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Prevention of Pin Track Infection in External Fixation with Silver Coated Pins: Clinical and Microbiological Results

A. Massè,[1] A. Bruno,[1] M. Bosetti,[2] A. Biasibetti,[1] M. Cannas,[2] P. Gallinaro[1]

[1] Dept. of Orthopaedics, Traumatology and Occupational Medicine, University of Torino, Italy

[2] Dept. of Medical Sciences, Human Anatomy, University Piemonte Orientale "A. Avogadro," Novara, Italy

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Abstract: Pin tract infection is a frequent complication of external fixation; according to literature its frequency ranges from 2–30%. The recent introduction of silver coating of polymeric materials was found to decrease bacterial adhesion; its clinical use with Foley catheters and central venous catheters led to significant results. To verify the ability of the same silver coating to decrease the bacterial colonization on external fixation screws, a prospective randomized study was carried out on 24 male patients; a total of 106 screws were implanted in the lower limb to fix femoral or tibial diaphyseal fractures: 50 were coated with silver and 56 were commercially available stainless steel screws. Although the coated screws resulted in a lower rate of positive cultures (30.0%) than the uncoated screws (42.9%), this difference was not statistically significant (*p* = 0.243). the clinical behavior of the coated screws did not differ from that of the uncoated ones. Furthermore, the implant of silver-coated screws resulted in a significant increase in the silver serum level. These results led us to consider it ethically unacceptable to continue this investigation. © 2000 John Wiley & Sons, Inc. J Biomed Mater Res (Appl Biomater) 53: 600–604, 2000

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INTRODUCTION

One of the main causes for loss of stability in external fixation is pin tract infection, which is found in literature to occur in 2–30% of cases .[1-5] In a study of pin tract infection, Mahan reported 75% of screw tips cultured positive at removal, with a higher rate of Gram positive (Staphylococcus epidermidis, Staphylococcus aureus) as compared to Gram negative (Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis)[3]; the same bacterial species have been found in chronic osteomielitis.[6,7]

From an historical point of view, it is worth mentioning the experience of Parkhill, who managed to reduce pin track infection by using silver screws more than a century ago.[8] More recently, the introduction of silver-coated Foley catheters lead to a statistically significant reduction of bacteriuria in patients who had undergone prolonged catheterization.[9-13] Moreover, the use of silver-coated central venous catheters in parenteral nutrition was shown to significantly decrease the rate of sepsis.[14,15] Recently, silver coating of stainless steel screws, implanted in sheep iliac bone and inoculated with *Staphylococcus aureus*, was found to be effective in reducing the number of colony-forming units when compared with uncoated screws.[16]

A prospective randomized study was carried out to investigate whether the same silver coating was able to decrease the bacterial colonization of 316L stainless steel screws used in external fixation of diaphyseal fracture of the lower limb.

MATERIAL AND METHODS

This study was approved by the Regional Ethical Committee.

Twenty-four male patients (mean age 34.7 years; range 18–47 years) affected by diaphyseal fracture of the tibia or the femur to be treated with monolateral external fixator underwent the implant of 106 screws; 50 of these screws were silver-coated (40 in tibia, 10 in femur), while 56 were uncoated (46 in tibia, 10 in femur). The screws were removed at a mean of 109 days for the silver-coated screws, of 113 days for the uncoated screws.

The output variables considered were: the silver blood level, the inflammation, and the mechanical anchorage scores according to Mahan,[3] the rate of positive screw-tip cultures at the extraction.

All data were recorded in a custom database and analyzed with a software package (SPSS 8.01, SPSS Comp.). Statistical significancy was stated at $p \leq 0.05$ for all the tests performed.

Correspondence to: Dr. A. Massè, Università degli studi di Torino, Osp. CTO, Via Zuretti 29, 10126 Torino, Italy (e-mail: alessandro.masse@CTO.UNITO.it)

Patient Selection and Surgical Procedure

Patients were asked to give their informed consent before to taking part in the study. Exclusion criteria were: open fractures more than degree IO1 according to the AO classification,[17] diabetes or history of other diseases or treatment that might increase the risk of infection. In order to have a group of patients homogeneous as far as the antibiotic treatment goes, the more severely open fractures were excluded.

AISI 316L stainless steel cortical screws for external fixation (ORTHOFIX, Verona, Italy) were fully silver coated by SPIArgent method (SPIRE Corporation, Bedford, MA). This method is based on ion-beam assisted deposition of silver from the vapor-phase.

Rifampicin (2 g) was administered to the patients preoperatively. We never used a postoperative antibiotic therapy.

Both the coated and uncoated screws were implanted on each patient. All screws within a screw clamp were of the same kind (coated or uncoated) to avoid interference due to contiguity infections. The choice of screw to be implanted on each clamp was made at random at the time of surgery.

The number of screws implanted on each side of the fixator was either two or three, depending on the fracture pattern and the bone quality, and was decided intraoperatively by the surgeon.

Silver Blood Level Measurement

Blood samples were taken previous to surgery, at 7 days, and at 1 and 2 months after surgery, after the removal of the screws. The silver level was measured in the whole blood by graphite furnace Zeeman atomic absorption spectrophotometry (Perkin–Elmer 4100 ZL). All the blood samples were frozen and analyzed at one time to avoid calibration problems. The Friedman test was used to check the presence of any difference among the silver blood levels retrieved from the same patient at the different observation times. The correlation between the silver blood level and the number of the silver screws implanted at each observation time was analyzed by the Pearson's correlation coefficient.

Clinical Evaluation

After discharge, patients were asked to provide pin care by cleaning the pin tract with iodate disinfectant three times per week.; Patients were then followed monthly, up to the fracture healing.

Inflammation was scored for each pin tract at 1 and 2 months and at the time of the removal of the fixator at 1 and 2 months and at the removal of the fixator; the scoring system was that proposed by Mahan, which ranges from 0–4, as the sum of the points given for the presence at the pin tract site of tenderness, erythema, heat and purulent discharge.[3]

At the end of the treatment, screw extraction was performed after cleaning the tract with 7.5% iodate water disinfectant and washing out any residual disinfectant with sterile saline solution.

The use of a dynamometer screwdriver to measure the strength of both insertion and removal of the screws was found to be ineffective due to the high number of measurements out of range. The mechanical anchorage at removal was, therefore, scored**,** again according to Mahan,[3] as follows: 0 = no motion; 1 = slight motion; 2 = definite motion; 3 = gross motion; 4 = "pulls out by hand." Inflammation scores and mechanical anchorage score were compared for the silver-coated and uncoated screw groups by the Newman–Keuls test.

The Wilcoxon rank test was used to compare the mean scores of coated and uncoated screws in each single patient, to avoid the variable represented by inter-individual differences in the quality of pin tract care among patients.

Screw Tip Culture

A 2-cm sample was taken from the tip of each screw with a sterile bolt cutter, and placed in a sterile box for microbiologic examination; samples were then rolled on bloodagar plates (5% sheep eritrocytes, "Columbia," Becton Dickinson) using plastic forceps. The number of CFU was recorded after 24 h of incubation at 35°C. The Yate's Chi-square test was used to compare the overall rate of positive cultured tips both in the study and control screw groups.

Surface Analysis

To check the presence of modifications of the surface morphology and/or composition induced by the implant, surface microanalysis was performed on the threaded portion of two silver-coated screws sterilized but not implanted, and on two silver-coated screws implanted in a tibia and removed after 3.5 months. Scanning electron microscopy (SEM) and energy-dispersive X-ray analysis (EDAX) were performed on a PHILIPS XL 20 Scanning Electron Microscope equipped with EDAX based on a lithium-drifted silicon detector (Oxford Instruments, Oxford, UK).

EDAX was carried out on 10 points for each sample, at 25 keV. The comparison between the results of the implanted/not implanted coated screws was performed with the Mann–Whitney test.

RESULTS

Silver Blood-Level Measurement

The preoperative silver blood level was always below the reading threshold of the spectrophotometer (0.20 μg/L). It rose to a median of 2.79 at 7 days post-op (range 0.26–11.08), 2.85 at 1 month (range 1.08–14.88), 3.12 at 2 months (range 0.2–20.55), 1.08 at removal (range 0.20–7.22) (Fig. 1); the difference between the preoperative and the postoperative blood silver values was always statistically significant ($p < 0.001$), while no significant variation was found in the

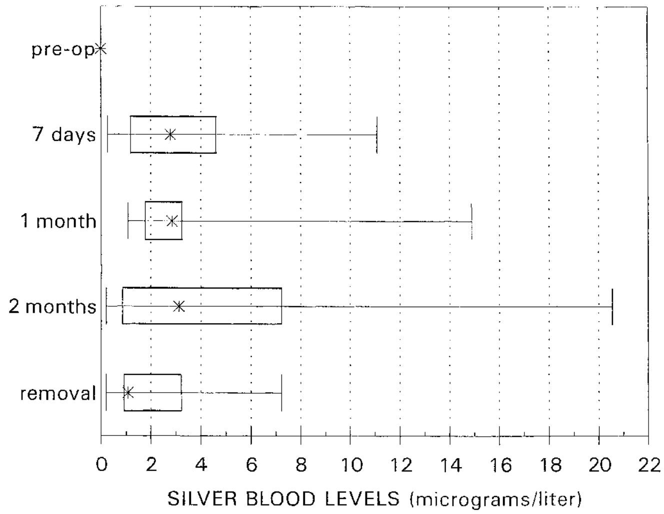


Figure 1. Tukey box-whiskers plot of the silver levels measured on whole blood. Each mark represents from left to right, respectively, the 1, 25, 50, 75, and 100 percentiles. The left and right whiskers of the plot represent the bottom and the top one-quarter of the data, while the box represents the middle 50%. Inside the box, the 50th percentile (median) is indicated. The preoperative silver blood-level was always below the reading threshold of the spectrophotometer (0.20 μg/L). The normal silver blood-value is reported in the literature as below 14 μg/L.[18]

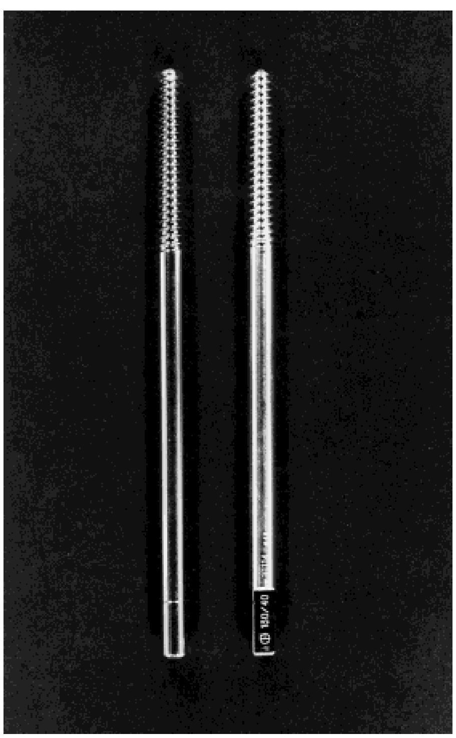


Figure 2. The screws used in this study were AISI 316L stainless steel cortical screws (ORTHOFIX, Verona, Italy); on the left, a commercially available screw; on the right, a screw coated with the SPI-Argent method. In some cases, a spotted brownish discoloration appeared on the surface of the coated screws after autoclave sterilization, probably due to oxidation; these screws were not implanted.

TABLE I. Results of the Cultures of the Tips of Silver Coated and Uncoated Screws

	50 Silver-Coated Screws	56 Uncoated Screws
Staph. aureus	8	11
Staph. coagulase negative	2	5
Staph. epidermidis	2	3
Staph. simulans	1	2
Staph. capitis	0	2
Bacillus species	1	0
Corynebacterium	1	0
Enterococcus faecalis	0	1

silver blood level from the postoperative measurement up to removal ($p = 0.19$).

The 7th day silver blood-value was significant related to the number of the silver screws ($p = 0.002$, $r = 0.565$), as was the second month value ($p = 0.014$, $r = 0.492$).

Clinical Evaluation

The clinical behavior of the silver-coated screws did not differ significantly from that of the uncoated ones; indeed, the inflammation score was comparable in the coated and uncoated screw groups. This result was seen at all the observation times. Furthermore, the mechanical anchorage score did not differ significantly in the two groups under examination.

Screw Tip Culture

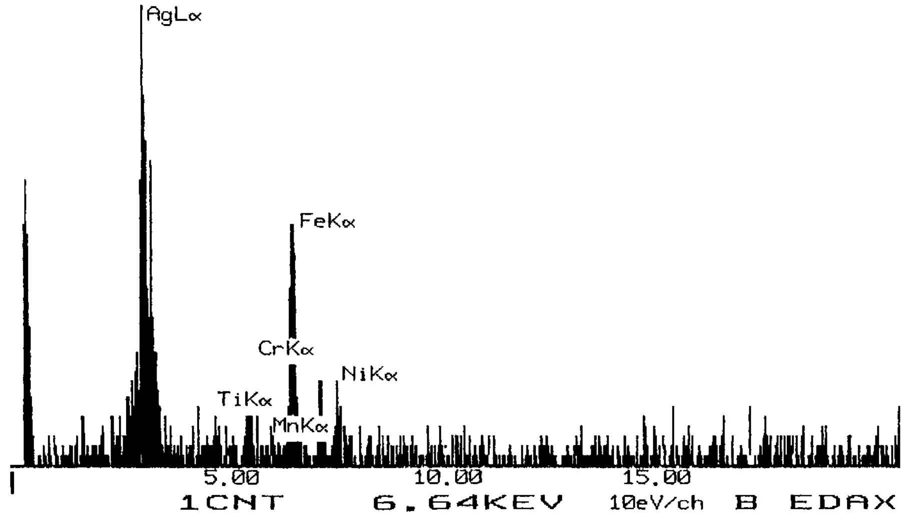
The overall rate of positive cultures was 36.8% (39 cases), with 15 screw tips (30.0%) in the silver-coated group and 24 (42.9%) in the group of uncoated screws. This difference was not statistically significant ($p = 0.243$, $power = 0.585$).

There was no evidence of polimicrobal colonization of the screw tips. *Staphylococcus aureus* was the most frequently cultured (19 screw tips, 48.7%); other cultured bacteria were *Staphylococcus coagulase* negative (7 screw tips, 17.9%), *Staphylococcus epidermidis* (5 screw tips, 12.8%), *Staphylocccus simulans* (3 screw tips, 7.8%), *Staphylococcus capitis* (2 screw tips, 5.1%) and Bacillus species, *Corynebacterium*, *Enterococcus fecalis* (1 screw tip, 2.6%) (Table I). No difference was found among the species of cultured bacteria in the silver-coated and uncoated screw groups.

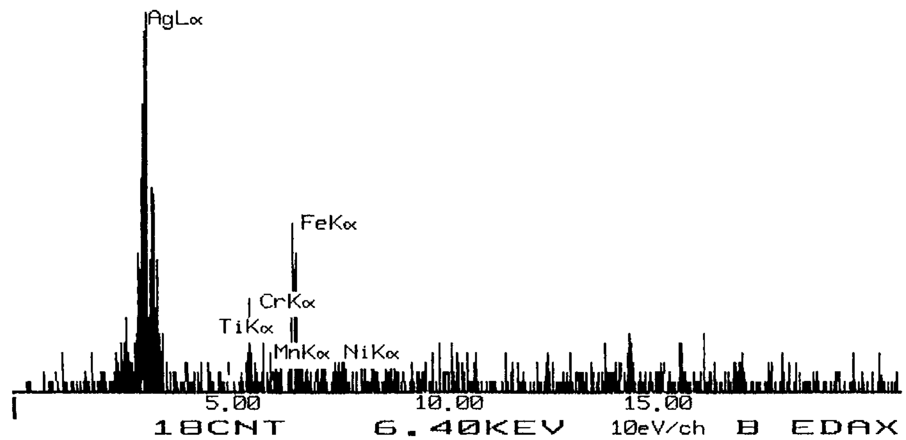
Surface Analysis

The SPI-ARGENT coating results in the deposition of silver droplets with an approximate diameter of 50–150 nm evenly distributed on the surface, as already found by Wassal.[18] The same morphologic characteristics were found both in the implanted and not implanted screws.

EDAX analysis indicated an almost identical surface composition in the silver-coated screws implanted and not implanted, with the presence of a high amount of silver [Figs. 3(a), (b)].



a



b

Figure 3. Energy dispersive X-ray analysis at 25 keV of (a) SPI-Argent coated screw sterilized but not implanted, and (b) Spi-Argent coated screw removed 3.5 months after the implant. No significant difference in the surface composition can be found.

DISCUSSION

There were no significant modifications in blood silver levels in the samples taken at different times. This observation shows that, even if a certain amount of silver ions bind to the peri-implantar connective tissues, the ion release rate remained almost unaltered throughout the observation period. Furthermore, the EDAX analysis did not show evidence that the implant induced any difference in the surface composition.

Although literature reports normal silver blood value as being below 14 μg/L,[19] we always recorded preoperative silver levels below the reading threshold of the spectrophotometer (2 μg/L). In all but two postoperative blood samples, the silver levels were also within the normal range. The measured values that exceeded this threshold were 14.88 and 20.55 μg/L. These values were recorded in the case with the highest number of coated screws, a young man with 6 femoral coated screws; noteworthy is the fact that the femoral screw has the highest ion-releasing surface implanted. This observation is in agreement with the correlation we found between the number of coated screws and the silver blood levels, and could lead to some concern as to the implantation of multiple silver-coated screws in patients with multiple fractures. It must be remarked that the only reports concerned with the systemic effects of silver are related to the extensive use of oral medications containing silver, which has been shown to cause a condition known as argyria, represented by a pronounced slate-gray discoloration in the exposed skin.[20] Webster did not report any side-effects in patients treated for severe chronic osteomyelitis with daily application of electrically activated silver dressing.[21]

The overall rate of screw tips colonized by bacteria recorded in this study was 36.8%, that is, less than one-half the rate of infection reported by Mahan.[3] This may be explained by the exclusion criteria used in our study, aimed at obtaining a group of patients homogeneous as to the infection risk, and/or by the use of different protocol for pin site care and antibiotic profilaxis.

The low overall infection rate decreased the power of the statistical test performed (*power* = 0.585). This means a high probability of beta error, which implies the risk of not detecting the real differences between the groups. With these remarks, the rate of positive cultured tips was 13% lower in the silver-coated screw group when compared to the uncoated group. Collinge, in an *in vivo* study performed on the same coating by directly inoculating Staphylococcus aureus in the pin tracts in 6 sheep, recorded a 22% reduction of infection in the silver coated group.[16] This value, observed in experimental conditions, seems to be comparable with our findings.

The results of this study are only in partial agreement with the reports on the clinical use of the same silver coating on polymeric surfaces for the prevention of sepsis and cystitis. Indeed, with the limits of the experimental design, the advantage given by the silver coating over the stainless steel seems to be limited to a reduction in the number of positive cultures from screw tips, which is not statistically significant. A possible explanation is given by the *in vitro* study of the bacterial adhesion on silver-coated and uncoated stainless steel samples performed by Wassal.[18] The incubation itself of the samples with human serum was found to significantly reduce the bacterial adhesion, even if the adhesion was still significantly lower in the SPI-Argent coated samples. In the same way, the adhesion of the serum proteins to the screw surface could reduce by itself the ability of the bacteria to adhere to the surface, thus obscuring AG/control differences.

Further clinical studies performed on a randomly selected population could led to a more precise quantification of the cost-effectiveness of this coating when applied to external fixation screws. However, with the absence of any clinical advantage, the lack of a significant decrease in the positive cultures from screw tips and the increase in the blood silver levels led us to consider it ethically unacceptable to continue this investigation.

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