Prosthetic joint infections (PJI) are a major complication of arthroplasties. Treatment consists of surgically exposing the infected appliance, irrigating the wound with antibiotics, coupled with tissue debridement. The effectiveness of using antibiotics in the irrigation fluid is debatable; especially against bacterial biofilms growing on infected prosthetic materials (titanium [Ti], polymethyl methacrylate bone cement [PMMA], and ultra-high molecular weight polyethylene [UHMWPE]). The purpose of this study was to investigate the effectiveness of two antiseptics (povidone-iodine [PI] and chlorhexidine digluconate [CHX]) in killing Staphylococcus epidermidis (a leading cause of PJI) biofilms on Ti, PMMA, and UHMWPE. S. epidermidis biofilms on Ti, PMMA, and UHMWPE disks anchored together with suturing material were exposed to 0.313% PI or 1.25% CHX for 15 minutes. Another trial was performed using 0.0781% PI and 0.0195% CHX for 4 minutes. Both antiseptics in both trials significantly reduced CFU of S. epidermidis on all orthopedic implant materials. With no treatment: polyethylene had a log 10 average of 5.1 CFU, titanium had a log 10 average of 4.5 CFU, and PMMA had a log 10 average of 5.3 CFU. Both trials of the antiseptic baths (PI and CHX) nearly sterilized all three materials completely; the log 10 average of the treated implant materials was 0.45 CFU. The results suggest that antiseptics might serve as alternatives to antibiotics in treating PJI.