SUMMARY

Bone grafting is frequently used to regenerate bone tissue lost due to trauma, and/or pathology. There are several surgical techniques, used alone or in combination with natural or synthetic graft materials that are used to achieve alveolar bone augmentation with varying degrees of predictability. Several synthetic calcium phosphate bone replacement graft materials have been investigated over the years as alternatives to autografts, which are considered to be the gold standard, in spite of the fact that they require a second surgical site for bone harvesting which impacts patient morbidity. One of the main issues with synthetic materials is the variable rate and extent of resorption resulting in poor long-term stability due to limited new bone infiltration into the graft material. To overcome this, our collaborative group have developed bone substitute graft materials consisting of dicalcium phosphate (monetite) that incorporate in their matrix a novel bone anabolic conjugate of a bisphosphonate (alendronate) and the potent bone activating EP4 receptor agonist known as C3. The primary objective of this proposed research is to investigate whether the novel conjugate drug released via the matrix of the bioresorbable cement grafts has the potential to achieve rapid, enhanced and clinically significant bone regeneration in the vertical bone augmentation model and that the newly formed bone is physiologically active. The long-term objective is to bring a product to the market which will ultimately benefit millions of patients undergoing maxillofacial reconstruction and alveolar bone augmentation prior to dental implant placement.

PROGRESS

Fabrication of the grafts: Monetite grafts were prepared by conversion of preset brushite cement discs. The cements were produced at P/L mixing ratio of 1.5 using de-ionized water containing the C3 drug (0.1% by weight) or no drug. Monetite grafts were prepared next by conversion of set brushite discs utilizing wet heat transformation performed via autoclaving

Characterization of the grafts: The phase purity of prepared monetite grafts with and without C3 will was confirmed using X-ray diffraction (XRD). Microstructural morphology of the prepared monetite grafts was examined with a scanning electron microscope (SEM). The compressive strength will be measured before implantation.

Animal model and surgical procedure: The calvaria bone of 24 white male New Zealand rabbits was used and grafts with and without C3 drug (n=12 each) will be stabilized by titanium osteosynthesis screw (1.5 mm screw head diameter and 7 mm screw length) on either side of the midline. Total 24 animals, 2 grafts per animal, 2 time points of 6 weeks and 12 weeks. Grafts with C3 drug (n=12) and grafts without drug (n=12) for each time point.

Analysis: After sacrifice, the implant sites were retrieved, and analysis performed. Histomorphometric analysis of the implanted area from the images of histological coronal sections crossing the center of grafts was performed using a microscope. Bone growing within the grafts, as well as the area occupied by the remaining unresorbed graft material was identified and measured.

PROJECT AIMS, DELIVERABLES AND TIME-LINE

The research plan was to evaluate the osteoconductive potential of the monetite grafts containing a novel C3 conjugate in their matrix with the following specific aims:

-Preparation of monetite biomaterial grafts with conjugate C3: Preparation and characterization of monetite grafts with conjugate incorporated in the matrix and modifying processing conditions to optimize material properties to those required for specific bone applications. (1-3 months) [COMPLETED]

-Confirm efficacy in rabbit calvaria implant model: Study both measuring quality and quantity of new bone formation for vertical bone augmentation in a rabbit calvarial implantation model. Prepare manuscript for publication (4-12 months). [COMPLETED]

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