Assessment of B2A Peptide-Enhanced Ceramic Granules in an Instrumented Sheep Model of Interbody Lumbar Spinal Fusion

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Introduction: Although synthetic osteoconductive materials are routinely utilized in orthopedics, their use in lumbar spinal fusion has been limited. B2A is a synthetic, receptor-targeted peptide that amplifies the biological response of rhBMP-2 (1). B2A also amplified in vivo biological response in osteopromotive environments expected to contain BMP-2: when combined with demineralized bone matrix (DBM)(2) or when combined with ceramic scaffolds and used in rabbit long bone defects (without DBM) where it accelerated bone repair (2). Furthermore, in a rabbit posterolateral spinal fusion model, B2A coated ceramic granules enhanced autograft (3). The purpose of the present study was to evaluate the safety and effectiveness of B2A peptide-enhanced ceramic granules (B2A/G) versus synthetic granules when mixed with autograft and used in an instrumented sheep interbody fusion model.

Materials and Methods: Sixteen adult sheep underwent instrumented spinal arthrodesis. In each animal, posterior instrumentation (pedicle screw/rod) and a rectangular PEEK interbody spacer was placed in two, single-level procedures using an anterolateral retroperitoneal approach. Ceramic granules (hydroxyapatite-tricalcium phosphate) were coated with several concentrations of peptide to produce B2A/G. All granule preparations were mixed 1:1 with morselized iliac crest autograft. The animals were assigned to four treatment groups with an n=8. Group I consisted of uncoated granules (G; granule control); groups II-IV received granules without heterotopic ossification or other untoward events. This study compares favorably with a previous investigation comparing B2A/G versus granules alone in a rabbit posterolateral model. In both studies, B2A/G containing 50-, 100-, or 300-μg B2A/cc (B2A/G).

During the procedure, the anterolateral aspects of the L2-L3 and L4-L5 vertebral bodies were exposed. A discectomy was performed and the vertebral endplates removed to a dimension to accept a PEEK spacer (Signus Medical LLC, Tetris®). Once the implant space was prepared, the PEEK spacers were packed according to a treatment randomization schedule and securely implanted within the disc space. After fluoroscopic verification of the implanted cages, the two operative levels (L2-L3 and L4-L5) were then instrumented with polyaxial pedicle screw and rod systems (Zimmer, Silhouette®) using standard techniques.

After 4 months, spinal fusion was assessed by computed tomography (CT; Dedicated Imaging, Inc., Baltimore, MD). One mm axial sections were reformatted and four blinded orthopedic surgeons evaluated fusion status using the following definition: at least two sagittal slices with contiguous bone from endplate to endplate without signs of radiolucencies within the PEEK spacer. CT images were also utilized to determine the incidence of spinal stenosis and / or ectopic calcification.

Results: The animals tolerated the surgery well, returned to normal activity within 24 hours, and had recoveries without complications. Based on gross examination at the time of necropsy, there were no significant intra- or peri-operative complications – vascular, neurologic or infectious. The local tissues from all animals were considered unremarkable and without evidence of ectopic bone formation or other significant histopathologic changes. Radiographic analysis demonstrated no incidence of implant migration or fracture. Moreover, there was no evidence of spinal stenosis.

The granule control group (0 ug B2A) had the least fusion (5/8 fused; 63%). All B2A/G groups had more unions (7/8; 88%) than controls. There were four cases in which ossification spanned the operative levels anterior or lateral to the cage. This was considered secondary to the animals' normal healing response and unrelated to graft material. Importantly, two of these four cases occurred in the control group, which lacked the B2A coating.

Discussion: There is a clinical need for synthetic, osteoinductive materials that can consistently and safely increase fusion rates for lumbar spine fusions. Currently used allograft extenders have concerns over both safety and reproducibility and both allograft and synthetic osteoconductive materials are not optimal extenders for lumbar spinal fusion.

These studies established the feasibility of using B2A/G with autograft to increase the prevalence and quality of the spinal fusion using instrumentation. B2A/G increased fusion rates in this animal model compared with uncoated granules without heterotopic ossification or other untoward events. This study compares favorably with a previous investigation comparing B2A/G versus granules alone in a rabbit posterolateral model. In both studies, B2A/G containing 50-, 100-, or 300-μg B2A/cc produced higher fusion rates than granules alone (3). Furthermore, this study suggests that synthetic, osteo-inductive B2A/G may provide a safe, more reliable and more effective alternative to current bone grafting materials.

B2A has a unique mechanism of action in that, although it interacts with receptors for BMP-2, it appears to augment BMP-2-mediated osteoinduction and bone repair, and thus requires an osteopromotive environment. In the current study, the autograft bone and/or decorticated endplate may have provided the necessary signals for B2A action.

Because both safety and effectiveness was demonstrated in a sheep model that closely mimics the human application, these results warrant B2A/G evaluation in a clinical setting.


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