TISSUE ENGINEERING IN CRITICAL SIZE MANDIBULAR BONE DEFECTS.  
AN ANIMAL STUDY IN BEAGLE DOGS.

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INTRODUCTION: Mandibular bone tissue engineering it’s always a challenge. The structural and functional anatomic “restitutio ad integrum”; is the final objective of all kind of reconstructive surgery. Autologous bone grafting is the “gold standard” for mandibular reconstruction. Iatrogenic problems with possible donor site morbidity and bone reabsorption of non-vascularized grafted bone are frequent problems. So, many osteoinductive and osteoinductive substances are currently in study worldwide. Osteogenic growth factors might be an excellent alternative for bone generation if they can be carried and delivered properly and biological and biomechanic properties of the induced bone are similar to the normal bone. β-Tricalcium phosphate (TCP) and polylactic acid (PLA) derivatives have been used alone as osteoconductive substances and are actually considered good growth factors carriers. Transforming growing factor β (TGF-β1, TGF-β2 and TGF-β3) and their receptors are found in endochondral and intramembranous ossification sites. Transforming growing factor β3 (TGF-β3) deserves relevance when intramembranous osteogenesis is involved, as in the mandible.

OBJECTIVES: To evaluate, in a Beagle dog model, the capacity of different osteodynamics substances for bone tissue regeneration in a critical size mandibular bone defect. To compare two osteoconductive substances [β-TriCalcicPhosphate (TCP) granules and Poly(L/DL-lactide) sponges 70/30 (PLA)] with a potentially osteogenic growth factor [transforming growth factor β3 (TGF-β3)] and the “gold standard” method of cancellous bone grafting.

METHODS: 30 Beagle dogs, 21-24 months old, divided by five groups with 6 dogs each. By a new surgical extra-oral approach, a 30 mm long full-thickness unilateral critical mandibular bone defect was surgically created including the periosteum, after six months previous edentation. Mandibular stabilization with an AO 2.4 mm titanium locking reconstruction mandibular bone plate. Surgical defect filling groups: 1) humerus autologous cancellous bone; 2) TCP alone; 3) PLA alone; 4) TCP+TGF-β3 and 5) PLA+TGF-β3. A thermoplastic (70ºC) custom-made poly(L/DL-lactide) 80/20 biodegradable membrane for reconstructed area surrounding. Euthanasia at 26th week. Qualitative and quantitative bone evaluation: 1) radiography and contact radiography; 2) Quantitative Computed Tomography densitometry; 3) nondestructive mechanical tests; 4) histomorphological evaluation including intravital fluorochromes; 5) vascular evaluation with Indian Ink injection per mortem.

RESULTS: The cancellous bone graft group presented 3 mandibles (50%) with a structure that can be considered good for normal use, 2 with incomplete bone formation and 1 with minimal bone formation. Minimal bone formation was found with PLA alone or TCP alone, whereas TCP plus TGF-β3 resulted in a partial bone bridging. With PLA plus TGF-β3 no significant bone formation resulted but an exuberant cellularity and angiogenesis could be observed.

CONCLUSION: The osteodynamic substances studied can’t achieve a normal good bone formation as cancellous bone graft generally does. The experimental growth factor used (TGF-β3) seems to have a high capacity for mesenchymatous cells stimulation of angiogenesis and/or osteogenesis with significant activity differences between different carriers. Further investigation for establishment of the appropriate carrier seems to be recommended.