JOGNN

CONTEMPORARY PERSPECTIVES

# Avoiding Chlorhexidine Burns in Preterm Infants

Mariano Paternoster, Massimo Niola, and Vincenzo Graziano

**Correspondence**
Mariano Paternoster, PhD, Department of Advanced Biomedical Sciences, School of Medicine, University of Naples Federico II, Via Pansini 5, Edificio 20, 1° piano, Naples 80131, Italy.
mariano.paternoster@unina.it

**Keywords**
chemical burns
chlorhexidine
malpractice claims
preterm infants

**ABSTRACT**

Chlorhexidine is a skin antiseptic agent frequently used for off-label indications in NICUs. Changes to the safety labeling of chlorhexidine products for use in preterm infants were recently made because of the risk of severe chemical burns. We provide tips for a safer use of chlorhexidine to prevent injury in newborns and to help health care professionals protect themselves against burn injury claims.

*JOGNN, 46, 267–271; 2017.* http://dx.doi.org/10.1016/j.jogn.2016.10.007

Accepted October 1 2016

Mariano Paternoster, PhD, is an assistant professor in the Department of Advanced Biomedical Sciences, School of Medicine, University of Naples Federico II, Naples, Italy.

Massimo Niola, PhD, is an associate professor in the Department of Advanced Biomedical Sciences, School of Medicine, University of Naples Federico II, Naples, Italy.

Vincenzo Graziano, PhD, is an assistant professor in the Department of Advanced Biomedical Sciences, School of Medicine, University of Naples Federico II, Naples, Italy.

The authors report no conflict of interest or relevant financial relationships.

Chlorhexidine is a local antiseptic that has an important role in the prevention of catheter-associated bloodstream infections (Marschall et al., 2014). Its application to a newborn's umbilical cord reduces all-cause neonatal mortality (Imdad et al., 2013). However, as of today, there are insufficient safety data to recommend the use of chlorhexidine in infants less than 2 months of age (Chapman, Aucott, & Milstone, 2011; O'Grady et al., 2011). Accordingly, less effective alternative agents, such as povidone–iodine or alcohol, are used instead (Garland et al., 2001).

Over the years, several researchers reported severe chemical burns associated with the use of alcohol-based or water-based chlorhexidine solutions for skin antisepsis before invasive procedures in neonates (Andersen, Hart, Vemgal, & Harrison, 2005; Espuny et al., 2010; Kutsch, & Ottinger, 2014; Lashkari, Chow, & Godambe, 2012; Mannan, Chow, Lissauer, & Godambe, 2007; Reynolds, 2005; Sivathasan, Sivathasan, & Vijayarajan, 2010; Upadhyayula, Kambalapalli, & Harrison, 2007). Such events raise serious concerns, especially when considering that chemical burns in infants who weigh less than 1,500 g can be life threatening (Tamma, Aucott, & Milstone, 2010).

Despite being contraindicated in this age group, chlorhexidine is frequently used for off-label indications in NICUs for infants younger than 2 months of age (Bryant, Zerr, Huskins, & Milstone, 2010; Tamma et al., 2010) without causing major adverse effects if used safely (Curry, Honeycutt, Goins, & Gilliam, 2009; Taylor et al., 2011). *Off-label* means the use of a medication in a different manner from that specified in the drug regulatory agency–approved packaging label or insert (Stafford, 2008). Off-label use arises through many pathways but in NICUs usually entails the use of drugs for the unapproved subpopulations of the tiniest newborns.

In recent years, major American and European health associations and agencies, although recognizing the effectiveness of chlorhexidine for the prevention of infection in premature newborns, have provided a number of reports on its potential risks and safe use. For example, in 2011, the American Pediatric Surgical Association Outcomes and Clinical Trials Committee reported that the use of alcohol-based chlorhexidine as a cutaneous antiseptic decreased the risk of catheter colonization and/or catheter-related bloodstream infections compared with 10% povidone–iodine (Huang et al., 2011). However, recommendations were made to use it with care in neonates and premature infants because it could increase the risk of skin irritation for systemic absorption (Huang et al., 2011). In May 2012, the U.S. Food and Drug Administration Center for Drug Evaluation and Research

**Changes to the safety labeling of chlorhexidine products were recently made in the United States and Europe because of the risk of chemical burns in preterm infants.**

followed suit and approved changes to the safety labeling of chlorhexidine-based topical antiseptic products. The new label reiterated once again instructions to use the antiseptic with care in premature newborns or infants younger than 2 months of age because of an increased risk of irritation or chemical burns (U.S. Food and Drug Administration, 2012).

Likewise, in June 2014, the UK Medicines and Healthcare Products Regulatory Agency urged British physicians to use chlorhexidine solution with maximum care after severe adverse effects occurred in 28 infants born at less than 32 weeks gestation who were treated with the solution within the first few days of life (Siddique, 2014). In particular, in the Drug Safety Update, issued by the same agency, health care providers were urged to administer the chemical with extreme caution, and the following safety measures were recommended: (a) to apply only the minimum amount of chlorhexidine solution required without allowing it to accumulate, (b) to remove any excess solution and any soaked materials, drapes, or gowns from the skin, and (c) to monitor patients frequently to detect and manage cutaneous adverse effects at an early stage (UK Medicines and Healthcare Products Regulatory Agency, 2014b).

Later that year, European health officials revisited the safety issue. Indeed, in September 2014, the European Medicines Agency Pharmacovigilance Risk Assessment Committee approved changes to the safety labeling of chlorhexidine products for use in infants and issued the following statements: "Use with care in newborn babies, especially those born prematurely," "Use with care in neonates, especially those born before 32 weeks of gestation and within the first 2 weeks of life," and "May cause chemical skin burns" (pp. 5–6). The European Medicines Agency Pharmacovigilance Risk Assessment Committee also recommended that all relevant hospital physicians, nursing staff, and pharmacists responsible for neonatal/pediatric intensive care units be officially informed about the increased risks of skin-related adverse events. In short, the agency reported that the risk of severe chemical injuries after exposure to alcohol-based or water-based chlorhexidine solutions was higher in preterm infants, especially those born before 32 weeks gestation and within the first 2 weeks of life. Therefore, it cautioned providers to administer the minimum amount of chlorhexidine solution required to avoid accumulation in skin folds or underneath an infant's body. Furthermore, the agency recommended the removal of any soaked materials, drapes, or gowns from the skin. Finally, it pointed out the importance of closely monitoring patients to detect and manage cutaneous adverse effects at an early stage.

In November 2014, a new edition of the Drug Safety Update was issued by the UK Medicines and Healthcare Products Regulatory Agency (2014a) with further instructions on how to manage the potentially excessive quantities of chlorhexidine in multidose containers.

Successively, Beresford (2015) published in the *Journal of Neonatal Nursing* the data of the European review. In this article, he reported all the data pored over by the European review, including yellow card data on chlorhexidine adverse reactions, published literature, and cumulative reviews from companies with authorized medicinal chlorhexidine solutions.

Overall, 44 cases of chemical burns after the application of chlorhexidine solutions were identified. Most occurred in extremely premature infants born at 26 or fewer weeks gestation or in infants who weighed less than 1,000 g at birth. Twenty-nine cases occurred after exposure to alcohol-based chlorhexidine solutions (0.5% and 2% chlorhexidine gluconate in 70% alcohol), whereas 11 cases occurred after exposure to 2% aqueous solutions. In five cases, the chemical injury resolved but with severe sequelae, including scaring, discoloration, and keloid formation. Death was reported in five cases. Four of these deaths were judged to be attributable to comorbidities associated with preterm birth. However, severe chemical injuries were also considered as a possible contributory cause, as suggested by the severe skin burns found on the back of one of these infants. In summary, the author identified the common use of chlorhexidine in NICUs for off-label indications while highlighting that different hospitals were recommending the use of a variety of different strengths and types of solutions despite not having clear guidelines or data on their safety.

## Nursing Implications

The health cautionary reports issued by health care agencies will undoubtedly promote a growing awareness of the risks of chlorhexidine-related burns. Although current data are scarce,