LETTER

Limitations on the use of platelet concentrate as a graft material and scaffold for bone regeneration.

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Bone is a dynamic an important component of our body that is constantly being appositioned and reabsorbed. However, aging and chronic diseases modify its biological homeostasis producing large bone defects, hypocalcification and even fractures. Actually, tissue engineering applies knowledge of bioengineering, cell transplantation and the manufacture of biological substitutes that can restore and maintain normal bone function *(Cypher & Grossman, 1996)*. For this purpose, it is necessary to have a graft material that meets the biological properties of autogenous bone: to have an osteogenic, osteoconductive and osteoinductive potential, with a rapid incorporation and consolidation *(Cypher & Grossman, 1996)*. Currently in the market there are deproteinized bone substitutes of human / animal origin or synthetic biomaterials. Mineral substitutes come in common from a bone that can be freeze dried or demineralized and deproteinized, so its mineral base is generally based on tricalcium phosphate particles *(TCP)* and Hydroxyapatite crystals. On the other hand, the scaffold of human / animal origin is marketed as Demineralized Bone Matrix *(DBM)* and consists of decalcified bone *(residual calcium <5%)* with a collagen matrix and the presence of bone-inducing growth factors capable of stimulating the activation and migration of osteogenic stem cells and progenitor cells, and induce revascularization *(Campana et al., 2014)*.

While mineral substitutes and DBM have demonstrated their effectiveness in bone formation, new findings have shown that the type and quality of bone is not biologically similar to the subject's native bone, with a scar-like acellular bone without lacunas typically seen between osteoclasts in resorbing bone surfaces *(Mordenfeld et al., 2010)*. It has also been demonstrated that the effect of new bone formation is limited by the waiting time for the maxillae to incorporate, absorb and regenerate the graft material. The presence of intact graft particles up to fourteen years *(Iezzi et al., 2007)*, with the constant presence of large giant cells around the particulate and a constant size of the original particles *(40–400 μm)* have been observed and a lower percentage of new laminar bone formation *(between 14% and 40%) (Mordenfeld et al., 2010)*

According to these antecedents, the use of the patient's own blood as scaffold would allow to form the required bone. This is possible to achieve through the controlled centrifugation of blood by obtaining platelet concentrates in a fibrin network and releasing growth factors and bioactive proteins to initiate and accelerate tissue repair and regeneration *(Altmeppen*

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et al., 2004). Compared with the most widely used scaffolds, platelet concentrates combine some important advantages such as high efficiency and cellular distribution *(Swartz et al., 2005)*, adhesion capacity *(Rosso et al., 2005)*, being cost-effective and safe for the patient, decreasing the potential risk of immune reaction or infection by a foreign body.

The first uses in the oral and maxillofacial territory were described in 1997 and defined as platelet-rich plasma *(PRP) (Marx et al., 1998)* and then in 2001 the second generation called platelet-rich fibrin *(PRF)* defined with biological characteristics much higher than its predecessor, mainly due to its metabolic capacity on osteoblasts in the production of alkaline phosphatase and osteocalcin *(Wang et al., 2017)*.

There are several studies in animal model that demonstrate the effectiveness of the use of platelet concentrate in the formation of biologically stable bone compared to the use of inorganic or collagen matrices *(Skwarcz et al., 2019)*, and even favor the repair of exposed fractures *(Dülgeroglu & Metineren, 2017)*. However, in models of maxillary sinus lift elevation in sheep showed that the use of PRF had lower bone density compared to the use of autogenous bone-allograft mixture, and even presenting remains of the platelet concentrate after 9 months of surgery *(Ocak et al., 2017)*. Therefore, the use of platelet concentrate *(PRP, PRF or its derivatives)* should be analyzed with caution, since there are reports that analyze the risk of bias presented in the reports highlighting important limitations in terms of low quality and high heterogeneity, hindering the understanding of the achievement of the observed results to be used in a general way in the daily clinic.

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