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ANTIBACTERIAL RESORBABLE COATING OF ORTHOPAEDIC IMPLANTS: AN IN VITRO AND IN VIVO STUDY

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Summary Statement: An Implant Disposable Antibacterial Coating (i-DAC®) is described, consisting of a fully resorbable, biocompatible hydrogel, able to release antibacterial and antibiofilm agents. Direct application of the hydrogel on implants prevented infection occurrence in an *in vitro* model of peri-prosthetic infection.

Introduction: Biofilm-related infections are among the main reasons for failure of joint prosthesis with high associated social and economical costs (1, 2, 3). Bacterial adhesion and subsequent biofilm formation have been shown to develop early after biomaterials implant into the human body, when a "race to the surface" takes place between the host's cells and the colonizing bacteria eventually present at the surgical site (4). Providing an antibacterial/antibiofilm coating of the implant may then play a strategic role in preventing biofilm related infections. Here we report the results of a series of *in vitro* and *in vivo* studies, partially performed under the European 7th Framework Programme (Implant Disposable Antibiotic Coating, IDAC, collaborative research project # 277988), concerning a fully resorbable, biocompatible antibacterial hydrogel coating (DAC®, Novagenit, Italy). The patented hydrogel, a co-polimer comprising of hyaluronic acid and a polylactic acid, has been designed to be mixed with various antibacterial agents and applied directly on the implant at the time of surgery, being fully resorbed within few days.
Patients & Methods: The tested hydrogel (DAC®, Novagenit, Italy) is a derivative of a low molecular weight hyaluronan, grafted with poly-D,L-lactic acid and provided in powder form. At the point of care, the powder is hydrated with the antibiotic or antibiofilm solution, thus generating the final compound to be applied onto the implant surface. *In vitro* studies were conducted using DAC® coating on different biomaterials, including titanium, chrome-cobalt and polyethylene discs. The release of different antibacterial agents, including vancomycin, ciprofloxacin, meropenem, gentamycin, amikacin, tobramycin, clindamycin, doxycyclin, linezolid, NAsalycilate and N-acetylcisteine, adequately mixed with the hydrogel, has been tested by means of gas chromatography and microbiological methods. *In vivo* studies were then performed on 35 rabbits divided in 7 groups. Animals were implanted with an intramedullary titanium rod in their femur, with a known inoculum of methicillin-resistant *Staph. aureus* and vancomycin-loaded DAC® at different concentrations (2% and 5%) and compared with controls.
Results: Regardless of the tested material, *in vitro* studies showed the ability of the hydrogel to be loaded and to sustain the release of the following antibacterial/antibiofilm compounds for up to 96 hours: vancomycin, ciprofloxacin, meropenem, gentamycin, amikacin, tobramycin, clindamycin, doxycyclin, linezolid, NAsalycilate, N-acetylcisteine. *In vivo* studies showed a bacterial load reduction ranging from 94% to 99.9% using vancomycin-loaded DAC®, compared to controls.
Discussion/Conclusion: DAC®, a fast-resorbable antibacterial coating (5), showed the ability to be loaded with various antibacterial compounds and the ability to provide a highly significant reduction of bacterial colonization of implanted biomaterials in an animal model, opening a new pathway to local prevention and treatment of biofilm-/implant-related infections.

References

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