What is the Optimal Protocol of Intraoperative Irrigation with Povidone-Iodine Solution to Prevent Periprosthetic Joint Infection? In Vitro Investigation

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INTRODUCTION:

To prevent periprosthetic joint infection (PJI), many surgeons employ antiseptic and antibacterial agents during intraoperative irrigation. Dilute povidone-iodine irrigation has demonstrated efficacy in numerous cases, offering advantages such as cost-effectiveness, no risk of bacterial resistance, and broad antimicrobial properties. Clinical reports have shown that irrigation with a 0.35% diluted povidone-iodine solution for 3 minutes reduces PJI incidence. Basic in vitro experiments have also highlighted the effectiveness of a 0.13% povidone-iodine solution in eradicating staphylococci while exhibiting minimal cytotoxicity. However, these experiments did not replicate actual PJI conditions or verify the impact on biofilm. Furthermore, the timing of intraoperative irrigation, for example, when and how often it is appropriate and effective, remains unexplored. This study aimed to investigate the optimal concentration and timing of dilute povidone-iodine irrigation to prevent PJI.

METHODS:

In this in vitro study, Ti-6Al-4V washers were used as implants. A bacterial suspension of 1-5 × 107 CFU/ml was prepared using methicillin-sensitive Staphylococcus aureus (MSSA: ATCC#25923), capable of forming biofilms. Clean washers were placed in 1 ml of Tryptic Soy broth (TSB) medium, with 20 µL of the bacterial suspension added. The washers were then exposed to three different irrigation solutions (saline, 0.13% povidone-iodine, and 0.35% povidone-iodine) for 3 minutes at four different time intervals (15 minutes, 30 minutes, 60 minutes, and 120 minutes), followed by a return to TSB medium. This process was repeated until 120 minutes had elapsed. Finally, the washers were exposed to 1 ml of saline, and the bacteria present in the solution were assessed as floating bacteria, while those adhering to the washer's surface were evaluated as biofilm bacteria.

Quantitative Evaluation Using the Spread Plate Method: The spread plate method was used to assess floating bacteria in the saline solution. The washers were then rinsed twice with sterile water to remove non-adherent and floating bacteria. Subsequently, the washers were placed in 5 ml microtubes containing 3 ml of PBS. The solution was vortexed and sonicated to destroy biofilm on the washers. The remaining bacteria in the PBS were evaluated as biofilm bacteria using the spread plate method.

Qualitative and Quantitative Evaluation Using Fluorescence Microscopy: The washers were rinsed to remove suspended and non-adherent bacteria, and biofilms were stained using a biofilm viability kit. The biofilm coverage on the washers was examined using fluorescence microscopy. The percentage of washer surfaces covered by biofilm was determined, separately assessing live and dead bacteria.

Cytotoxicity Evaluation: Human osteoblasts were cultured and adjusted to 90% confluence. The wash solutions were administered at four different time patterns (15, 30, 60, and 120 minutes) and then aspirated after 3 minutes of exposure. The cells were detached and subjected to a cytotoxicity assessment using a cell proliferation assay reagent.

RESULTS:

Quantitative Evaluation Using the Spread Plate Method: Evaluation of suspended bacteria revealed that both 0.13% and 0.35% diluted povidone-iodine irrigations successfully eradicated MSSA in all time patterns, whereas saline failed to do so. Evaluation of biofilm bacteria demonstrated that irrigating with 0.13% and 0.35% povidone-iodine solutions every 30 minutes eliminated bacteria. (figure 1, 2)

Qualitative and Quantitative Evaluation Using Fluorescence Microscopy: Perfusion of 0.13% diluted povidone-iodine and 0.35% diluted povidone-iodine solutions within 30 minutes resulted in less coverage by live bacteria compared to other time intervals. No significant difference was observed in coverage by dead bacteria across all irrigation patterns.

Cytotoxicity Assessment: 0.35% diluted povidone-iodine irrigation exhibited significant cytotoxicity in all time patterns compared to the control (saline) irrigation. Conversely, 0.13% diluted povidone-iodine irrigation displayed significant cytotoxicity at 15-minute intervals but showed no significant cytotoxicity at 30, 60, and 120 minutes. (figure 3)

DISCUSSION AND CONCLUSION: This in vitro study suggests that irrigating with 0.13% and 0.35% diluted povidone-iodine solutions may be more effective against MSSA than saline irrigation. However, if more than 60 minutes elapsed before washing, bacteria formed a biofilm, reducing the irrigation's effectiveness. Considering cytotoxicity, irrigating with a 0.13% diluted povidone-iodine solution every 30 minutes was identified as the optimal irrigation protocol for preventing PJI.

Figure 2

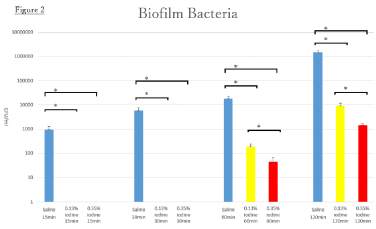

Figure 3

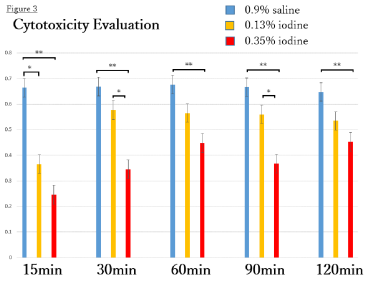

Figure 1