SH72: What is the role of topical wound antiseptics (dilute betadine lavage, acetic acid, chlorhexidine, hydrogen peroxide, or antibiotics added to the irrigation solution) in treating shoulder prosthetic joint infection?

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Response: There are no clinical studies evaluating the role of topical wound antiseptics in the treatment of prosthetic shoulder infection. While in vitro studies suggest effect of topic wound antiseptics in decreasing bacterial burden, clinical studies are needed.

Strength of Recommendation: Limited

Delegate Vote: 53 (100%) agree; 0 disagree; 0 abstain

Rationale: A comprehensive literature review was performed to identify all studies on the role of topical wound antiseptics in treating shoulder prosthetic joint infections. Searches for the terms "betadine lavage", "intrawound antiseptic", "acetic acid", "chlorhexidine", "hydrogen peroxide", "antibiotic irrigation solution", "one-stage debridement", "two-stage debridement", "prosthesis retention", "revision arthroplasty", "shoulder arthroplasty", "shoulder peri-prosthetic joint infection", "shoulder prosthetic joint infection", "PJI", "infection control", "recurrence" and "success rate" were performed using the search engines Pubmed, Embase and Google Scholar which were searched through November 2024. We also reviewed the references of identified articles to maximise the number of studies. Inclusion criteria were all English studies (Level I-IV evidence) that reported on the use of topical wound antiseptics in the treatment of shoulder prosthetic joint infection. Exclusion criteria were non-English studies, non-human studies, retracted papers, case reports, and review papers. PRISMA (preferred reporting items for systematic reviews and meta-analyses) criteria were followed.

As no studies are looking at the role of topical wound antiseptics in treating shoulder PJI, we will discuss some in vitro studies, and evidence relating to other joints which formed the basis of our recommendation. However, it is important to recognise the differences between PJI in shoulder arthroplasty compared to other joints with regards to the micro-organisms involved and the presentations and chronicity of infections. The evidence available is often related to hip and knee arthroplasty, or the in vitro model studies have been designed with hip and knee arthroplasty in mind.

The use of Providone-Iodine is well established in the prevention of surgical site infections and PJI however the evidence is limited with regards to its use in *treating* prosthetic joint infection. Multiple studies have shown its efficacy against multiple microorganisms biofilms including those involved in PJI in vitro. However, there are differences across the studies with regards to the concentration of antiseptic used (Prekumar et al, 2020) (Goswami et al, 2019) (Cichos et al, 2019) (Gilotra et al, 2015). There is a clinical study by Riesgo et al (2018) comparing the use of dilute povidone-iodine with vancomycin powder in 36 PJI involving the hip and knee compared with a matched cohort of patients managed with saline irrigation without antibiotic powder. Although there was no statistically significant difference in reinfection rates between the two groups, there was a 45% relative risk reduction and overall DAIR success rate ranged from 63% to 83.3%. This

may suggest there is a role for the use of dilute povidone-iodine however the evidence is limited, and in vivo evidence relating to the shoulder is not available.

Hydrogen peroxide again has very limited in vivo evidence. There is in vitro evidence showing its efficacy in reducing a broad spectrum of bacterial biofilm (Glynn et al, 2009) (Lu and Hansen, 2016), and there is also in vitro evidence of synergistic effect when combined with povidone-iodine against 3 bacterial (*S.Aureus*, *Pseudomonas aeruginosa* and *E.Coli*) and various fungal pathogens, with its combined use being bactericidal as opposed to bacteriostatic when used separately (Zubko and Zubko, 2013)

Chlorhexidine Gluconate effects are proven in in-vitro studies, having been shown to decrease MRSA biofilm load and *S.epidermis* biofilms. (Schwechter et al, 2011) (Frisch et al, 2017). Its use has been described in prosthetic joint infections in hip and knee replacements, either by a scrub brush technique (Barros et al, 2019) or irrigation (Bryen et al, 2009) however the authors don't comment on volume or concentration. Once again there is no clinical evidence with regards to shoulder prosthetic joint infection.

Acetic acid has in vitro evidence against *Pseudomonas aeruginosa* and *S.aureus* (MSSA) biofilms (Williams et al, 2017) (Tsang et al 2018), and Williams et al (2017) showed success (87%) with the use of a 3% acetic acid soak during TKA PJI management using DAIR, two-stage revision and arthrodesis. Again, there is no clinical evidence with regards to shoulder arthroplasty and limited evidence against a range of micro-organisms common in prosthetic joint infections.

Preformulated irrigation solutions are readily available and are marketed as an option. O'Donnell et al (2021) conducted an in vitro study comparing the efficacy of various antiseptic solutions (Bactisure, Irrisept, Providone-iodine, Vashe and Prontosan) against clearing the biofilm formed by various clinically relevant micro-organisms (*Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Staphylococcus epidermis*, *Cutibacterium acnes*). Providone-iodine was found to be most effective against nascent MRSA biofilms, whilst Bactisure had the greatest effect against mature *pseudomonas* biofilms. When the data was pooled the results found statistically greater reductions in all biofilm formation with the use of either Providone-iodine or Bactisure. Whilst this study provides some interesting in vitro evidence and includes micro-organisms that cause prosthetic joint infections in the shoulder, there are limitations in the study, and these may be particularly relevant when translating this into clinical practice. The biofilms that the antiseptic solutions were tested against were only 4 hours and 72 hours old. In clinical practice it is likely the timescale for the formation of these biofilms will be much longer, and therefore, whether the efficacy on more mature biofilms is unknown. As this was an in vitro study, a key element that was missing was also pressure application, which is commonly used in clinical practice to try and mechanically disrupt bacteria as part of the therapeutic effect. Each antiseptic solution was only tested against single organisms, which sometimes is not the case in clinical practice. Finally, there are many other topical antiseptic solutions that weren't included in this study, and the study does provide useful in vitro information.

There is a further in-vitro study by Kia et al (2021) looking at the effectiveness of different topical adjuvants in reducing biofilm formation on orthopaedic implants. They looked at the effectiveness of Bactisure, Providone-Iodine (Betadine) and Chlorhexidine Gluconate solution (Irrisept) in reducing biofilm formation of *Staphylococcus aureus*, *Staphylococcus epidermis* and *Cutibacterium acnes* inoculated on Cobalt Chrome, Titanium and Stainless Steel discs. They found a significant reduction in biofilm formation of *C. acnes*, *S. aureus* and *S.epidermidis* at 48 hours and 72 hours for all topical adjuncts tested, but they did find Bactisure demonstrated the greatest reductive potential. Like many other in-vitro studies though, they used CFU (colony forming unit) quantification to judge effectiveness, and we know that this method may underestimate the residual contamination

that persists due to difficulty in detecting certain aspects of the mature biofilm. As the study had a maximal time point of 72 hours, it is hard to know how this translates into clinical practice We are also unaware of the clinically meaningful reduction in CFU.

This discussion highlights the limited evidence available about the use of topical antiseptics to treat shoulder prosthetic joint infections, particularly related to clinical in vivo studies. We would encourage clinical studies to look at this important question.

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