred for developmental assessment by his health visitor. His community paediatrician diagnoses speech and language delay. His mother reports he first sat independently at 9 months and walked at 17 months.

Structured clinical question

In a male child with speech delay who walks prior to 18 months old [patient], does requesting serum creatine kinase