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REGULAR ARTICLE

Using isopropyl alcohol impregnated disinfection caps in the neonatal intensive care unit can cause isopropyl alcohol toxicity

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ABSTRACT

Aim: The safety of SwabCap alcohol impregnated disinfection caps was questioned in our unit because of malfunctions in luer access valves. We examined whether SwabCaps affected the integrity of two luer access valves and were associated with alcohol injected into the lines.

Methods: Our bench test study included seven circuits using SmartSite or CARESITE valves exposed to two environmental temperatures. Passive circuits consisted of a 96-hour contact system using SwabCap without other interventions. Active circuits consisted of nine sham injections during a 24-hour period, with the SwabCap replaced after each injection. The active control circuit used isopropyl alcohol impregnated pads to disinfect valves. Isopropyl alcohol was measured at the extremity of all active circuits by gas chromatography

Results: The visual appearance of all SmartSite valves and 67% of the CARESITE valves was changed by SwabCap use. The mean isopropyl alcohol dosages were 52 mmol/L in the SmartSite and 8 mmol/L in the CARESITE at room temperature and 73 and 7 mmol/L, respectively, at 35°C. No alcohol was found in the control circuit.

Conclusion: The SwabCap altered the valves' appearance and allowed significant amounts of isopropyl alcohol to be injected. It should not be used for neonates without further research.

INTRODUCTION

Alcohol impregnated disinfection caps are intended to prevent microbial contamination of luer access valves. An *in vitro* study with these caps showed that there were significantly less micro-organisms on the valves than without disinfection or with pledget disinfection (1). In clinical studies in neonates, children and adults, isopropyl alcohol impregnated disinfection caps significantly reduced central line contamination, the density of organisms present on the valves and central line associated bloodstream infections (2–4). When we used the SwabCap (Excelsior Medical, Neptune, NJ, USA), a 70% isopropyl alcohol impregnated disinfection cap, in our institution for a month, five luer access valves malfunctioned in three patients. This made us question the safety of SwabCap for our vulnerable population. Isopropyl alcohol is a solvent used in industry and in medicine as a disinfectant and an antiseptic. It is not intended for intravenous injection. It remained unclear whether using the SwabCap could lead to intravenous injections of isopropyl alcohol. The first objective of the study was to evaluate, *in vitro*, whether contact with the SwabCap affected the luer access valve's appearance and, or, function. The second objective was to ascertain whether

Abbreviations
mL, Millilitre; NICU, Neonatal intensive care unit.

Key notes

- The safety of alcohol impregnated disinfection caps was questioned in our unit because of malfunctions in luer access valves.
- This bench test showed that isopropyl alcohol impregnated disinfection caps changed the appearance of two types of luer access valves and led to the injection of significant isopropyl alcohol amounts into the lines connected to these valves.
- Isopropyl alcohol impregnated disinfection caps should not be used in neonates without further research.

isopropyl alcohol could be injected intravenously with the drug after the SwabCap was removed.

METHOD

Study design and setting

This bench test study was held in June 2013 at CHU Sainte-Justine, Montreal, Canada, a level three paediatric centre. Seven different circuits were developed using two different luer access valves and exposed to two different environmental temperatures. Each circuit was repeated three times. To determine whether the SwabCap changed the appearance (colour, cracks or leaks) and, or, the function of the luer access valve, we built a prolonged duration passive use circuit (Fig. 1). The SwabCap stayed in contact with the luer access valve for 96 hours, which is interval recommended by the Centers for Disease Control and Prevention to replace tubing. Observational data were regularly recorded for each circuit during this time. To determine whether the SwabCap was associated with the intravenous injection of isopropyl alcohol, an active circuit (Fig. 2) was developed. Nine sham drugs injections were performed hourly and 24 hours after the beginning of the study, through the luer access valve after removal of the SwabCap. After each injection, a new SwabCap was replaced on the luer access valve, as it is designed for single use. Each sham drug injection consisted of an initial 0.5 millilitre (mL) of 0.9% sodium chloride acting as the rinsing agent then a 0.3 mL of 0.9% sodium chloride acting as the sham drug, ending with 0.5 mL of 0.9% sodium chloride to complete rinsing. This design corresponds to the clinical reality of intravenous central line drug injections in the neonatal intensive care unit (NICU). All injected fluids were collected using a needle in a glass vial closed by a latex cap to avoid alcohol evaporation (Fig. 2). Observational data included visual inspection of the colour and for the presence of cracks or leaks and the presence of fluid in the luer access valves or the tubing. Functional data included testing for resistance during injections, the presence of complete obstruction and the luer access valves' return to their initial state after injections. Standard care in our institution during the study period consisted of disinfecting the luer access valve before injections using friction

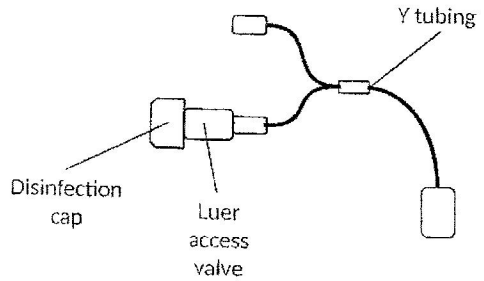

Figure 1 Diagram of passive circuit.

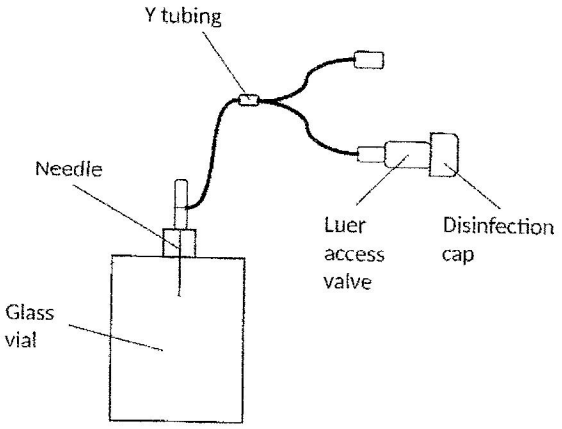

Figure 2 Diagram of active circuit.

with an isopropyl alcohol pad for 15 seconds followed by a drying time of 15 seconds. This method was used as the control circuit.

Equipment and environment

This study tested two luer access valves. The first was the SmartSite valve (Alaris CareFusion, San Diego, CA, USA), which was in use in our institution when the first SwabCap related incidents became apparent. The second was the CARESITE valve (B Braun, Melsungen, Germany), which was in use in our institution during the study period as a result of a change in intravenous pumps. To mimic the true clinical conditions in the NICU, active circuits were tested at room temperature in a standard NICU room and in an incubator set at 35°C, the typical temperature necessary for a very low birthweight preterm baby.

Isopropyl alcohol dosage

Isopropyl alcohol quantification was blindly carried out in the specialised biochemistry laboratory in our institution. The levels of isopropyl alcohol were measured by gas chromatography equipped with a flame ionisation detector by diluting the samples with an aqueous solution containing internal standard. Additional information on the isopropyl alcohol dosage used provided on request.

Isopropyl alcohol critical threshold

Toxic plasmatic isopropyl alcohol concentrations are unknown for neonates and especially for the preterm infant. Based on paediatric studies (5), we speculated that the toxic threshold for neonates would be at 25 mg/dL. Extrapolating from data on ethylic alcohol, we determined that the critical plasmatic concentration was 1% of the toxic threshold. Taking into account that the most vulnerable neonatology patient can weigh as little as 500 g, and using a volume of distribution of isopropyl alcohol of 0.9 L/kg given the high water composition of preterm neonates, the isopropyl alcohol critical concentration in the vial glass of

the active circuits was estimated to be 14 mmol/L, based on a single injection in the circuit.

RESULTS

The appearance of the valves was modified in all the SmartSite valves tested and in 67% of the CARESITE valves. Discoloration and inflation of the valve's fanfold piece occurred for all SmartSite valves. Loss of transparency was noted in 89% of SmartSite valves. The possible presence of fluid inside the valve was seen in 67% of SmartSite valves. Figures 3 and 4 provide examples of how the appearance of the SmartSite valves changed during the bench test. The changes in the CARESITE valves included loss of transparency and the possible presence of fluid in the valves. No luer access valve malfunctioned. Mean isopropyl alcohol dosages for each sample of each active circuit are presented in Table 1. These show that the mean isopropyl alcohol dosages were 52 mmol/L in the SmartSite and 8 mmol/L in the CARESITE at room temperature and 73 mmol/L in the SmartSite and 7 mmol/L in the CARESITE at 35°C. No alcohol was found in the control circuit.

DISCUSSION

This bench test found that there were significant appearance changes in the luer access valves, particularly the SmartSite valves, when they were connected to the SwabCap. In all the samples, isopropyl alcohol passed from the SwabCap to the vial through the luer access valve and isopropyl alcohol concentrations exceeded the critical estimated limits for a preterm baby weighing 500 g. The isopropyl alcohol concentrations of the SmartSite valves that were visibly modified by the SwabCap, were higher than with the CARESITE valves. No measurable isopropyl alcohol was found in the circuits of the valves disinfected with isopropyl alcohol pads.

It is very worrying to find large quantities of isopropyl alcohol in the line that is usually connected to the patient to give him or her common drugs in neonatology. How isopropyl alcohol passed from the SwabCap into the line is unknown. Maybe some alcohol stayed on the surface of the luer access valve when the SwabCap was removed, resulting in alcohol being injected into the line with the sham drug. It is also possible that isopropyl alcohol slowly invaded the luer access valve when the SwabCap was connected, so that the luer access valve lost its seal, leading to the passage of alcohol. The presence of alcohol in the valve could interact with the injected drugs, potentially resulting in inactivation or precipitation of the medication. Isopropyl alcohol levels reached in the bench test could lead to intravenous isopropyl alcohol intoxication in a neonate. Clinical symptoms of such intoxication can include neurologic signs such as drunkenness, headache, dysarthria, nystagmus, ataxia (5), central nervous system depression up to coma and respiratory depression. Digestive manifestation can also occur, such as abdominal pain, nausea, vomiting (5) and haemorrhagic gastritis (6). Severe intoxication can present as hypotension, pseudo-renal failure (7), hepatic dysfunction, haemolytic anaemia (8) and haemorrhagic tracheobronchitis.

Figure 3 Photograph of a sample of scenario three at the end of the 24-hour period showing discoloration and inflation of the fanfold part of SmartSite valve connected to the SwabCap (on the right) compared to control SmartSite valve (on the left).

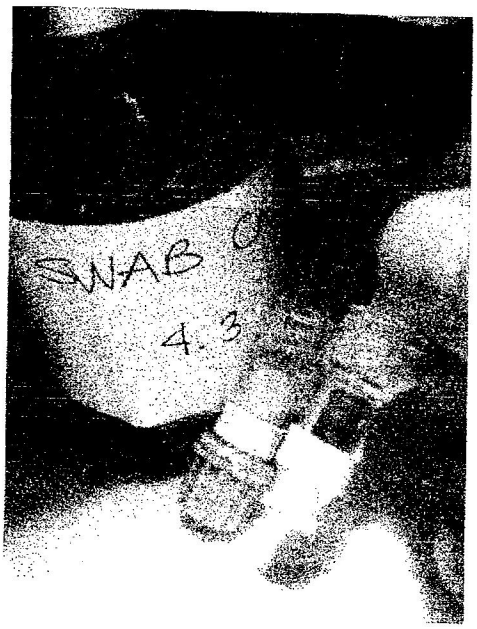

Figure 4 Photograph of a sample of scenario four eight hours after the beginning of the bench test showing total loss of transparency of the SmartSite valve connected to the SwabCap (on the left) compared to a control SmartSite valve (on the right).

Table 1 Results of isopropyl alcohol dosage by gas chromatography for each circuit. Theoretical isopropyl alcohol critical concentration was calculated to be 14 mmol/L for a 500 g neonate

Circuit type	Temperature	Isopropyl alcohol dosage in collected fluids (mmol/L)			
		Sample 1	Sample 2	Sample 3	Mean
SwabCap on SmartSite valve	Room temperature	49.49	58.43	46.76	51.56
	Incubator 35°C	45.16	94.73	77.93	72.61
SwabCap on CARESITE valve	Room temperature	14.10	5.72	5.21	8.34
	Incubator 35°C	6.99	8.13	5.94	7.02
Isopropyl alcohol pad on CARESITE valve (Control)	Room temperature	0.00	0.00	0.00	0.00

The usual isopropyl alcohol intoxication routes in adults are voluntary (9) or accidental ingestion. Reported cases of isopropyl alcohol intoxication in neonates and infants are rare and of different aetiologies. A full-term boy with gastroschisis died after accidental exposition to isopropyl alcohol inhalation caused by the humidifier of his ventilator (10). A boy of 21 days went into a hypotonic coma because his mother applied isopropyl alcohol pads to his umbilicus at each diaper change (11). A two-year-old boy who received an isopropyl alcohol bath to treat fever presented with haemorrhagic gastritis (6). Transcutaneous absorption is possibly the primary cause of systemic toxicity in infants because of the increased dermal absorption and larger surface area. Transplacental isopropyl alcohol intoxication occurred in a neonate whose mother had taken polysubstances days before birth (12). The baby suffered from hypotension, hypotonia and seizures. Isopropyl alcohol and acetone were found in his blood. These neurological and digestive symptoms can be wrongly interpreted as prematurity-related complications and not as signs of isopropyl alcohol intoxication. All the possible effects of intravenous isopropyl alcohol injection are unknown, in particular the effect on neurologic development of a preterm baby. Isopropyl alcohol toxicity is enhanced by the *in vivo* metabolism that produces acetone, which has a half-life of 10–30 hours in adults. Repeated injections may involve accumulations of acetone, which could not be measured in our *ex vivo* model. Estimated isopropyl alcohol critical concentrations were carried out using the pharmacokinetics of a single injection. In clinical practice, intravenous injections are repeated and isopropyl alcohol is slowly metabolised in premature babies. This could result in accumulations of isopropyl alcohol *in vivo* that would reach higher plasmatic concentrations than the ones assessed in this bench test study.

Even though the isopropyl alcohol quantities found in the line were different between the two types of luer access valves tested, the presence of alcohol is, in itself, of concern. The type of valve used did not seem to be the problem. The SwabCap could be as efficient, but safer, if it contained less isopropyl alcohol. Also, allowing a drying time after removal of the SwabCap and before drug injection could decrease the amount of alcohol injected in the line. This study has some limitations. A bench test study is not an *in vivo* study. No tests were carried out to measure the isopropyl alcohol doses in the urine or the blood of NICU patients exposed to the SwabCap, as it was immediately removed from the unit when the issues related to the luer access valves were observed.

CONCLUSION

Although the use of isopropyl alcohol impregnated disinfection caps has proved to be beneficial in reducing central line associated bloodstream infections rates in the literature, the presence of significant amounts of isopropyl alcohol in the line when the SwabCap was used, in this study, seems unsafe for term and preterm neonates. More research should be carried out on alcohol impregnated disinfection caps in neonates. Disinfecting luer access valves with isopropyl alcohol pads remains safe, as no detectable isopropyl alcohol was found at the end of the line with this method.

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