LOCAL APPLICATION OF POOLED HUMAN IgG TO PREVENT POSTOPERATIVE SPINAL IMPLANT INFECTIONS


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**Introduction:** Postoperative spinal implant infection still occurs at a significant rate, despite the use of antibiotic prophylaxis and the decrease in postoperative total joint replacement infection rates. The increasing frequency of methicillin resistant *Staphylococcus aureus* (MRSA) associated with these infections, combined with the increase in immunocompromised patients (geriatric-, obese- and HIV-infected individuals) adversely impact healthcare costs and underscore the need for new anti-infective strategies. The local application of pooled human immunoglobulins (IgG) is studied as a new strategy to fight infection, independent of antibiotic resistance mechanisms. Pooled human polyclonal IgG represents all IgG subclasses and idiotypes and has broad-spectrum titers against most contemporary pathogens, potentiating natural immune mechanisms against pathogens in wound sites. A novel *in vivo* spinal implant infection model in rabbits\(^1\) was used to assess anti-infective properties of an IgG wound lavage against high levels of MRSA inoculation. This model has the advantage of simultaneously using three independent surgical sites in one animal permitting comparison of control sites with infected sites both with and without implanted biomaterials.

**Methods:** Sixteen New Zealand white rabbits (2.5 – 3.0 kg) were anaesthetized, dorsums were shaved, prepared with povidone-iodine solution and covered with sterile drapes. A 25mm dorsal skin incision was made longitudinally in the midline above vertebra Th13 (see Figure: A). After complete exposure, the spinous process (1) was excised, creating a laminectomy defect (see Figure: B), not violating the integrity of the ligamentum flavum. The defect was lavaged with either 1ml of 1wt% IgG solution or 1ml of sterile saline solution. From the left side of the animal, a 0.85mm diameter threaded K-wire (stainless steel ASTM F-138) was screwed through the transverse process (2), allowed to cross the defect, and fastened into the right transverse process (see Figure: C). The defect was then lavaged again with 1ml of either IgG or sterile saline. The site was subsequently challenged with 500 Colony Forming Units (CFU) MRSA for 60 seconds, followed by the final lavage with 1ml of either IgG or sterile saline. After closing the fascia and skin, the animal was uncovered and again prepared for similar implantation/infecion at level L3, followed by the same procedure at level L6. New sterile equipment was used for each site, and all rabbits had one saline-lavaged site and two 1wt% IgG-lavaged sites. Animals were sacrificed after day 7 or day 28, and bacteria were enumerated from tissue-biopsies (skin, fascia, muscle, transverse processes, lamina and fibrous debris from the defect) and the implant by plating serial dilutions onto nutrient agar. The same surgeon performed all procedures, no systemic antibiotics were administered and the use of IgG or saline lavage was blinded. Earlier studies with MRSA demonstrated that cross-contamination does not occur between the three implant sites.\(^1\)

**Results:** Nine of the 12 rabbits in the 7-day study developed a consistent biomaterial-centered infection in their positive control site (MRSA+saline lavage) and were included in the study. The difference in bacterial enumeration between 18 IgG lavaged sites (mean=4.0x10\(^7\) CFU/gram) and 9 saline lavaged sites (mean=3.2x10\(^7\) CFU/gram) was significant (p=0.003, t-test). Biofilm formation on the implants in IgG lavaged sites assessed after sonication of the K-wires was also significantly lower (p=0.04, t-test). The four rabbits in the 28-day long-term study all healed their infections, regardless of the treatment applied.

**Discussion:** IgG wound lavage significantly reduced bacterial burden and biofilm formation over regular saline lavage in postoperative, biomaterial-centered MRSA infections in a rabbit spinal implant infection model. Passive local immunotherapy as an IgG wound lavage to prevent biofilm-formation, seeding of pathogens, and resulting biomaterial-centered infection is suggested as a new anti-infective strategy complementary to i.v. antibiotic prophylaxis.

**Reference:**

**Figure legend:**
*Cranial view on rabbit lumbar-region vertebra. After complete exposure of the spinous process (A), and the creation of a laminectomy defect (B), a 0.85mm stainless steel threaded K-wire was drilled through both transverse processes and challenged with 500 CFU MRSA for 60sec.*

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*Poster Session - The Spine - VALENCIA FOYER
46th Annual Meeting, Orthopaedic Research Society, March 12-15, 2000, Orlando, Florida 0365*