Effect of hormone levels, gender, body mass index, age and life-style parameters on human craniofacial bone regeneration with tricalcium phosphate grafts

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Introduction: Augmentation of the maxillary sinus has become a well-established pre-implantology procedure for alveolar ridge augmentation of the posterior maxilla. Over the last decade, the use of tricalcium phosphate (TCP) particles as alloplastic bone graft material for sinus floor augmentation procedures (SFA) has received increasing attention in implant dentistry.[1,2] However, little is known regarding the effect of patient-specific parameters such as hormone levels, gender, body mass index (BMI), age and life-style parameters on bioactive ceramic stimulated bone regeneration. Expanding this knowledge base, however, is of great importance, with respect to tailoring and optimizing treatment regimes for individual patients in view of pursuing an individualized orofacial medicine. The objective of this study was to elucidate the associations between these patient-specific factors and bone formation after SFA, when utilizing a bioactive TCP grafting material.

Methods: The study comprised a consecutive series of 120 participants, 60 women (ranging in age from 30-79 years, mean 60.7 years) and 60 men (aged 24-80, mean 58.3). In all patients SFA was required in order to facilitate dental implant placement in the posterior maxilla. Since the residual alveolus was 1-3 mm in height, a staged approach was used. Medical history and lifestyle information was obtained by questionnaire. This was in addition to determining the BMI. Levels of serum estradiol (E2), total testosterone (TT), free testosterone, sex hormone binding globulin (SHBG), and the free androgen index (FAI) were measured by radioimmuno-assay (RIA) and electrochemoluminescent-immunoassay (ECLIA). SFA was performed using a combination (10:1 ratio) of pure synthetic ß-TCP granules with a porosity of 65% and a grain size of 700 to 1400 µm and autogenous bone chips. Dental implants were placed 6 months after SFA. At implant surgery when preparing the implant bed, cylindrical biopsies, 2.5 mm in diameter and 8 mm long, were sampled using a trephine drill. The tissue samples were fixed in an alcohol based fixative Histochoice (Amresco, USA) and processed for hard tissue histology using a methodology, which facilitated performing immunohistochemical analysis on resin embedded undecalcified hard tissue sections, as described previously.[1,3] Immunohistochemical staining was performed using primary antibodies specific to collagen type I (Col I), alkaline phosphatase (ALP), osteocalcin (OC) and bone sialoprotein (BSP).[1,3] First, histomorpho-metric evaluation of the sections was performed. To this end, a rectangular area 6 mm^2 in size was defined in each section at a distance of 3 mm from the native alveolar crest. The bone area fraction was measured using a light microscope in combination with a digital camera (Colourview III) and SIS Analysis software (Olympus, Germany).[1,3] Second, semi-quantitative analysis of the immunohistochemical staining was performed. A scoring system quantified the amount of staining observed using light microscopy. A score of (+++), (++) and (+) corresponded to strong, moderate or mild, whereas a score of (0) correlated with no staining.[1,3] The Wilcoxon rank-sum U test, Spearman correlations and linear regression analysis were used to explore the association between bone formation and BMI or hormonal factors.

Results: Six months after sinus floor augmentation partial resorption of the grafting material had occurred. The residual granules were partially embedded in newly formed bone, which was predominantly lamellar bone without any signs of inflammatory tissue response in any of the patients. Good bone bonding behavior was observed as well as bone formation within the degrading particles. This was accompanied by expression of Col I, ALP, BSP and OC in osteoblasts of the newly formed bone in contact with the TCP particles. Linear regression analysis and spearman correlations revealed significant associations between BMI as well as logE2 and bone formation with BMI ($p=0.03$, F-test) and logE2 ($p<0.045$) being significantly positively associated with the amount of bone formation in men (Fig. 1), while in female patients there was no statistically significant association between BMI ($p=0.45$) or Log E2 and the amount of bone formation even after adjustment for age and smoking status. Histomorphometry revealed trends toward greater bone formation and osteogenic marker expression with non-smokers compared to smokers.

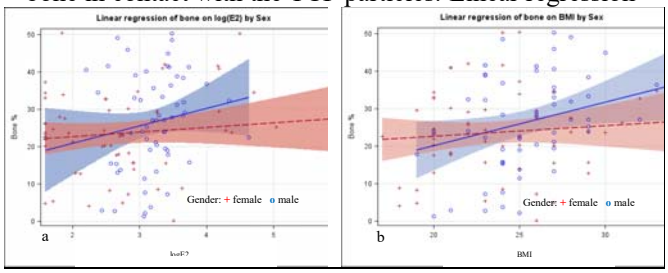

Figure 1 depicts the graphs for the linear regression analyses employed to explore the associations between: a. TCP stimulated bone formation (bone area fraction) and log (E2), b. bone formation and BMI for male and female patients, 6 months after SFA.

Discussion / Conclusions: In male patients, higher E2 levels and higher BMI enhanced TCP stimulated craniofacial, i.e. intramembranous bone repair, which is in agreement with the orthopedic literature dealing with osteoporosis related issues.

References:
[1] Knabe C. Biomaterials 2008;29:2249-2258.
[2] Bohner M. Mater Today 2010;13:24-30.
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