Annex J: Cochrane review

Skin preparation with alcohol versus alcohol followed by any antiseptic for preventing bacteraemia or contamination of blood for transfusion.

Review information

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What's new

Date	Event	Description

History

Date	Event	Description

Abstract

Background

Blood for transfusion may become contaminated at any point between collection and transfusion and may result in bacteraemia (the presence of bacteria in the blood), severe illness or even death for the blood recipient. Donor arm skin is one potential source of blood contamination, so it is usual to cleanse the skin with an antiseptic before blood donation. One-step and two-step alcohol based antiseptic regimens are both commonly advocated but there is uncertainty as to which is most effective.

Objectives

To assess the effects of cleansing the skin of blood donors with alcohol in a one-step compared with alcohol in a two-step procedure to prevent contamination of collected blood or bacteraemia in the recipient.

Search strategy

We searched the Cochrane Wounds Group Specialised Register (March 10 2009); The Cochrane Central Register of Controlled Trials (CENTRAL) *The Cochrane Library* 2009, Issue 1; Ovid MEDLINE - (1950 to February Week 4 2009); Ovid EMBASE - (1980 to 2009 Week 9); and EBSCO CINAHL - (1982 to February Week 4 2009). We also searched the reference lists of key papers.

Selection criteria

All randomised trials (RCTs) comparing alcohol based donor skin cleansing in a one-step versus a two-step

process that includes alcohol and any other antiseptic for pre-venepuncture skin cleansing were considered. Quasi randomised trials were to have been considered in the absence of RCTs.

Data collection and analysis

Two review authors independently assessed studies for inclusion.

Main results

No studies (RCTs or quasi RCTs) met the inclusion criteria.

Authors' conclusions

We did not identify any eligible studies for inclusion in this review. It is therefore unclear whether a two-step, alcohol followed by antiseptic skin cleansing process prior to blood donation confers any reduction in the risk of blood contamination or bacteraemia in blood recipients, or conversely whether a one-step process increases risk above that associated with a two-step process.

Plain language summary

Alcohol, with or without an antiseptic, for preparing the skin before blood collection, to prevent bacteraemia or contamination of blood for transfusion.

When blood is collected from blood donors for transfusion it may become contaminated during collection, storage or transfusion. Blood contamination can cause bacteraemia (the presence of bacteria in the blood), severe illness or even death in the blood recipient. When blood is being taken from donors, the skin on the arm of the donor is one potential source of contamination, so it is usual to cleanse the arm with an antiseptic first, and both one-step and two-step alcohol based regimens are commonly used, however there is uncertainty about which regimen is the most effective for reducing the microbial load (the number of microscopic bacterial organisms) on the donor arm. We looked for studies that compared the use of alcohol alone versus the use of alcohol followed by another antiseptic to clean the arm before the needle is inserted to draw blood, but we did not find any relevant studies. It is currently unclear whether donor skin cleansing with a one-step alcohol based regimen reduces the risk of blood contamination compared with a two-step alcohol based regimen during blood donation.

Background

Complications associated with the infusion of blood and blood-related products have reduced in recent years, due to considerable advances in detecting transfusion-related viral pathogens, such as human immunodeficiency virus (HIV) and hepatitis C and B virus (HCV and HBV). In contrast, bacteraemia, resulting from bacterial contamination of blood products continues to be an ongoing problem (Sandler 2003; Wagner 2004). Exogenous contamination of donor blood may occur at any point during collection, storage and transfusion (McDonald 2001). One of the sources of contamination is thought to be the donor's skin, as a result of inadequate skin cleansing (de Korte 2006; McDonald 2006).

Description of the condition

Bacteraemia, or the presence of bacteria in the blood, is a potentially fatal condition. It is associated with high rates of morbidity (Hakim 2007; Sligl 2006). Microorganisms may enter the blood stream through almost any organ (for example the lungs following pneumonia), through a surgical site, or via an implanted device such as an intravenous catheter. Prognosis is related to the virulence of the infective organism, severity of the sepsis at diagnosis and the underlying health of the patient (Herchline 1997). Although the aetiology of bacteraemia is often difficult to identify, transfusion-transmitted infection is a rare cause. The incidence of bacterial transmission through donated blood is estimated at between 1 per 100,000 and 1 per 1,000,000 units for packed red blood cells, and between 1 per 900 and 1 per 100,000 units for platelets (Walther-Wenke 2008). Fatalities are associated with 1 in 8,000,000 red cell units and 1 in 50,000 to 500,000 white cell units (Wagner 2004). The reason for higher rates in platelet transfusion is thought to be because frozen platelets are thawed and stored at room temperature before infusion and if they are not used immediately there is an opportunity for any organisms that may be present to multiply before the product is transfused. Further reduction of infection rates depends on ensuring that blood for transfusion is free of contaminants. One way of achieving this is through careful preparation and cleansing of the donor's skin at the collection site.

Description of the intervention

There is no standard method for cleansing the site on the blood donor's skin from which the blood will be taken (generally the cubital fossa, or the inner aspect of the elbow). However, alcohol, followed by an application of povidone iodine has been traditionally used (Shahar 1990; Kiyoyama 2009). Consequently, the interventions of interest for this review are skin cleansing with alcohol (usually 70% isopropyl alcohol) for skin preparation in a one-step process, compared with a two-step process involving alcohol followed by povidone iodine or other antiseptic solution. Antiseptics are antimicrobial substances that are applied to living tissue or skin to reduce the possibility of infection, sepsis or putrefaction. They should generally be distinguished from antibiotics that destroy bacteria within the body, and from disinfectants, which destroy microorganisms found on non-living objects. Alcohol is widely used prior to venepuncture and is available from a number of manufacturers as easy-to-use disinfection wipes. Isopropyl alcohol is a flammable, colourless liquid; also known as 2-propanol (MSDS

2006).

How the intervention might work

Alcohol kills most bacteria and fungi by acting on lipid and protein components of the cell. It is less effective against viruses (Adams 2007). Isopropyl alcohol has some advantages over other products because it requires a shorter contact time to achieve antisepsis. For example some two-step procedures take up to two minutes to perform, which is considered too long for some blood bank services (McDonald 2006). Antiseptics are toxic to living tissues as well as bacterial cells, some antiseptics are true germicides, capable of destroying microbes (bacteriocidal), whilst others are bacteriostatic and only prevent or inhibit their growth (Morgan 1993).

Why it is important to do this review

Although a range of antiseptics has been used to cleanse the skin of the donor arm, a two-step process, including alcohol and iodine is widely used (Shahar 1990; Kiyoyama 2009). The effectiveness of this regimen, and other forms of cleansing has been evaluated in a number of studies by measuring the microbial load on the donor arm (Cid 2003; Follea 1997; Goldman 1997; McDonald 2001; Wong 2004) and any contamination of platelet concentrates de Korte 2006; Lee 2002) however it remains unclear whether isopropyl alcohol alone is as effective as alcohol plus povidone iodine (or any other antiseptic) in preventing the clinical consequences of contaminated blood. This review question was brought to us by the World Health Organisation (WHO) and a scoping search did not identify any existing systematic review which had previously addressed this question.

Objectives

To assess the effects of cleansing the donor arm with alcohol in a one-step regimen compared with a two-step regimen including alcohol followed by any other antiseptic to prevent donor blood contamination or recipient bacteraemia.

Methods

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing a one-step alcohol regimen with any two-step regimen that includes alcohol followed by another antiseptic for pre-venepuncture skin cleansing were considered. Cluster randomised trials and crossover trials were also eligible for inclusion. Quasi randomised trials were to have been considered in the absence of RCTs.

Types of participants

Studies enrolling people of any age and in any setting, having venepuncture and blood collection were eligible, irrespective of whether the venepuncture was for the purpose of blood donation. Studies should also include follow up from the recipients of the donated blood in order to measure outcomes occurring in the recipient.

Types of interventions

Studies which compared one-step donor skin cleansing with alcohol (any concentration or application method) with a two-step method which involved alcohol (any strength or application method) followed by any other antiseptic (any concentration or application method) were eligible.

Types of outcome measures

At least one of the primary outcomes was to have been reported for the study to be considered for inclusion in the review.

Primary outcomes

- Bacteraemia in the blood recipient (the presence of bacteria in the blood stream) as measured by blood culture.
- Blood product contamination (blood products include whole blood, platelets, red blood cells or any other product derived from the blood collection) at any time between collection and transfusion as detected most commonly by blood culture.

Proxy outcome measures, such as skin contamination or skin colonisation, were not considered for several reasons. Namely, any antiseptic will reduce levels of microflora on the skin and swabbing skin for bacteria is really a 'sampling procedure' which is subject to inconsistencies in sampling. In addition, a positive skin culture does not automatically mean that the blood collected for transfusion will be positive for bacteria (in the same way that a positive skin culture before surgery does not mean the person will develop a surgical site infection).

Secondary outcomes

- Death of the blood recipient, attributed to the transfusion.
- Any adverse effects in the blood recipient associated with the transfusion. This may include sepsis (a grouping of signs such as fever, chills, or hypotension), septic shock (severe disturbances of temperature, respiration, heart rate or white blood cell count) or multiple organ dysfunction syndrome (altered organ function in a severely ill patient that requires medical intervention to prevent death).

Search methods for identification of studies

Electronic searches

We searched the following databases:

Cochrane Wounds Group Specialised Register (Searched March 10 2009);
The Cochrane Central Register of Controlled Trials (CENTRAL) –*The Cochrane Library* 2009, Issue 1;
Ovid MEDLINE – 1950 to February Week 4 2009;
Ovid EMBASE – 1980 to 2009 Week 9;
EBSCO CINAHL – 1982 to February Week 4 2009.

The Cochrane Central Register of Controlled Trials (CENTRAL) was searched using the following strategy:

#1 MeSH descriptor Blood Specimen Collection explode all trees
#2 MeSH descriptor Blood Transfusion explode all trees
#3 MeSH descriptor Blood Donors explode all trees
#4 (blood NEXT collection*) or (blood NEXT donor*) or (blood NEXT donation*):ti,ab,kw
#5 (collection NEAR/1 blood) or (donation NEAR/1 blood):ti,ab,kw
#6 ven*puncture NEXT site*:ti,ab,kw
#7 (#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8 MeSH descriptor Antisepsis explode all trees
#9 MeSH descriptor Anti-Infective Agents, Local explode all trees
#10 MeSH descriptor Iodine Compounds explode all trees
#11 MeSH descriptor Povidone-Iodine explode all trees
#12 MeSH descriptor Alcohols explode all trees
#13 MeSH descriptor Disinfectants explode all trees
#14 MeSH descriptor Disinfection explode all trees
#15 skin NEXT preparation:ti,ab,kw
#16 disinfect*:ti,ab,kw
#17 ("alcohol" or "alcohols" or iodine or povidone-iodine or chlorhexidine):ti,ab,kw
#18 (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)
#19 (#7 AND #18)

The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in Appendix 2, Appendix 3 and Appendix 4 respectively. The Ovid MEDLINE search was combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision) (Lefebvre 2008). The Ovid EMBASE and EBSCO CINAHL searches were combined with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2008). There was no restriction on the basis of date or language of publication.

Searching other resources

Reference lists of articles retrieved in full were searched.

Data collection and analysis

Selection of studies

Titles and abstracts identified through the search process were independently reviewed by two review authors. Full reports of all potentially relevant studies were retrieved for further assessment of eligibility based on the inclusion criteria. Differences of opinion were settled by consensus or referral to a third review author. There was no blinding to study authorship when we did these assessments.

Data extraction and management

We had planned to extract the following data, where available (to be extracted by one review author and checked by a second review author):

- details of the trial/study (first author, year of publication, journal, publication status, period);
- setting and country of study;
- source of funding;
- inclusion and exclusion criteria;
- baseline characteristics of participants (age, sex);
- aspects of morbidity of the blood recipients, e.g. predictors of susceptibility to bacteraemia;
- number of participants in each arm of the trial;
- description of intervention (type, duration);
- description of control intervention (type, duration);
- details and duration of follow up;
- primary and secondary outcomes (by group);
- design / methodological quality data as per risk of bias criteria;
- unit of randomisation (where relevant);
- unit of analysis;
- results and primary statistical analysis.

Assessment of risk of bias in included studies

Two review authors were to independently assess study risk of bias using the Cochrane Collaboration tool (Higgins 2008a).This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues (e.g. co-interventions)(see Appendix 1 for details of criteria on which the judgements were to have been based). Blinding and completeness of outcome data would have been assessed for each outcome separately and we had planned to complete a risk of bias table for each eligible study.

We planned to contact investigators of included studies to resolve any ambiguities. We also planned to include data from duplicate publications only once, but to retrieve all publications pertaining to a single study to enable full data extraction and risk of bias quality assessment.

For any eligible study, we planned to present assessment of risk of bias using a 'risk of bias summary figure', which presents the judgments in a cross-tabulation of study by entry. This display of internal validity indicates the weight the reader may give the results of each study.

Measures of treatment effect

For individual trials, effect measures for categorical outcomes (e.g. rates of bacteraemia) would have included relative risk (RR) with its 95% confidence interval (CI). For continuous outcomes, we planned to use the mean difference (MD) or, if the scale of measurement differed across trials, standardized mean difference (SMD), each with its 95% CI. For any meta-analyses (see below), for categorical outcomes the typical estimates of RR with their 95% CI would have been calculated; and for continuous outcomes the weighted mean difference (WMD) or a summary estimate for SMD, each with its 95% CI, would have been calculated.

We planned to analyse data using The Cochrane Collaboration's Review Manager 5 software.

Dealing with missing data

If outcome data had remained missing despite our attempts to obtain complete outcome data from authors, we would have performed an available-case analysis, based on the numbers of patients for whom outcome data were known. If standard deviations were missing, we would have imputed them from other studies or, where possible, computed them from standard errors using the formula $SD = SE \times \sqrt{N}$, where these were available (Higgins 2008b).

Assessment of heterogeneity

Heterogeneity would have been assessed visually and by using the chi-squared statistic with significance being set at $p < 0.10$. In addition, the degree of heterogeneity would have been investigated by calculating the I^2 statistic (Deeks 2008). If evidence of significant heterogeneity had been identified ($I^2 > 50\%$), we would have explored potential causes and a random-effects approach to the analysis would have been used if a meta-analysis had been appropriate.

Assessment of reporting biases

Reporting bias would have been assessed using guidelines in the Cochrane Handbook for Systematic Reviews of Interventions (Sterne 2008).

Data synthesis

Where appropriate, results of comparable trials would have been pooled and the pooled estimate together with its 95% CI would have been reported. We planned to conduct a narrative review of eligible studies if statistical synthesis of data from more than one study was not possible or considered not appropriate.

Subgroup analysis and investigation of heterogeneity

We planned to analyse potential sources of heterogeneity using the following subgroup analysis: concealment of allocation (adequate versus not reported).

Sensitivity analysis

We planned to undertake a sensitivity analysis to explore the effect of excluding studies where concealment of allocation was unclear

Results

Description of studies

We did not find any randomised or quasi-randomised controlled trials that met the inclusion criteria.

Results of the search

Our initial search identified 457 citations of which 19 were considered potentially relevant. Full copies of these papers were obtained and reviewed independently by two review authors, however, none met the inclusion criteria.

Included studies

No studies were included.

Excluded studies

The Table: Characteristics of excluded studies contains reasons for excluding 19 potentially eligible studies. In summary, two citations were for unsystematic literature reviews (Blajchman 2004; Wendel 2002) eight trials did not compare the eligible interventions (Calfee 2002; Choudhuri 1990; Little 1999; Mimoz 1999; Schifman 1993; Sutton 1999; Suwanpimolkul 2008; Trautner 2002). Eight studies were not randomised or quasi randomised controlled trials (Kiyoyama 2009; de Korte 2006; Goldman 1997; Lee 2002; McDonald 2006; Pleasant 1994 Shahar 1990; Wong 2004). One study examined techniques for quantifying bacterial reduction (Follea 1997).

Risk of bias in included studies

No studies were included.

Effects of interventions

We did not identify any eligible randomised or quasi randomised controlled trials, nor were we able to identify any ongoing trials.

Discussion

We have been unable to identify any trials addressing the effectiveness of alcohol alone compared with alcohol followed by any other antiseptic to prevent bacteraemia from transfused blood or blood products. This may be because infusion related bacteraemia is a relatively rare event and very large trials would be needed to investigate the effect of donor-arm cleansing. Sepsis rates for platelet transfusions are around 1:50,000 and for red cell transfusions around 1:500,000 (Sandler 2003). Therefore mounting a trial large enough to detect differences in clinical outcomes, based on products used for arm cleansing, would be prohibitively expensive and lengthy.

Because of this, surrogate measures, such as contamination of stored blood have been used to evaluate antisepsis efficacy. However, again, we found no trials that compared alcohol alone with alcohol followed by any other antiseptic for cleansing the donor skin. A number of studies used the surrogate outcome of post-cleansing skin microbial load at the venepuncture site however we excluded such studies *a priori* on the grounds that this is a surrogate outcome of unproven validity; it is not known how skin contamination relates to blood recipient outcomes. Moreover none of these trials compared a one-step with a two-step cleansing process (de Korte 2006; Follea 1997; Goldman 1997).

Whilst we did identify two studies that compared the effects of the eligible interventions they were otherwise ineligible for important methodological reasons and did not meet our pre-specified study design eligibility criteria. The first compared blood culture contamination following pre-venepuncture cleansing with 70% alcohol for one minute followed by povidone iodine solution for an additional minute with brief swabbing of the skin three to five times with 70% alcohol. Patients who were suspected of having bacteraemia had two blood samples taken; once using the two-step method and once with the standard method. Unfortunately it appeared from the report that the order in which the methods were used was not randomised and samples may have been taken from the same or a closely adjacent site with an unreported time lapse between sampling. Of the 181 cultures tested in each group, eight (4.4%) were positive in the two-step group compared with six (3.3%) in the one-step preparation group (no statistically significant difference) (Shahar 1990). The second study potentially suffers from important selection bias in that the treatment groups were in different settings as well as receiving different modes of skin cleansing and compared blood culture contamination rates between patients in whom blood had been drawn in the emergency department and who received a one-step 70% alcohol cleansing with inpatients who received a two-step 70% alcohol followed by povidone iodine procedure. Although there was a statistically significant difference in positive culture rates in favour of the one step process (189 (6.6%) positive cultures in the one-step group versus 248 (8.9%) in the two step, alcohol plus iodine group ($p = 0.0015$) (Kiyoyama 2009) this study was not eligible for inclusion in the review due to the inherent risk of selection bias (inpatients and emergency department patients may well be at different levels of risk of positive blood culture). Thus whilst the authors presented additional data to suggest that baseline positive blood culture rates were similar between inpatients and emergency department patients the risk of selection bias remains and this study was excluded (Kiyoyama 2009).

In conclusion there is currently no evidence of a difference in either blood contamination or bacteraemia when donor skin is cleansed pre-venepuncture with a one-step alcohol based process or a two-step alcohol plus antiseptic process. This lack of evidence for a difference however results from a complete absence of research and therefore a real difference cannot be discounted. Until better evidence emerges, decisions about which mode of pre-blood donation skin cleansing to use are likely to be driven by convenience and cost. It is also important to note that arm cleansing is only one of the points at which blood contamination may occur. Careful collection and storage of blood and blood products, and systematic surveillance to detect bacterial contamination can all contribute to the safety of patients requiring blood transfusions. Eliminating all bacteria from stored blood may not be possible. So, following relevant clinical guidelines (for example UK BTS Guidelines 2005) for collection and for detecting bacterial contamination in stored blood, both at the time of collection and at the time of issue, may be the most effective way of reducing infusion related bacteraemia (Yomtovian 2006).

Summary of main results

We did not identify any eligible studies for inclusion in this review. It is therefore unclear whether a two-step, alcohol followed by antiseptic skin cleansing process prior to blood donation confers any reduction in the risk of blood contamination or bacteraemia in blood recipients (or conversely whether a one-step process increases risk above that associated with a two-step process).

Potential biases in the review process

Biases in the review process were minimised as far as possible by adhering to the guidance provided by the Cochrane Handbook (Higgins 2008). We believe that publication bias is unlikely in this case; whilst no trials met the inclusion criteria , this is probably due to the difficulty and expense associated with mounting a trial large enough to answer the question.

Authors' conclusions

Implications for practice

We did not find any eligible randomised or quasi randomised controlled trials. Until further research emerges, decisions about which mode of pre-blood donation skin cleansing to use are likely to be driven by convenience and cost. It is also important to note that arm cleansing is only one of the points at which blood contamination may occur.

Implications for research

Cleansing the donor skin before taking blood for transfusion is important, but conducting a trial to compare the effects of using specific antiseptics on bacteraemia rates would be logistically difficult given the relatively rare event rate. It may be possible to estimate the effects of disinfecting with alcohol alone versus alcohol plus other antiseptics on blood contamination rates but this would still require very large sample sizes to detect clinically important differences. Alternatively, high quality observational studies may provide additional information to guide practice. A future comprehensive evidence synthesis that summarised the evidence for all competing alternative approaches to pre-blood donation skin cleansing would be worthwhile.

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Contributions of authors

Joan Webster: designed the review, checked the search results and all papers retrieved in full, wrote the review draft, responded to the peer referee feedback, made an intellectual contribution to the review and approved the final review prior to submission. Guarantor of the review

Sally Bell-Syer: coordinated the review, edited the review draft, responded to the peer referee feedback, made an intellectual contribution to the review and approved the final review prior to submission.

Ruth Foxlee: designed the search strategy, conducted the literature searches and retrieved papers. Edited the search methods section and responded to the peer referee feedback and approved the final review prior to submission.

Declarations of interest

none known

Differences between protocol and review

Nil

Published notes

This rapid review was undertaken at the request of the World Health Organisation (WHO). This organisation framed the review question but they did not provide funding or influence its publication.

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Blajchman 2004

Reason for exclusion	Narrative, non-systematic literature review

Calfee 2002

Reason for exclusion	None of the four study arms involved a two-step skin preparation process.

Choudhuri 1990

Reason for exclusion	Comparison of two one-step processes; alcohol swab compared with iodine swab.

de Korte 2006

Reason for exclusion	Single arm study evaluating a double-swab isopropyl alcohol disinfection process.

Follea 1997

Reason for exclusion	Examined techniques for quantifying bacterial reduction by comparing a three-step process with no skin disinfection.

Goldman 1997

Reason for exclusion	Abstract only available and it was unclear how patients where allocated to groups. Though this was not likely to have been randomised or quasi-randomised because one group was treated in a particular way on the basis that they were allergic to iodine. Also there was no one-step, alcohol-only skin preparation group.

Kiyoyama 2009

Reason for exclusion	Not a randomised or quasi-randomised controlled trial. Two independent groups were considered; one group from an inpatient ward was treated with isopropyl alcohol + povidone-iodine and the other from an emergency department was treated with isopropyl alcohol alone.

Lee 2002

Reason for exclusion	Not a randomised or quasi-randomised controlled trial. Comparison of two two-step processes in consecutive time periods. Cetrimide/ chlorhexidine solution + isopropyl alcohol compared with povidone-iodine + isopropyl alcohol.

Little 1999

Reason for exclusion	Povidone-iodine was compared with iodine tincture, i.e. not a comparison of a one-step with a two-step skin preparation.

McDonald 2006

Reason for exclusion	An uncontrolled before and after evaluation of a two-step process involving isopropyl alcohol + tincture of iodine.

Mimoz 1999

Reason for exclusion	Povidone-iodine compared with chlorhexidine, i.e. not a comparison of a one-step with a two-step skin preparation.

Pleasant 1994

Reason for exclusion	Only available in abstract form; no information to suggest this was a randomised controlled trial; attempts to contact the authors were unsuccessful.

Schifman 1993

Reason for exclusion	Comparison of two two-step processes, namely, isopropyl alcohol pads + povidone-iodine swabs compared with isopropyl alcohol/acetone scrub + povidone-iodine dispenser.

Shahar 1990

Reason for exclusion	Not a randomised or quasi-randomised controlled trial; the venepuncture site was cleansed with a two-step process after which a culture was taken, at a later time point the venepuncture site was cleansed with a one-step process after which a culture was taken. The two samples were collected from the same person but it is not clear from the report if the two venepuncture sites were different, if there was a possibility of cross contamination between sites and what time period separated the sampling process..

Sutton 1999

Reason for exclusion	Isopropyl alcohol (IPA) compared with no IPA skin preparation, i.e. not a comparison of a one-step with a two-step skin preparation.

Suwanpimolkul 2008

Reason for exclusion	Chlorhexidine in alcohol compared with povidone-iodine, i.e. not a comparison of a one-step with a two-step skin preparation.

Trautner 2002

Reason for exclusion	Chlorhexidine gluconate compared with iodine tincture, i.e. not a comparison of a one-step with a two-step skin preparation .

Wendel 2002

Reason for exclusion	Narrative, non-systematic literature review.

Wong 2004

Reason for exclusion	An uncontrolled before and after study of a one-step process involving chlorhexidine gluconate.

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Excluded studies

Blajchman 2004

Blajchman MA, Goldman M, Baeza F. Improving the bacteriological safety of platelet transfusions. Transfusion Medicine Reviews 2004;18(1):11-24.

Calfee 2002

Calfee DP, Farr BM. Comparison of four antiseptic preparations for skin in the prevention of contamination of percutaneously drawn blood cultures: a randomized trial. Journal of Clinical Microbiology 2002;40(5):1660-5.

Choudhuri 1990

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de Korte 2006

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Folléa G, Saint-Laurent P, Bigey F, Gayet S, Bientz M, Cazenave JP. Quantitative bacteriological evaluation of a method for skin disinfection in blood donors. Transfusion Clinique et Biologique 1997;4(6):523-31.

Goldman 1997

Goldman M, Roy G, Fréchette N, Décary F, Massicotte L, Delage G. Evaluation of donor skin disinfection methods. Transfusion 1997;37(3):309-12.

Kiyoyama 2009

Kiyoyama T, Tokuda Y, Shiiki S, Hachiman T, Shimasaki T, Endo K. Isopropyl alcohol compared with isopropyl alcohol plus povidone-iodine as skin preparation for prevention of blood culture contamination. Journal of Clinical Microbiology 2009;47(1):54-8.

Lee 2002

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Little 1999

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McDonald 2006

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Mimoz 1999

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Pleasant 1994

Pleasant H, Marini J, Stehling L. Evaluation of three skin preps for use prior to phlebotomy. Tranfusion 1994;34(Supp):14S.

Schifman 1993

Schifman RB, Pindur A. The effect of skin disinfection materials on reducing blood culture contamination. American Journal of Clinical Pathology 1993;99(5):536-8.

Shahar 1990

Shahar E, Wohl-Gottesman BS, Shenkman L. Contamination of blood cultures during venepuncture: fact or myth? Postgraduate Medical Journal 1990;66(782):1053-8.

Sutton 1999

Sutton CD, White SA, Edwards R, Lewis MH. A prospective controlled trial of the efficacy of isopropyl alcohol wipes before venesection in surgical patients. Annals of the Royal Collegeof Surgeons of England 1999;81(3):183-6.

Suwanpimolkul 2008

Suwanpimolkul G, Pongkumpai M, Suankratay C. A randomized trial of 2% chlorhexidine tincture compared with 10% aqueous povidone-iodine for venipuncture site disinfection: Effects on blood culture contamination rates. The Journal of Infection 2008;56(5):354-9.

Trautner 2002

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Classification pending references

Data and analyses

Figures

Sources of support

Internal sources

- Department of Health Sciences, University of York, UK

External sources

- No sources of support provided

Feedback

Appendices

1 *Criteria for a judgment of 'yes' for the sources of bias*

1. Was the allocation sequence randomly generated?

Yes, low risk of bias
A random (unpredictable) assignment sequence.
Examples of adequate methods of sequence generation are computer-generated random sequence, coin toss (for studies with two groups), rolling a dice (for studies with two or more groups), drawing of balls of different colours, dealing previously shuffled cards.

No, high risk of bias
- Quasi-randomised approach: Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number
- Non-random approaches: Allocation by judgement of the clinician; by preference of the participant; based on

the results of a laboratory test or a series of tests; by availability of the intervention.

Unclear
Insufficient information about the sequence generation process to permit judgement

2. Was the treatment allocation adequately concealed?

Yes, low risk of bias
Assignment must be generated independently by a person not responsible for determining the eligibility of the participants. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about whether the person is eligible to enter the trial. Examples of adequate methods of allocation concealment are: Central allocation, including telephone, web-based, and pharmacy controlled,randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.

No, high risk of bias
Examples of inadequate methods of allocation concealment are: alternate medical record numbers, unsealed envelopes; date of birth; case record number; alternation or rotation; an open list of random numbers any information in the study that indicated that investigators or participants could influence the intervention group.

Unclear
Randomisation stated but no information on method of allocation used is available.

3. Blinding was knowledge of the allocated interventions adequately prevented during the study?

Was the participant blinded to the intervention?

Yes, low risk of bias
The treatment and control groups are indistinguishable for the participants or if the participant was described as blinded and the method of blinding was described.

No, high risk of bias
- Blinding of study participants attempted, but likely that the blinding could have been broken; participants were not blinded, and the nonblinding of others likely to introduce bias.

Unclear

Was the care provider blinded to the intervention?

Yes, low risk of bias
The treatment and control groups are indistinguishable for the care/treatment providers or if the care provider was described as blinded and the method of blinding was described.

No, high risk of bias
Blinding of care/treatment providers attempted, but likely that the blinding could have been broken; care/treatment providers were not blinded, and the nonblinding of others likely to introduce bias.

Unclear

Was the outcome assessor blinded to the intervention?

Yes, low risk of bias
Adequacy of blinding should be assessed for the primary outcomes. The outcome assessor was described as blinded and the method of blinding was described.

No, high risk of bias
No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding

Unclear

4. Were incomplete outcome data adequately addressed?

Was the drop-out rate described and acceptable?

The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given.

Yes, low risk of bias
If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias. (N.B. these percentages are arbitrary, not supported by literature);
No missing outcome data;
Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias);
Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups;
Missing data have been imputed using appropriate methods.

No, high risk of bias

Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups;

Unclear

Were all randomised participants analysed in the group to which they were allocated? (ITT analysis)

Yes, low risk of bias
Specifically reported by authors that ITT was undertaken and this was confirmed on study assessment, or not stated but evident from study assessment that all randomised participants are reported/analysed in the group they were allocated to for the most important time point of outcome measurement (minus missing values) irrespective of non-compliance and co-interventions.

No, high risk of bias
Lack of ITT confirmed on study assessment (patients who were randomised were not included in the analysis because they did not receive the study intervention, they withdrew from the study or were not included because of protocol violation) regardless of whether ITT reported or not

'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.

Unclear
Described as ITT analysis, but unable to confirm on study assessment, or not reported and unable to confirm by study assessment.

5. Are reports of the study free of suggestion of selective outcome reporting?

Yes, low risk of bias
If all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the final trial report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment. Alternatively a judgement could be made if the trial report lists the outcomes of interest in the methods of the trial and then reports all these outcomes in the results section of the trial report.

No, high risk of bias
Not all of the study's pre-specified primary outcomes have been reported;
One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. sub scales) that were not prespecified;
One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect);
One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis;
The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

6. Other sources of potential bias:

Were co-interventions avoided or similar?

There were no co-interventions or there were co-interventions but they were similar between the treatment and control groups.

Was the compliance acceptable in all groups?

The review author determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the treatment intervention and control intervention(s). For example, ultrasound treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each participant attended or if participants completed the course of an oral drug therapy. For single-session interventions (for example: surgery), this item is irrelevant.

2 Ovid MEDLINE search strategy

1 exp Blood Specimen Collection/
2 exp Blood Transfusion/
3 exp Blood Donors/
4 (blood collection$ or blood donor$ or blood donation$).ti,ab.
5 ((collect$ adj1 blood) or (donat$ adj1 blood)).ti,ab.
6 ven?puncture site$.ti,ab.
7 or/1-6
8 exp Antisepsis/
9 exp Anti-Infective Agents, Local/
10 exp Iodine Compounds/
11 exp Povidone-Iodine/
12 exp Alcohols/

13 exp Disinfectants/
14 exp Disinfection/
15 skin preparation.ti,ab.
16 disinfect$.ti,ab.
17 (alcohol$1 or iodine or povidone-iodine or chlorhexidine).ti,ab.
18 or/8-17
19 7 and 18

3 Ovid EMBASE search strategy

1 exp Blood Sampling/
2 exp Blood Transfusion/
3 exp Blood Donor/
4 (blood collection$ or blood donor$ or blood donation$).ti,ab.
5 ((collect$ adj1 blood) or (donat$ adj1 blood)).ti,ab.
6 exp Vein Puncture/
7 ven?puncture site$.ti,ab.
8 or/1-7
9 exp Antisepsis/
10 exp Topical Antiinfective Agent/
11 exp Iodine/
12 exp Povidone Iodine/
13 exp Chlorhexidine/
14 exp Alcohol/
15 exp Disinfectant Agent/
16 exp Disinfection/
17 skin preparation.ti,ab.
18 disinfect$.ti,ab.
19 (alcohol$1 or iodine or povidone-iodine or chlorhexidine).ti,ab.
20 or/9-19
21 8 and 20

4 EBSCO CINAHL search strategy

S19 S9 and S18
S18 S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17
S17 TI (alcohol or alcohols or iodine or povidone-iodine or chlorhexidine) or AB (alcohol or alcohols or iodine or povidone-iodine or chlorhexidine)
S16 TI disinfect* or AB disinfect*
S15 TI skin preparation or AB skin preparation
S14 (MH "Disinfectants")
S13 (MH "Alcohols+")
S12 (MH "Povidone-Iodine")
S11 (MH "Iodine")
S10 (MH "Antiinfective Agents, Local+")
S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S8 TI venepuncture site* or AB venepuncture site*
S7 (MH "Venipuncture+")
S6 TI blood donation* or AB blood donation*
S5 TI blood donor* or AB blood donor*
S4 TI blood collection* or AB blood collection*
S3 (MH "Blood Donors")
S2 (MH "Blood Transfusion+")
S1 (MH "Blood Specimen Collection+")