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Defensive Antibacterial Coating (DAC®) for prevention of infection in ACL reconstruction: a feasibility study

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SUMMARY
Defensive Antibacterial Coating (DAC) is a hydrogel, Conformité Européene (CE)-marked medical device, intended to be used as a disposable, quickly bioresorbable antibacterial coating for implants. The present feasibility study investigated the application of DAC on the grafts, in addition to IV prophylaxis, during anterior cruciate ligament (ACL) reconstruction.

KEY WORDS
ACL; Anterior cruciate ligament reconstruction; DAC; Defensive Antibacterial Coating; prophylaxis

INTRODUCTION

Orthopaedic implants are commonly used for the fixation or the reconstruction of bones or tendon and ligaments. Bacterial infections on implanted material are a serious adverse complication in this type of surgery (1), often requiring further procedures, resulting in discomfort and risk for the patient. Antibacterial materials with non-fouling properties, capable to release drug immediately after the procedure and for at least during the following 6 h, and preferably up to 48–72 h, have been used to cover the critical period of bacterial colonization and proliferation at the site of surgery (2,3).
Biodegradable polymeric materials are resorbable, do not require a second procedure to remove them, reduce foreign body reactions, and may increase the release of drug at the site of implant. Moreover, the rate of drug release from the polymer matrix may be modulated by controlling the degradation processes of the materials. Researchers from Stanford University and the consensus meeting on periprosthetic joint infections suggested that "coatings of devices would be most useful in the prevention and treatment of implant-associated infection" (4–6).
For these reasons, recently, a fast-resorbable hydrogel coating (Defensive Antibacterial Coating [DAC®], Novagenit Srl, Mezzolombardo, Italy) which works as a physical barrier and that can be intra-operatively loaded with various antibacterials, has been developed 1. DAC is composed of covalently linked hyaluronan and poly-D,L-lactide, which undergo complete hydrolytic degradation within 72 hours. During this time, DAC completely releases a variety of antibacterials at concentrations ranging from 2% to 10%. DAC is effective with various antibiotics and antibiofilm agents *in vitro* (7) and is safe and effective *in vivo* in rabbit models

of highly contaminated implant both with (8) and without systemic antibiotic prophylaxis (9).
Infection of the graft after arthroscopic ACL reconstruction is an uncommon but devastating post-operative complication, and many factors may lead to infection, including comorbidities, such as diabetes, smoking, previous surgery or concomitant open surgical procedures (10–15). Increased operative time, additional or larger incisions, long tourniquet inflation time, or use of a drain may also contribute (10–12,16). An infection after ACL reconstruction may result in poorer clinical outcomes, reduced function, pain, arthrofibrosis, early osteoarthritis and graft failure with later revision (17–21).
The aim of the present feasibility study is to report the safety of the use of DAC in patients undergoing anterior cruciate ligament reconstruction using semitendinosus and gracilis tendon autograft.

MATERIAL AND METHODS

The present study was conducted following the ethical standards of the journal (22). All patients undergoing ACL reconstruction by the same surgeon (NM) using an identical surgical technique in the same hospital after obtained informed consent were included in the present study. Inclusion criteria were symptomatic ACL deficiency, a history of trauma, a positive Lachman test and pivot shift test, and MRI confirming the ACL rupture. All patients had chronic anterior cruciate ligament insufficiency and had undergone a six to 12 weeks period of physiotherapy. All of them had developed symptomatic instability and had experienced at least one episode of instability before being scheduled for surgery. Patients with concomitant chondral and/or meniscal injuries were excluded, as were patients undergoing simultaneous high tibial osteotomy, ACL reconstruction revision, multiligament injury patients, or patients who underwent ACL reconstruction using a graft different from hamstrings tendons.
The same surgical technique was performed in each patient, with systemic intravenous pre-operative cephalothin 2 g injection before tourniquet inflation to achieve adequate plasma levels pre-incision.
A single endoscopic assisted incision technique was used with a four-strand ipsilateral hamstring autograft and anatomic femoral tunnel drilling via the anteromedial portal was performed. Graft fixation was accomplished with a 7x25 mm titanium interference screw in all subjects in both the femoral and tibial tunnels. Weightbearing as tolerated with crutches was immediately after surgery, without brace and an accelerated rehabilitation program was supervised by physical therapist, aiming to achieve full extension by 2 weeks and full range of motion by 6 weeks.
During ACL reconstruction, hamstring harvest grafts, still attached to the tibia, were wrapped with DAC.
The preparation of the DAC hydrogel during surgery was performed according to the manufacturer's instructions. In brief, the prefilled syringe, containing 300 mg of sterile DAC powder, was filled with a solution of 5 mL sterile water for injection and the desired antibiotic. This allowed the antibiotic-loaded hydrogel with a DAC concentration of 6% (w/v) and an antibiotic concentration ranging from 20-50 mg/mL to be prepared in 3–5 min. The surgeons can choose the antibiotic from a list of antibacterials previously tested, including gentamicin, vancomycin, daptomycin, meropenem, rifampicin, and ciprofloxacin [7]. In the present report, a dose of 250 mg of vancomycin was used.
Following routine preparation of the graft and the tibial and femoral tunnels, the DAC was directly spread onto the surface of the graft (7–9). After the graft had been inserted in the joint and fixed with a femoral and a tibial interference screw, the remaining hydrogel was applied at the tibial tunnel aperture and over the portion of the graft which remained attached to the hamstring insertion at the pes anserinus.

RESULTS

A total of 25 consecutive patients underwent the index procedure (10 female (40%) and 15 male (60%) patients), with a mean age of 22.48 ± 5.9 years. All patients underwent a standardised postoperative rehabilitation program, and were followed-up at weeks 2, 6, 12, and at 6 and 12 months post-operatively by the operating surgeon. All patients were advised to notify the surgeon if they had increasing pain, swelling or fever at any time during this period. Within the observation period, no patients developed a graft failure. No patient developed an infection after the ACL reconstruction surgery. One patient developed a post-operative blood effusion and underwent knee aspiration. Culture yielded negative results, with no signs of bacterial infection. There were no adverse events from the use of DAC.

DISCUSSION

The present feasibility study reported the efficacy and safety in the use of DAC and vancomycin in ACL deficient patients undergoing reconstruction with hamstring tendons autografts (5,23). Concerning efficacy, this report is in line with previous data from *in vivo* (7,8) and recent clinical trials on the use of DAC for total hip and knee cementless or hybrid total joint arthroplasty (24).
Antibacterial coatings have been effective in reducing septic complications, but their application to orthopaedic procedures has been relatively limited (9). The high biocompati-

bility and the short time needed for resorption of DAC (1,25) make the occurrence of longer-term side-effects unlikely.
We are aware of the limitations of the present report: we included a small number of patients, follow up was limited to one year, and this was not a randomized controlled trial. However, we set out to undertake a feasibility investigation, and the report fulfils its initial scope.

CONCLUSIONS

The use of prophylactic Defensive Antibacterial Coating (DAC) loaded with vancomycin on hamstring grafts for ACL reconstruction is safe and effective. More studies with a greater number of patients and longer follow-up are needed to draw more definitive conclusions on the role of this coating device in the prevention of infection following ACL reconstruction.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests

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