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Would it Possible to Turn Muscle into Bone?

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Description

The challenge of treating large osseous defects presents a formidable problem for orthopedic and maxillofacial surgeons. The present method of choice to replace lost tissue is autologous bone grafting, but supplies of autologous bone are limited and harvesting of the graft is associated with donor site morbidities [1]. Artificial biomaterials offer much promise, but do not, by themselves, supply the osteo-progenitor cells needed for bone formation. Moreover, there are often issues with resorption of the scaffold used in the biomaterial, coupled with inadequate vascularization. To address this shortfall, the use of a muscle flap that can act as a bio-reactor for the growth of mesenchymal stromal cells, which can then provide a composite bone mineral for maxillofacial reconstruction has been reported [2]. The role of muscle in bone regeneration has not been studied extensively, however there is proof that muscle has the propensity to induce bone formation because of its intrinsic osteogenic potential when exposed to osteogenic stimuli including bone matrix substitutes and bone morphogenic proteins [3-5]. The most accepted mechanism behind bone formation is that an inflammatory response at the surgical site, and the presence of oestrogenic stimuli amplify the signalling of exogenous BMP-7, triggers the MAPK pathway, as explained by Hassel et al. [6].

To our knowledge there was only been one report on complete bone regeneration in long bones using an induced muscle graft which was injected with an adenovirus vector encoding BMP-2 [3]. An Induced pedicle muscle flap was used to reconstruct critical sized defect in the mandible was also reported [2-4]. Similar surgical techniques, using skeletal muscle flaps injected with a BMP-2 adenovirus, have been used to reconstruct large cranial bone defects which reported variable results [4]. This latter study reported that insufficient vascularization, and differences in the mechanism of bone formation between partial bones and long bones, could be reasons behind the suboptimal results that were obtained. Our previous work has, however, demonstrated the remarkable potential of the use of muscle flaps, along with an injectable bio-cement loaded with BMP and seeded with rBMSCs, to induce bone formation for the reconstruction of bony defects. However, this latter study was conducted as a single cohort study group.

With regard to the fate of the muscle graft, complete muscle transformation was noted, with the tissue becoming a loose connective tissue full of osteoblast, pre-osteoblasts, with a small number of myocytes. This may indicate there were possible metaplastic changes occurring to transform the muscle cells into bone-forming cells.

On the other hand, experimental group which were grafted with the un-treated muscle graft, was retain its vascularization and look like connective tissue, that rich with colonies of cells resembling resemble bone marrow cells, with no evidence of tissue necrosis or the presence of inflammatory cells. One could infer that the muscle was essentially acting as bioreactor for endogenous cells and exogenous rBMSCs as well as it acts as rich source of blood supply.

Conclusion

Therefore, it is reasonable to imagine that osteogenesis follows the route of intramembranous ossification, initiated by the presence and the differentiation of mesenchymal stem cells into osteoblasts inside the vascularized muscle, which essentially acts as a bioreactor for the injected cells. Bone cement and BMP then play role in inducing cells differentiation and bone regeneration. We thought it would have been ideal to perform similar study in larger animal model, using autologous BMSCs and in a critical size defect in mandible, as this region is the main challenge in maxillofacial reconstruction. Within the limitation of the conducted study so far, the concept of using muscle graft as in-situ bio-reactor for bone engineering was approved.

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