INFLUENCE OF PLATELET RICH PLASMA ON OSSEOINTEGRATION IN CONTROLLED DIABETIC PATIENTS

by

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LIST OF ABBREVIATIONS

Platelet rich plasma	PRP
Microliter	µl
Millimeter	mm
Standard Deviation	SD
Milliliter	ml
Newton	N
Celsius	C
Percent	%
Temporal Subtraction	SR
Resonance Frequency Analysis	RFA
Scanning Electron Microscopy	SEM
Newton centimeter	Ncm
milliAmpere	mA
kiloVolt	kV
megaHertz	MHz
Orthopantomogram	OPG
Charged coupled device	CCD

PENGARUH PLATLET YANG KAYA PLASMA TERHADAP OSEOINTEGRASI DALAM KALANGAN PESAKIT DIABETES TERKAWAL

ABSTRAK

Kadar kejayaan implan pergigian dalam kalangan pesakit diabetes terkawal adalah lebih rendah berbanding pesakit normal dan melihatkan kepada bilangan pesakit diabetes yang ramai, penyelesaian dan pembaikan amat diperlukan. Pesakit diabetes mempunyai kadar penyembuhan tulang dan luka yang lebih lambat jika dibandingkan dengan pesakit normal. Objektif kajian ini adalah untuk memperbaiki kadar kejayaan dengan menggunakan implan yang invasif secara minimum untuk mengurangkan saiz luka dan juga penggunaan plasma yang kaya dengan platlet autogenus (PRP) untuk menggalakkan penyembuhan tulang. Ini adalah ujian klinikal bukan secara rawak yang menggunakan rekabentuk 'split-mouth' dan terdiri daripada pesakit-pesakit yang dipilih dari klinik diabetes di Hospital Universiti Sains Malaysia. Dengan menggunakan protokol surgeri satu peringkat, sejumlah 28 implan 'Mini Drive Lock' (Intra-lock® USA) dengan kepanjangan 10, 11.5, 13 dan mempunyai diameter 2.0 mm dari 2.5 mm telah disisipkan pada pesakit-pesakit edentulus dan separa edentulus. Pesakit-pesakit yang digolongkan sebagai pesakit diabetes terkawal mempunyai HbA1c = 7 atau kurang, FBS = 7 mmol/L atau kurang, RBS = 10 mmol/L atau kurang. Jumlah saiz sampel ialah 14 pesakit, setiap pesakit menerima dua implan (n=28 implan, 14 = ujian dan 14 = terkawal) di mana satu implan (tanpa PRP) telah diletakkan dan satu lagi implan (dengan PRP) diletakkan pada bahagian lateral kontra rahang yang sama. Implan-implan telah diletakkan pada maksila atau mandibel setiap pesakit. Keputusan

daripada 14 implan ujian dan 14 implan terkawal adalah dilaporkan. Penilaian ketumpatan radiografi telah dilakukan pada minggu ke 3, minggu ke 6 dan minggu ke 9 selepas implan diletakkan. Pengukuran telah dilakukan pada 5 titik di sekeliling implan-implan menggunakan histogram dan densitometri dengan perisian VIXWIN 2000 Ver. 1.8. Sejumlah 28 implan telah diletakkan, satu implan tidak mencapai kestabilan primer pada kedudukannya disebabkan oleh kekurangan kelebaran tulang dan telah ditanggalkan dan ia tidak dianggap sebagai kegagalan untuk bercantum. Pada minggu ke 9, kesemua 27 implan mini yang telah diletakkan menunjukkan oseointegrasi pada radiograf. Secara statistiknya keputusan menunjukkan tiada perbezaan secara signifikan di antara ketumpatan radiograf kedua-dua kumpulan (P=0.125) semasa kajian dijalankan. Walaubagaimana pun implan-implan mini telah berjaya pada minggu ke 9. Kajian menunjukkan tiada perbezaan secara signifikan dalam penyembuhan luka antara kumpulan PRP dan bukan PRP dalam kalangan pesakit diabetes terkawal. Kedua-dua kumpulan menunjukkan oseointegrasi yang baik secara radiografi dan kestabilan implant telah dikekalkan sepanjang 9 minggu walaupun 'loading' telah dilakukan dengan serta-merta. Penggunaan prosedur implan yang invasif secara minimum dapat membantu membaiki penyembuhan luka tisu lembut dan oseointegrasi dalam kalangan pesakit diabetes, dengan atau tanpa PRP. Kesimpulannya, penyembuhan luka untuk pesakit-pesakit diabetes amat bergantung kepada keparahan trauma tisu. Oleh itu penekanan tehadap teknik pemasangan implant patut diambil kira.

INFLUENCE OF PLATELET RICH PLASMA ON OSSEOINTEGRATION IN CONTROLLED DIABETIC PATIENTS.

ABSTRACT

Success rates of dental implants in controlled diabetics is less than normal patients and considering the large number of diabetic patients a solution and improvement is needed. Diabetic patients are known to have delayed bone and wound healing compared to normal patients. The objective of this study was to improve success rates by employing a minimally invasive implant to decrease the size of the wound and autogenous platelet rich plasma (PRP) to enhance the bone healing. This was a Non-randomized clinical trial employing a split-mouth design consisting of patients selected from the diabetic clinic at the Hospital University Sains Malaysia. Using a one-stage surgical protocol, a total of 28 Mini Drive Lock implants (Intra-lock® USA) implants with lengths of 10, 11.5, 13 and a diameter of 2.0 mm of 2.5 mm were inserted in edentulous and partially edentulous patients. Patients included as controlled diabetic had HbA1c = 7 or less, FBS = 7 mmol/L or less, RBS = 10 mmol/L or less. Total sample size was 14 patients, each patient received two implants (n=28 implants, 14 = trial & 14 = control), where one implant (without PRP) is placed, and another implant (with PRP) is placed on the contra lateral side of the same jaw. Implants were placed in the maxilla or the mandible in each patient. Results of 14 test and 14 control implants is reported. Radiographic density evaluation was done at 3, 6 and 9 weeks after placement. Measurements were done at five points around the implants using histogram and densitometry with the VIXWIN

2000 Ver. 1.8 software. A total of 28 implants were placed, 1 implant did not attain primary stability at placement due to lack of bone width and was removed, it was not considered failure to integrate. At 9 weeks all 27 mini implants placed showed osseointegration on radiographs. Statistically, results showed no significant difference between radiographic density of the two groups (P=0.125) during the time period of the study, however mini implants were successfully followed up at 9 weeks. This study showed no significant difference of wound healing when comparing groups of PRP and non-PRP in controlled diabetic patients. However both groups have shown good osseointegration radiographically and the stability of implants was still maintained over the period of nine weeks although with immediate loading. The use of minimally invasive implant procedure can help to improve the soft tissue wound healing and bone osseointegration in diabetic patients with or without PRP. In conclusion the wound healing in diabetic patients is highly dependant upon the severity of tissue trauma, therefore emphases on implant placement technique should be considered.

CHAPTER 1

INTRODUCTION

1.1. Background

The focus of modern dentistry is geared towards the prevention of oral soft and hard tissue loss. The field of implant dentistry has brought a great change in the way dentists treat edentulous spaces and prevent bone loss.

When a tooth is lost, the alveolar bone is lost in width and height. In some cases the bone resorbs beyond the alveolar bone and into the basal bone (Palmer *et al.*, 2002). Study done on bone have revealed that under physiological load bone loss ceases or is minimized (Mische, 1999). This physiological load can be achieved when dental implants are placed in these edentulous sites. Since the load applied by implant treatment prevents bone loss, implant dentistry is in fact preventive dentistry and a method of bone preservation. As time went by improvements took place in implant dentistry, less traumatic, simpler, less time consuming and economical implants were developed (Worthington, 2005). An attempt to improve the implant success rate and decrease the time of functional loading became the goal of implant dentistry.

Diabetes Mellitus is a medical concern when it comes to implants and poses a threat to implant success as patients in this category have certain impairments which must be addressed. In diabetic patients the osteoclastic activity is accelerated and osteoblastic activity is decreased which results in impaired bone healing in type II diabetics (Suzuki *et al.*, 2005). The diabetic population of

the world including Malaysia makes up a large part of those needing dental care, especially implants. However due to economic and medical concerns they often are not treated.

The average number of missing teeth between the ages of 55-65 is 10, which underlines the need for dental implants at a later age. The partially edentulous population above the age of 65 years has lost an average of 17.9 teeth. At the age of 65 and above diabetes mellitus affects more than 18.4% of all individuals (Misch, 1999)

When dentists want to place implants in diabetic patients apart from other problems they face, two major problems concerning long term success. These are the impaired bone and soft tissue healing (Balshi and Wolfinger, 1999). To overcome this problem, implants which have a minimally invasive surgical procedures would be of choice. Apart from this, an adjunct to the healing process such as growth factor would also be of great help.

1.2 Osseointegration as a criterion for implant success

The definition of osseointegration is the structural and functional connection between ordered living bone and the surface of a load carrying implant (Branemark *et al.*, 1992). Watzek described osseointegration or bone growth around an implant similar to healing-in or stable osteosynthesis as observed in closely approximated bone fragments (Watzek, 1996). This process of bone formation is dependent upon osteoblasts and osteoclast for bone formation and resorption respectively. Thus if this process is hindered in any way the process

of osseointegration would be affected directly. Hence in diabetic patients the osseointegration process must be measured to determine if implants are successful.

Scientists have tried to quantify and measure osseointegration in order to successfully load implants when they are integrated or defer loading of implants till such time as they are integrated enough. Other reasons for implant osseointegration evaluation have been to find the best implant materials, ideal surface properties and the effects it may have on osseointegration.

Various methods for measuring osseointegration were suggested. Radiographs, computerized tomography, resonance frequency analysis, periotest, digital subtraction radiography and computer assisted digital image analysis using the help of software are some of the methods used (Misch, 2005).

1.3 Growth factors as an adjunct to bone healing

Growth factors are proteins which occur naturally and have the capability of stimulating cell proliferation and cell differentiation; these are involved in the daily growth and regeneration of cells of the body. If an injury takes place, the growth and regeneration of the injured part of the body is methodically carried out and rebuilt with the help of growth factors. These growth factors work in such a way where some cause inhibition and others cause proliferation and differentiation.

Of many sources of growth factors, platelets are one of the known sources. The alpha granules contain up to seven different growth factors (Marx, 2004). Platelets are a fraction of whole blood which can be separated by means of gradient density centrifugation, with this came the idea of using them as a source of growth factors. Hence, platelet rich plasma (PRP) meaning platelet in a small quantity of plasma was introduced. Many studies in the past have shown promising results with platelet rich plasma where as others have shown little benefit. Platelet rich plasma is used since its discovery about 10 years ago in vertical and horizontal bone height reconstructions, bone grafts, sinus lift procedures, as coatings on implants. It has been used in medical field in articular cartilage avulsion cases, diabetic foot ulcer treatments and shown good results (Marx, 2004).

Attempts have been made to individually separate the growth factors. One such genetically engineered product was the recombinant human platelet derived growth factor beta-beta (PDGF-ββ) which is approved for use in diabetic foot ulcers. In several studies it has shown shorter healing times compared to normal control (Larsen *et al.*, 2004).The use of recombinant human keratinocyte growth factor (KGF-2) has shown good results in animal model but still has not been used in humans. However the food and drug administration has approved the use of recombinant bone morphogenetic protein-2 (rhBMP-2) in spinal fusion cases. A time will come when (rhBMP-2) will be available for human use as well in the maxillofacial region. Hence, platelet rich plasma remains a valuable source of growth factors and should be considered in medically

compromised and patients with systemic disease such as diabetics and post radiation therapy patients (Marx, 2005).

1.4 A new generation of implants

In recent years dental implants which are minimally invasive have emerged. Such implants would preserve bone and soft tissue which have been a problem with implant dentistry from the beginning. They would also be of advantage to the medically compromised patients such as diabetic patients due to their minimal wound inflicting nature.

Flapless procedures is suggested by many implant companies as they are minimally invasive, giving less discomfort and shorter healing time. The mini implant system satisfied the above mentioned criteria. There was a fundamental variation from the conventional implants in its bone preparation protocol and soft tissue management. This implant was first used as a provisional implant during the time of healing for the conventional implants, where it was used to support a denture or a temporary restoration and subjected to load from the day it was placed. The dentists noticed that at the time of removal of the mini implants, there was difficulty after 3 to 6 months and had osseointegrated most of the times (Griffitts *et al.*, 2005). Based on this finding the birth of the mini implant took place with slight modifications to the initial implant for adaptation to softer bone and harder bone resulting in variations in thread design.

Another interesting finding was that mini implant was adequately integrated which meant that the implant could be immediately functionally loaded, a new