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Highlights

- There is a lack of trial evidence directly comparing 2% chlorhexidine gluconate (CHG) in alcohol with other CHG solutions for the prevention of central venous catheter-related infections in hemodialysis patients.
- Although not statistically significant, there is a possible benefit from 2% chlorhexidine gluconate (CHG) in alcohol compared with routinely used CHG solutions.
- Findings add to the evidence base and can be used in future meta-analyses of similar studies.

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Brief report

Is 2% chlorhexidine gluconate in 70% isopropyl alcohol more effective at preventing central venous catheter-related infections than routinely used chlorhexidine gluconate solutions: A pilot multicenter randomized trial (ISRCTN2657745)?

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Key Words:

Hemodialysis
central venous catheters
chlorhexidine gluconate
skin cleansing
infection prevention
clinical trial

A pilot randomized trial in 3 Irish outpatient hemodialysis units compared 2% chlorhexidine gluconate (CHG) in 70% isopropyl alcohol with routinely used CHG solutions for central venous catheter exit site antiseptics. We found no significant difference between the groups for the prevention of catheter-related bloodstream infections (1/53 vs 2/52; relative risk [RR], 0.49; 95% confidence interval [CI], 0.05-5.25; $P = .55$) and catheter-associated bloodstream infections (1/53 vs 4/52; RR, 0.25; 95% CI, 0.03-2.12; $P = .16$).

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Central venous catheter (CVC)-related infections impact negatively on hemodialysis patients' quality of life.^{1,2} Effective preventive strategies include chlorhexidine gluconate (CHG) containing antiseptic solutions that minimize contamination of the CVC exit site and catheter hubs. There is a lack of trial evidence directly comparing 2% CHG in alcohol with other CHG solutions.³

To our knowledge, this is the first trial to evaluate 2% CHG in 70% isopropyl alcohol solution versus routine CHG solution for reducing CVC-related infections in hemodialysis patients.

METHODS

This pragmatic pilot randomized open-label trial took place at 3 outpatient hemodialysis units in Ireland from October 2010-October 2012. Patients were eligible if they were aged >18 years and on long-term hemodialysis using a permanent tunneled cuffed CVC inserted at least 4 weeks before trial entry. Exclusion criteria

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Funding/Support: Supported by CareFusion and PDI Healthcare.

Conflicts of Interest: None to report.

included unable to give informed consent, CVC used for purposes other than access for hemodialysis, known allergy to the interventions, CVC material not compatible with the interventions, using CVCs or dressings that were not standard practice for the unit, and patients unable to adhere to the trial protocol. A telephone randomization service used computer-generated stratified allocation sequences to allocate intervention and comparator solutions. Approval was granted by the Irish Medicine Board (CT 900/493/1) and the Institute Research Ethics Committee (REC 2010/27/03).

Trial interventions included ChlorPrep with Tint (CareFusion, San Diego, CA) for exit site cleansing and Sani-Cloth CHG 2% medical device wipes (PDI Healthcare, New York, NY) for catheter hub cleansing. Comparator participants received the routine CHG antiseptic agent for their dialysis facility: 0.5% CHG in 70% alcohol (Hydrex Pink, ECOLAB, Swindon, UK) or 0.05% aqueous CHG (Sterets [Unisept solution]; Medlock Medical, Oldham, UK). The frequency of the CVC dressing change was patient dependent.

The primary outcomes were CVC-related infection encompassing catheter-related bloodstream infection (CRBSI),⁴ catheter line-associated bloodstream infection (CLABSI),⁵ and local access infection.⁵ An independent microbiologist confirmed the outcome assessment blind to patient allocation.

Using intention-to-treat analysis, participants were followed-up to trial completion (12 months), primary outcome, or death and

Table 1
Baseline characteristics

Characteristic	2% CHG in alcohol (n = 53)	Comparator (n = 52)	P value*
Female	26 (49.1)	26 (50)	
Mean age ± SD	65.1 ± 14.45	64.9 ± 16.23	0.95 (0.88) [†]
CVC history			
Right jugular CVC	34 (64.2)	45 (86.5)	.01 [‡]
Left jugular CVC	16 (30.2)	6 (11.5)	.02 (0.03)
Right subclavian CVC	2 (3.8)	1 (1.9)	.57
Left subclavian CVC	1 (1.9)	0 (0)	.32
CVC locking solution			
Heparin	11 (20.8)	3 (5.8)	
Trisodium citrate	39 (73.6)	48 (92.3)	.01 (0.02)
Other	3 (5.7)	0 (0)	
Heparin and trisodium citrate	0 (0)	1 (1.9)	

NOTE. Values are n (%) or as otherwise indicated.

CHG, chlorhexidine gluconate; CVC, central venous catheter.

*P value χ^2 test (Fisher exact test).

[†]P value independent 2-sample *t* test (Mann-Whitney U test).

[‡]Same P value for χ^2 and Fisher exact test.

analyzed in accordance with their random allocation. Statistical tests were 2-tailed, with $P < .05$ considered statistically significant. Analyses included frequencies (numbers of participants with an event and percentages) and χ^2 or Fisher exact tests. The 2-sample independent *t* test and Mann-Whitney U test were used to estimate differences in group means.

RESULTS

Of the 201 patients with CVCs, 149 were eligible and 105 gave their consent to enter the trial. After randomization, 53 participants were assigned to the intervention and 52 to the comparator solution for their research site (0.5% CHG in alcohol [n = 42] or 0.05% aqueous CHG [n = 10]). Baseline characteristics are outlined in Table 1.

There were fewer catheter-related infections in the intervention group (n = 5/53, 9%) than in the comparator group (n = 10/52, 19%); this difference was not statistically significant (relative risk [RR], 0.49; 95% confidence interval [CI], 0.18-1.34; $P = .15$). The intervention solution, 2% CHG in alcohol, did not significantly reduce CRBSI (RR, 0.49; 95% CI, 0.05-5.25; $P = .55$), CLABSI (RR, 0.25; 95% CI, 0.03-2.12; $P = .16$), or local access infection (RR, 0.74; 95% CI, 0.17-3.13; $P = .68$) compared with the comparator solution.

In subcomparison analyses, 2% CHG in alcohol did not significantly reduce CRBSI (0/42 vs 2/42; RR, 0.20; 95% CI, 0.01-4.04; $P = .15$), CLABSI (1/42 vs 2/42; RR, 0.50; 95% CI, 0.05-5.31; $P = .56$), or local access infection (3/42 vs 4/42; RR, 0.75; 95% CI, 0.18-3.15; $P = .70$) compared with 0.5% CHG in alcohol. When compared with 0.05% aqueous CHG (n = 10), the differences for CRBSI (1/11 [9%] vs 0/10; RR, 2.75; 95% CI, 0.12-60.7; $P = .33$) and CLABSI (0/11 vs 2/10 [20%]; RR, 0.18; 95% CI, 0.01-3.41; $P = .12$) were not statistically significant.

Four (7%) participants (all treated with 2% CHG in alcohol) experienced a skin sensitivity reaction ($\chi^2_1 = 4.08$, $P = .04$; Fisher exact test: $P = .12$).

DISCUSSION

There was no clear difference between 2% CHG in alcohol and other routine CHG antiseptic solutions used in CVC exit site and catheter hub care in the prevention of CVC-related infections in

hemodialysis patients. Overall, 7% of participants experienced an adverse reaction (skin sensitivity) to the 2% CHG in alcohol solution, and it is possible that participants reacted to the food dye this contains rather than to the CHG.

A limitation of our pilot randomized trial is the relatively small sample size, which was insufficient to detect clinically relevant differences in catheter-related infections between the intervention and comparator solutions. However, this is a large sample for an Irish hemodialysis study, with the at risk population studied being all hemodialysis patients in a catchment area of 1 million people, of whom 50% were recruited. A chance imbalance at randomization caused the comparator group to have a significantly higher use of trisodium citrate CVC lock solution than the intervention group, but a meta-analysis of CVC antimicrobial and nonantibiotic lock solutions showed no significant effect on catheter-related infection in patients using trisodium citrate only.⁶ The pragmatic nature of our study meant that we compared the trial intervention with what was used routinely for outpatients in hemodialysis units in Ireland; therefore, comparator participants were allocated different strengths and volumes of CHG.

CONCLUSIONS

Our trial investigating the effectiveness of 2% CHG in 70% alcohol versus other routinely used CHG solutions in the prevention of CVC-related infections appears to be the first such comparison in hemodialysis patients.

Although not statistically significant, the results suggest a possible benefit from 2% CHG in alcohol compared with routinely used CHG solutions. Although we cannot draw firm conclusions for practice from this pilot trial, our findings add to the evidence base and can be used in future meta-analyses of similar studies.

Acknowledgments

We thank the dialysis units and the patients who took part in this randomized trial. We also thank CareFusion and PDI Healthcare for providing the investigational medicinal products free of charge. We also thank Simon-Noble Clarke (CareFusion) and Ron Tierney (PDI Healthcare) for their help.

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