Bone Reconstruction with a Bupivacaine-Loaded Injectable Calcium Phosphate Cement Can Reduce Postoperative Pain After Iliac Bone graft Harvesting Procedure in a Canine Model

Olivier J. Gauthier, DVM, PhD1, Xavier Plaetevoet, DVM2, Elise Verron, PhD3, Borhane H. Fellah, DVM, PhD4, Pascal Janvier, DVM, PhD4, Delphine Holopherne-Doran, DVM, PhD4, Jean-Michel Bouler, DVM, PhD4.

1Oniris College of Veterinary Medicine, Food Sciences and Engineering, Nantes, France, 2Oniris College of Veterinary Medicine, Food Sciences and Engineering, Nantes, France, 3INSERM U791, LIOAD, University of Nantes, Nantes, France, 4CEISAM, CNRS UMR 6230, University of Nantes, Nantes, France.

Disclosures:

Introduction: Donor site morbidity with persistent pain is the most common complication of iliac bone graft harvest, with a more severe pain from the donor site than from the primary surgical site in 15 to 50% of the cases.

The aims of our study were:
- To establish an animal model that would reproduce the human iliac crest bone graft harvesting procedure;
- To evaluate the induced pain after such a harvesting procedure;
- To evaluate the reconstruction ability of an injectable calcium phosphate bone cement to fill the iliac crest bone defect;
- To evaluate the benefit in pain relief obtained with a CaP cement loaded with bupivacaine compared to the same cement without any analgesic agent.

Methods: A 2 x 2 cm square bone defect was created with an orthopaedic bur on the iliac wing, mimicking a unicortical posterior iliac bone graft, on 12 adult female beagle dogs, according to European Community guidelines for the care and use of laboratory animals (2010/63/UE) after approval of the Local Animal Welfare Committee. Briefly, with the animal in lateral recumbency, a dorsal approach of the left iliac crest was performed. The middle gluteal muscle attachments were incised dorsally and cranially on the iliac crest, elevated and reflected ventrally together with the deep gluteal muscle to expose the whole iliac wing. The contours of the iliac bone defect were stamped with the bur, starting on the dorsal cortex and extending on the lateral one that was detached with an osteotome. The inner iliac trabecular bone was removed with the bur to expose the medial iliac cortex. Each dog was implanted unilaterally with either the bupivacaine-loaded CaP cement or the unloaded control one (figure 1). A few minutes after cement injection, the muscle flap was repositioned over the defect and the middle gluteal muscle attachments were sutured dorsally with absorbable sutures. Subcutaneous and skin sutures were routinely performed.

Postoperative evaluations were performed 6h, 12h, 24h after cement injection and every 24h until 7 days postop. They included physical and orthopedic examinations that defined a lameness score, a VAS (Visual Analogic Scale) score and a postoperative pain score using the 4A-Vet pain scale. Algometric sensitivity measurements with a Von Frey sensor were carried out by application of progressive pressure with a plastic cone on four predetermined locations until the animal reacted (between the two first lumbar vertebrae, laterally to the patellar ligament, medially to the iliocrest and on the iliocrest insertion of the middle gluteal muscle just over the surgical site). All measurements were done in triplicate. Rescue analgesia with morphine was available. Six months after the first surgery, the 6 animals that had received the control unloaded cement underwent the same surgical procedure on the contralateral iliac crest where the created bone defect was left unfilled to provide negative control sites. Osteointegration of the CaP cement was investigated with CT, microCT and histology. Then three conditions were compared: (i) the “CaP Cement + Bupi” group, (ii) the “Cement alone” group, and (iii) the “No cement” group. Statistical analysis was performed with ANOVA and post hoc Tukey test adapted for linear mixed effects model.

Results: Pain relief after cement bone filling was highly significant regardless the cement used, compared to unfilled surgical site conditions where significant postoperative pain was observed during the first 4 postoperative days. Bupivacaine-loaded CaP cement provided very local and short-term better pain relief compared to the unloaded cement, during the first 6 postoperative hours. CT-scan analysis confirmed the bone reconstruction of the iliac crest by the injected cement (figure 2) that remained in place and showed very good osteointegration on both microCT and histological analysis (figure 3), with induced porosity, osteoconduction properties and peripheral cement resorption and bone colonization.

Discussion: Our experimental model of iliac bone graft (i) Created significant postoperative pain, (ii) Showed significantly reduced postoperative pain when a CaP cement was used to fill the iliac crest harvesting site, loaded with bupivacaine or not, (iii) Restored the iliac bone morphology after cement injection. Bupivacaine local delivery provided early local but transitory analgesic effects.

Significance: The injection of CaP cement may be an effective bone augmentation method to decrease permanent induced local
pain and thus long-term morbidity after iliac crest harvesting procedure.

Acknowledgments:
