

On Platelet-Rich Plasma in Reconstructive Dental Implant Surgery

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i Hörsal A 404 vid Avdelningen för Biomaterialvetenskap, Medicinargatan 8b, våning 4, fredagen den 8:e december 2006, kl. 13.00 av

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Avhandlingen baseras på följande delarbeten:

- I **Thor A, Wannfors K, Sennerby L, Rasmusson L.** Reconstruction of the severely resorbed maxilla with autogenous bone, platelet-rich plasma and implants: 1-year results of a controlled prospective 5-year study. Clin Impl Dent Rel Res 2005;4:151-160
- II **Thor A, Franke.Stenport V, Johansson C, Rasmusson L.** Early bone formation in human bone grafts treated with platelet-rich plasma. Int J Oral & Maxillofac Surg 2006, Accepted.
- III **Thor A, Rasmusson L, Wennerberg A, Thomsen P, Hirsch J-M, Nilsson B, Hong J.** The role of whole blood in thrombin generation in contact with various titanium surfaces. Biomaterials 2006, In press.
- IV **Thor A, Sennerby L, Hirsch J-M, Rasmusson L.** Bone formation at the maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material –an evaluation of 20 patients treated with 44 Astra Tech implants. J Oral & Maxillofac Surg 2006, In press.
- V **Thor A, Hong J, Zellin G, Sennerby L, Rasmusson L.** Correlation of platelet growth factor release in jawbone defect repair – a study in the dog mandible Int J Oral & Maxillofac Impl 2006, Submitted.

Abstract

Background Severe atrophy of the edentulous maxilla may require augmentation before implants can be placed. Autogenous bone has been used for reconstruction in block or in particulated form. Platelet-rich plasma (PRP) has been suggested to enhance the healing of bone grafts, as activated platelets release autogenous growth factors (GFs) into the wound healing site. Additionally, the GFs of PRP are suggested to enhance the integration of implants into bone. However, controversies exist in the literature with respect to the effect of combining PRP with bone grafts, or implants, as the concept has been evaluated in different study models with a wide range of results.

Aims The first two Papers presented, evaluates the effects of PRP in conjunction with autogenous bone grafts and subsequent installation of implants. Paper III explores the thrombogenic properties *in vitro* of titanium in whole blood and PRP and also evaluates the potential effect of a fluoride titanium surface modification regarding the thrombotic response. Furthermore, a recently developed surgical procedure is evaluated in Paper IV, where simultaneous sinus mucosal lining elevation and installation of implants is performed without the addition of any graft material. Finally in Paper V, an attempt to correlate platelet count, GF release in PRP and its effect on bone formation is performed in a canine peri-implant defect model, where additionally, the modified surface from Paper III is further evaluated.

Materials & Methods In Paper I, 19 patients were subjected to autogenous bone grafting from the iliac crest to the maxillary sinus with or without PRP in a *split mouth* setting. Implants were installed (n=152) after 6 months of healing. Patients were followed with Resonance Frequency Analysis (RFA) and radiological follow-up up to 1 year after loading of implants. 3 months after grafting, biopsies were retrieved and micro implants installed in the grafted site, left to heal for 3 months and thereafter collected with surrounding bone, simultaneously with installation of dental implants. Biopsies from 3 and 6 months were evaluated regarding new bone formation and bone-implant contact in Paper II.

In Paper III, *in vitro* tests with the heparinised slide chamber model were performed. In this model, the tested biomaterial is the only part of a secluded chamber that is not furnished with heparin, and therefore the tested surface is allowed to cause thrombotic reactions in e.g. blood or PRP, that subsequently can be quantified regarding e.g. generation of thrombin and platelet activation.

Paper IV consisted of 20 patients, followed clinically and with radiographs for a minimum of 1 year. These patients were all subjected to elevation of the sinus mucosal lining, where a bone window was cut out in the sinus wall and replaced after installation of implants (n=44) consequently tenting the mucosal lining. In Paper V, 6 dogs were used. Peri-implant defects were created in the mandibles and implants with and without a fluoride titanium surface were installed. PRP or whole blood thereafter filled the defects before closing of the surrounding soft tissues and left to heal for 5 weeks before collection of samples for histomorphometric evaluations.

Results Paper I showed an overall survival rate of 98.7 % after 1 year in function and stable marginal conditions regardless use of PRP or not. RFA disclosed significantly higher values for the PRP side at abutment connection after 6 months but not at the 1 year follow up. Early bone healing was enhanced with PRP as evaluated in biopsies collected from grafts after 3 months of healing, however, no differences were found in biopsies with micro implants after 6 months.

Whole blood showed a stronger activation of the coagulation system, in Paper III, and a fluoride modification of a titanium surface seemed to augment the effect.

In Paper IV, the survival rate of implants was 97.7% after a minimum of 1 year of evaluation and the average bone gain was 6.51 mm. Marked bone formation was observed around implants also when installed in diminutive amounts of bone.

In Paper V, the use of PRP added no significant value to the healing of defects. Regardless of PRP or blood in the defects, a fluoride titanium surface modification enhanced the bone healing significantly.

Conclusions This thesis supports the use of PRP in augmentation with particulated autogenous bone due to enhanced early healing and enhanced handling abilities. The use of PRP and implants in combination can not be supported as a result of *in vitro* and experimental animal studies performed in this thesis. Implant surface characteristics seems to be more important. Bone grafts may be obviated during sinus lift surgery if the described method is used and will result not only in acceptable results of implant integration, but also in minimising morbidity of patients.

Keywords: autogenous bone graft, bone formation, coagulation, clinical study, complement, dental implant, experimental study, growth factors, platelet activation, platelet-rich plasma, sinus lift surgery, thrombogenicity

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