On tissue reactions to dentin as a bone substitute material

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Biotech-huset, Arvid Wallgrens Backe 20, Plan 5, Göteborg, torsdagen den 7/9 2017, kl. 13.00.

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Avhandlingen baseras på följande delarbeten

I. Al-Asfour A*, Farzad P*, Andersson L, Joseph B, Dahlin C. Host tissue reactions of non-demineralized autogenic and xenogenic dentin blocks implanted in a non-osteogenic environment. An experimental study in rabbits. Dent Traumatol. 2014;30:198-203 *Equal contribution

II. Farzad P, Al-Asfour A, Dahlin A, Andersson L, Dahlin C. Integration of dental implants in conjunction with grafted dentin. An experimental study in the rabbit maxilla. Oral Health Dent Manag 2015;5:289-293

III. Farzad P, Lundgren T, Al-Asfour A, Andersson L, Dahlin C. Integration and characterization of decalcified and non-decalcified dentin in conjunction with dental implants. An experimental study in rabbit tibia. In Manuscript

IV. Al-Asfour A*, Farzad P*, Al-Musawi A, Dahlin C, Andersson L. Demineralized xenogenic dentin and autogenous bone as onlay grafts to rabbit tibia. Implant Dent 2017;26:232-237. *Equal contribution

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER

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Abstract

Background Reconstruction of the jaws due to resorption of the alveolar crest may require bone augmentation prior to installation of endosseous implants. Active research on new bone graft materials with bone regeneration ability equivalent to autogenous bone but without the limitations of allogenic, xenogenic and synthetic bone are constantly ongoing. From clinical and experimental studies, it has been demonstrated that replanted In order to possibly modify treatment protocols and also exploring possible cost-benefit alternatives to commercially available bone replacement materials, there has been an increased interest to explore the use of human dentin as a source for graft material.

Aims The aim of the first study was to evaluate and compare the host tissue response to autogenous and xenogenic non-demineralized dentin blocks implanted in non-osteogenic areas, the abdominal connective tissue and femoral muscle of rabbits. The objective of the second study was primarily to evaluate the healing pattern of xenogenic non-demineralized dentin granules and dentin blocks grafted to maxillary bone of rabbits and secondarily to study integration of titanium micro-implants installed in grafted areas. In paper III, we sought to evaluate the healing pattern of xenogenic demineralized dentin granules and dentin blocks grafted to cavities created in tibial bone of rabbits, secondarily to study integration of titanium micro-implants installed in grafted areas and thirdly to investigate the morphological appearances and differences between demineralized and non-demineralized dentin by means of Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray (EDX). Finally, the objective of study IV was to compare the host tissue response and remodeling of onlay grafts of demineralized dentin in comparison to onlay bone grafts transplanted to the native tibial cortical bone wall.

Material and methods In study I, fifteen 6-month old New Zealand male white rabbits were used. Dentin autografts taken from the same rabbit and dentin xenografts taken from human premolars were implanted in abdominal connective tissue and femoral muscles. All rabbits were sacrificed after 12 weeks for light microscopic analysis. In study II, fifteen 6-months old New Zealand male rabbits were used. Dentin blocks and dentin granules from human premolars were implanted in cavities prepared on either side of the maxilla (n=15x2). After a healing period of 6 months, one micro implant (5 mm long, 2 mm in diameter) was installed in each surgical site. All rabbits were sacrificed 24 weeks after implant installation. The specimens were studied by light microscopic and histomorphometric analysis. Study III included twelve 6-month old New Zealand male, white rabbits. Dentin blocks and dentin granules from human premolars were implanted in cavities prepared on both tibial bones. Twelve hours prior to grafting the dentin grafts were rinsed in saline and demineralized on its surface by being placed in 24% EDTA neutral, pH7, for 12 hours. After a healing period of 24 weeks, one micro implant was installed in each surgical site. To characterize the grafts, twelve additional dentin blocks were prepared in standardized sizes. All samples were conditioned in 24% EDTA neutral, pH7, for 12 hours followed by a second x-ray analysis. Four samples were chosen for conventional SEM and energy dispersive X-ray analysis (EDX), both image mode and element analysis mode. In study IV, we used eight 6-months old New Zealand male rabbits. Standardized sized dentin blocks from human premolars and similar autogenous bone blocks, harvested from tibia were grafted as onlay blocks on each tibia (n=8x2). All animals were sacrificed after a healing period of 12 weeks. Descriptive histology as well as histomorphometric analysis of the remaining dentin, bone graft and soft tissue was determined using light microscopy.

Results Study I showed only minor signs of heterotopic bone formation. There were no significant differences between autografts and xenografts or grafts implanted in connective tissue or muscle with regards to tissue reactions except for a significant difference ($P = 0.018$) in findings of more local inflammatory cells in relation to grafts placed in connective tissue in the autograft group. In study II, no statistically significant difference could be observed in BIC and BA between dentin and native bone. Overall the BIC and percentage of new bone fill of the block specimens were higher than the same parameters for the particulate graft. Study III showed a tendency towards higher BIC and BA for the EDTA conditioned dentin in conjunction with installed implants, but the difference was not statistically significant. In addition, on the demineralized dentin surface the organic marker element C dominated, as revealed by EDX image mode. The hydroxyapatite constituents Ca, P and O were close to devoid on the dentin surface. A similar pattern was discerned from the semi-quantitative data analysis where the organic markers C and N dominated. Study IV showed that in general, both the dentin and bone block grafts were fused to the bone, resorbed and replaced by bone and connective tissue to a varying degree. Resorption cavities could be seen in the dentin with bone formation. Zones of osseous replacement resorption of the dentin could be noted. In both graft types, higher rate of bone formation was seen at the interface between graft and recipient site.

Conclusion Non-demineralized dentin, whether autogenous or xenogenic did not have the potential to induce bone formation when implanted in non-osteogenic areas such as the abdominal wall and abdominal muscle of rabbits. Limited or no bone contact between micro-implants and xenogenic non-demineralized dentin grafts could be seen. Demineralized xeno- genic dentin onlay grafts showed similar resorption characteristics as autogenous bone onlay grafts, being resorbed in a similar rate during 12 weeks. New bone formation occurred mainly in terms of replacement resorption in the interface between dentin/bone graft and native bone. The bone inductive capacity of the dentin material seemed limited although demineralization by means of EDTA indicated a higher BIC and BA value in conjunction with installed implants in the area.

Keywords: Grafted dentin, tissue reaction, bone blocks, dental implants, experimental study

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