Comparison of Wound Irrigation Solutions Using an *Ex Vivo* Human Bone Organ Culture Model Insight into Antibacterial Effectiveness and Host Cell Response

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INTRODUCTION:

It is estimated that by 2030 the number total joint arthroplasties will reach 3.5 million. As this number grows, the number of revisions increase with some estimates being as high as 12%. There are several mechanisms of failure with infection being the leading factor (29.3%). Use of intra-operative irrigation solutions which balance antimicrobial efficacy and host cell toxicity can be an effective strategy in reducing infection but there are many formulations from which surgeons are to choose. Evaluation of irrigation solutions are largely done in vitro; however, environmental conditions affect both bacterial metabolism and the antimicrobials themselves. In this study we evaluate 7 irrigation fluids using a human ex vivo organ culture methodology to best replicate the infection site. The solutions evaluated use an array of technologies and antimicrobial agents, including acids and surfactants, chlorhexidine gluconate (CHG), benzalkonium chloride (BZK), polyhexamethylene biguanide (PHMB), and povidone iodine (PI).

METHODS:

Viable human femoral heads were collected during total hip arthroplasty and 168 bone cores were harvested (Figure 1a). The cores were inoculated with *Staph. aureus* in media best replicating human serum. Half of the cores were treated with irrigation solutions and the remaining patient matched cores were exposed to saline. Surviving bacteria counts were compared both acutely and 24hrs after treatment. An additional 126 cores were exposed to each irrigation fluid and incubated in a dynamic bioreactor system (Figure 1b). These specimens were metabolically and histologically compared to saline controls from the same patient both acutely and two-weeks after exposure.

RESULTS:

Antibacterial efficacy tended to group according to formulation both acutely and 24hrs after exposure (Figure 2). Ethanol/acetic acid and PHMB containing solutions showed acute reductions greater than 3-log and 6-log 24hrs after exposure. Bactisure®, BIASURGE®, and Prontosan® had significantly larger reductions compared to Irrisept®, Surgiphor™, Vashe®, and Xperience® ($p<0.001$ – $p=0.02$) but not between each other ($p=0.083$ – $p=0.574$). All fluids tested decreased host cell metabolic activity but only the ethanol/acetic acid-treated samples were significant acutely ($p<0.001$). Significant metabolic differences were also seen between ethanol/acetic acid ($p<0.001$) and one PHMB formulation ($p=0.01$) two-weeks after exposure.

DISCUSSION AND CONCLUSION:

Using this methodology, ethanol/acetic acid and PHMB formulations tended to show greater reductions in survival of *S. aureus*. However, the acetic acid formulation also had the greatest impact on host cells. While standard in vitro cell culture has a place, the use of more complex models can provide additional insight as the biochemical environment impacts both bacteria and antimicrobial agents.

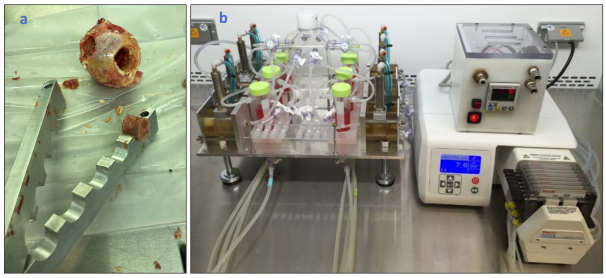

Figure1. a) Viable cancellous bone core harvest from a human femoral head. b) Bioreactor system with independent media circulation and pneumatic mechanical loading.

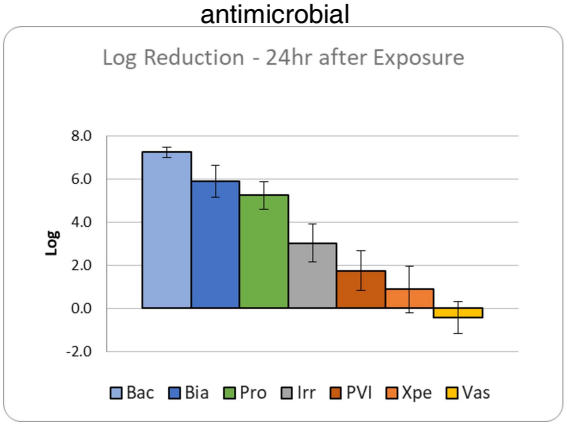

Figure 2. Chart showing log reductions of each irrigation fluid 24 hours after treatment.