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Silver microparticles plus fibrin tissue sealant prevents incisional hernias in rats

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ABSTRACT

Background: Open abdominal surgery is frequently complicated by the subsequent development of an incisional hernia. Consequently, more than 400,000 incisional hernia repairs are performed each year, adding over $15 billion per year to U.S. health-care expenditures. While the vast majority of studies have focused on improved surgical techniques or prosthetic materials, we examined the use of metallic silver microparticles to prevent incisional hernia formation through enhanced wound healing.

Materials and methods: A rodent incisional hernia model was used. Eighty-two rats were randomly placed into two control groups (saline alone and silver microparticles alone), and three experimental groups (0 mg/cm, 2.5 mg/cm, and 25 mg/cm of silver microparticles applied with a fibrin sealant). Incisional hernia incidence and size, tensile strength, and tissue histology were assessed after 28 days.

Results: A significant reduction of both incisional hernia incidence and hernia size was observed between the control groups and 2.5 mg/cm group, and between the control and 25 mg/cm group by nearly 60% and 90%, respectively ($P < 0.05$). Histological samples showed a noticeable increase in new fibrosis in the treated animals as compared with the controls, whereas the tensile strength between the groups did not differ.

Conclusions: The novel approach of using silver microparticles to enhance wound healing appears to be a safe and effective method to prevent incisional hernias from developing and could herald a new era of medicinal silver use.

Introduction

Five million open abdominal operations are performed annually in the United States.[1,2] Most patients recover without incident, but 15%-20% of patients develop incisional hernias.[3,4] Risk factors for hernia formation include morbid obesity, diabetes, smoking, and surgical site infection, placing an estimated 1.3 million abdominal surgery patients at high risk (>30%) for developing an incisional hernia each year.[1,5,6] The cosmetic deformity can lead to intestinal obstruction, bowel ischemia, enterocutaneous fistulas, and significant limitations on a patient's physical activity, gainful employment, and sense of overall well-being.[7,8] Thus, patients who develop an incisional hernia after abdominal surgery have considerably longer recovery times, a higher risk of death, and require an additional operation to repair the hernia. Accordingly, there are over 400,000 incisional hernia repairs each year, making it one of the five most common procedures

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performed by general surgeons and adding over $15 billion per year to U.S. health-care expenditures.[9,10]

Despite the magnitude and significance of incisional hernias, physicians, payers, and the biomedical technology industry are all primarily focused on improved repair materials and surgical techniques, instead of the optimal solution: prevention. However, the importance of prevention is recognized by several medical organizations.[11,12] In fact, the Society of American Gastrointestinal and Endoscopic Surgeons has identified finding a method or material that can be used at the time of a primary abdominal operation to prevent the development of an incisional hernia as a "top 10" research agenda item.[12] Furthermore, the European Hernia Society recently published a consensus document recommending how to best close abdominal incisions to avoid incisional hernia formation.[11]

For well over a century, the predominant strategy governing the repair of abdominal wall hernias has been "targeted fibrogenesis." Consequently, successful and durable hernia operations depend on the induction of fibrous scar tissue resulting from surgical manipulation of either native tissues or the placement of prosthetic materials in the area of myofascial weakness. In 1884, Bassini[13,14] inaugurated the era of anatomic inguinal hernia repair, proposing the detailed dissection and repositioning of the oblique abdominal muscles to buttress hernia defects in the groin with native muscle tissue. The use of prosthetics to reinforce defects in the abdominal wall followed soon thereafter. In 1894, Phelps reported the use of small silver coils (filigrees) during hernia repairs, exploiting the observation that as the implanted silver metal slowly disintegrated, it induced a local inflammatory response and wound fibrosis.[15-17] Despite impressive clinical results with hernia recurrence rates <0.5%, the use of silver wire prosthetics ended by the 1950's because of patient discomfort, from prosthetic hardening and seroma formation, occasional wound complications, and the advent of polymer chemistry that produced new prosthetic materials, especially polypropylene (Prolene), which was viewed as a superior alternative.

Because incisional hernias result from inadequate early wound healing,[18-20] we postulated that the prophylactic enhancement of myofascial wound healing would decrease subsequent hernia formation. We thought to leverage the clinical observations gleaned from the bygone use of metallic silver filigrees to repair hernias in a completely novel way to prevent incisional hernias instead. Specifically, we hypothesized that using microparticles of silver (5 μ-1 mm) rather than fine silver wire would preserve the therapeutic benefits of this unique metal, including enhanced fibrosis, yet avoiding the side effects that contributed to its abandonment. Furthermore, the positive wound-healing effect of metallic silver could be used to promote organized fibrosis along the abdominal wall incision during primary closure to prevent incisional hernia formation.

Materials and methods

Animals and surgical procedure

All procedures were performed with the prior approval of the University of California, San Francisco Institutional Animal Care and Use Committee under the protocol number AN091661. We used an established rat model in which at least 80% of the animals developed an incisional hernia.[21] Specifically, Sprague–Dawley rats (male, 250-300 g, Charles River, Cambridge, MA) were placed under isoflurane anesthesia; the ventral abdominal wall hair was shaved with electric clippers, and the surgical field was prepared with 70% alcohol. A 6 cm × 3 cm, rectangular, full-thickness skin flap based 2 cm lateral to the ventral midline was raised through the avascular prefascial plane, thereby separating the skin incision from the underlying fascial wound-healing environment. The 1:2 ratio of flap length to width was maintained to prevent ischemia of the skin flap. A 5-cm midline laparotomy incision was made, the intestines were manipulated, and then the myofascial incision was closed with two interrupted 5-0 plain catgut (rapidly absorbable) sutures placed 5 mm from the cut myofascial edges and one-third the distance from the cranial and caudal ends of the midline laparotomy incision, respectively, before the skin flap was closed with a continuous 4-0 vicryl suture to prevent intestinal evisceration. Immediately after the surgery, 0.4 mL of bupivacaine 0.25% was infused subcutaneously around the abdominal incision, and the rats were observed every 2 min until awake and resuming normal activity. Thereafter, the rats were returned to individual cages and monitored twice daily. At 12 and 18 h after operation, 0.05 mg/kg of buprenorphine was injected subcutaneously.

Application of silver microparticles and hernia measurement

To test our hypothesis, we used silver microparticles (<250 μ, Sigma Chemicals, St. Louis, MO) and a sterile fibrin tissue sealant (TISSEEL, Baxter Healthcare Corp, Hayward, CA) to localize the microparticles at the incisional site. A total of 82 rats were randomly placed into two control groups (saline alone and silver microparticles alone), and three experimental groups (0, 2.5, and 25 mg/cm of silver microparticles to be applied with fibrin tissue sealant). The experimental animals had 0.5 mL of fibrin tissue sealant topically applied on the closed abdominal incision, followed by one of the three doses of the silver microparticles. Animals in the control groups had either an equal volume of sterile saline (0.5 mL) or the high concentration of silver microparticles alone applied to their sutured myofascial incisions before skin closure. On day 28, all animals were inspected for the presence of an obvious abdominal protrusion (clinical hernia) and recorded as such. The animals were then euthanized, had their abdominal wall excised, and overlying skin carefully separated from the myofascial surface and hernia sac if present. Each specimen was carefully examined, and any gap between recti was measured. If a gap was found to be greater than 2 mm in diameter, it was classified as an anatomical hernia.[21] The total area of the myofascial defect was also determined by measuring the maximal transverse and cranial-caudal dimensions, and then calculated using the equation for an ellipse ($\pi \times r_1 \times r_2$; $r_1 = ½$ the transverse diameter and $r_2 = ½$ the craniocaudal diameter).

Tensile strength

We also wanted to determine if the application of silver microparticles would have an adverse effect on the normal