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Review

Antimicrobial coated implants in trauma and orthopaedics–A clinical review and risk-benefit analysis

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ABSTRACT

Implant-associated infections remain a major issue in orthopaedics and antimicrobial functionalization of the implant surface by antibiotics or other anti-infective agents have gained interest. The goal of this article is to identify antimicrobial coatings, for which clinical data are available and to review their clinical need, safety profile, and their efficacy to reduce infection rates.

PubMed database of the National Library of Medicine was searched for clinical studies on antimicrobial coated implants for internal fracture fixation devices and endoprostheses for bone surgery, for which study design, level of evidence, biocompatibility, development of resistance, and effectiveness to reduce infection rates were analyzed.

Four different coating technologies were identified: gentamicin poly(D, L-lactide) coating for tibia nails, one high (MUTARS®) and one low amount silver (Agluna) technology for tumor endoprostheses, and one povidone-iodine coating for titanium implants. There was a total of 9 published studies with 435 patients, of which 7 studies were case series (level IV evidence) and 2 studies were case control studies (level III evidence).

All technologies were reported with good systemic and local biocompatibility, except the development of local argyria with blue to bluish grey skin discoloration after the use of silver MUTARS® megaendoprostheses. For the local use of gentamicin, there is contradictory data on the risk of emergence of gentamicin-resistance strains, a risk that does not seem to exist for silver and iodine based technologies. Regarding reduction of infection rates, one case control study showed a significant reduction of infection rates by Agluna silver coated tumor endoprostheses.

Based on socio-economic data, there is a strong need for improvement of infection prevention and treatment strategies, including implant coatings, in fracture care, primary and revision arthroplasty, and bone tumor surgery. The reviewed gentamicin, silver Agluna, and povidone-iodine technologies have shown a good risk benefit ratio for patients. Further data from randomized control trials are desirable, although this will remain challenging in the context of infection prevention due to the required large sample size of such studies.

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Introduction

Orthopaedic implants, such as fracture fixation devices and total joint prostheses have proven their positive effect on patient quality of life. For both indications, metal implants based on their biomechanical properties are primarily used. Despite their known functional benefits, all implants exhibit a certain risk of deep infection. The link between an elevated infection risk in association with an implant was already suggested in 1957 by Elek et al. showing that the threshold for the establishment of an infection after intradermal injection of *S. aureus* was reduced from 1,000,000 bacteria when no foreign body was used to only 100 organisms when a silk suture was placed into the skin [1]. Further papers from Gristina [2] and Costerton et al. [3] identified the so-called “race for the surface” and biofilm formation of bacteria as key elements for the pathophysiology of implant-associated bone infections. The general idea of protection of the implant surface in order to positively influence the “race for the surface” and to prevent biofilm formation, is mainly based on the principle of local delivery of antimicrobial substances from Buchholz who discovered the release of antibiotics from PMMA bone cements into the local surrounding of the implant which paved to way to the prophylactic use of antibiotic-loaded bone cement in total joint arthroplasty [4]. For fracture fixation devices and uncemented total arthroplasty, the principle of local antimicrobial strategies to prevent colonization and biofilm formation on the implant surface is more difficult and the first clinically available technologies only emerged in the last years.

The purpose of this article is to perform a risk benefit analysis for antimicrobial coated implants for patients based on clinical data regarding questions on the clinical need, safety, including allergies and resistance risk, as well as their efficacy to reduce infection rates.

Materials and methods

Literature search

The author searched PubMed (1999 – present) databases of the National Library of Medicine with the following key words: “implant coating bone” (search 1) and “coated implant infection” (search 2) “gentamicin coating” (search 3) “silver coating” (search 4) on May 31; 2016. Only clinical studies on coated implants for internal fracture fixation devices and endoprostheses for bone surgery were included into the further review of data.

Analysis of clinical data

For all included clinical studies, indication, study design and level of evidence were reviewed [5]. Furthermore, number of patients, and particularly clinical data to identify potential risk and benefits regarding general biocompatibility, allergies, development of resistance and effectiveness to reduce infection rates were analyzed.

Results

Study selection and identified coating technologies

Literature research revealed 1542, 444, 99, and 1263 hits for search 1, 2, 3 and 4, respectively. Most articles on antimicrobial coatings were in vitro or in vivo animal experiments and most clinical papers reported on non-antimicrobial coatings, such as hydroxyapatite or other porous coatings. The search revealed nine clinical papers with four different antimicrobial coating technologies for which clinical data were reported (Table 1) [6–14].

The first one is a gentamicin poly(D, L-lactide) with ‘dipcoating process’ for tibia nails [6,7]. The second and third technology are based on different silver strategies with galvanic deposition of a relatively high amount elementary silver on the implant surface of tumor endoprostheses [8–11] or anodization of the titanium alloy followed by absorption of a relatively low amount of silver from an aqueous solution [12] for custom-made tumor endoprostheses. The fourth technology uses a povidone-iodine electrolyte-based process for iodine coating of megaendoprostheses and limb salvage systems [13,14].

Clinical data for the four different technologies

The 9 published studies included an overall patient number of 502 patients, of whom 20 patients of two studies of Hardes et al. [8,9] and 47 patients of the study of Tsuchiya et al. [13] and of Shirai et al. [14] might have been double included (Table 1). Therefore, with conservative estimate of real patient numbers, an overall number of 435 study patients can be assumed.

Seven of the nine studies are case series with level IV evidence, only the study of Hardest et al. [9] and Wafa et al. [12] on two different silver coating strategies for tumor endoprotheses can be considered as case control studies with level III evidence.

Gentamicin poly(D, L-lactide) matrix coating for tibia nails

This coating is based on a fully resorbable poly(D, L-lactide) matrix with gentamicin sulphate with an initial burst release of 40% release of the gentamicin within the first hour, 70% within the first 24 h and 80% within the first 48 h (from a 8 mm thick und 330 mm long UTN PROtect® (Synthes, Bettlach, Switzerland)) [15]. The total amount of antibiotic is depending on the surface area of the implant ranging from approximately 10 to 50 mg gentamicin depending on the size of the implant.

This coating was firstly available on the Unreamed Tibia Nail (UTN) PROtect® (UTN PROtect®; Synthes, Bettlach, Switzerland) based on the original UTN titanium alloy (Ti-6Al-7Nb) nail with CE-certification for this coated implant in August 2005.