

Effect of Diabetes in Osseointegration of Dental Implant - A Review

G. PAVYA¹ and N. ARAVINDHA BABU²

Department of Oral Pathology, Tagore Dental College, Chennai – 600127, India.
Professor, Department of Oral Pathology, Sree Balaji Dental College and Hospital,
Bharath University, Pallikaranai, Chennai - 600100, India.

DOI: <http://dx.doi.org/10.13005/bpj/703>

(Received: August 15, 2015; accepted: September 20, 2015)

ABSTRACT

Diabetes Mellitus is a pandemic metabolic disease prevailing globally and is characterized by chronic hyperglycemia due to absolute or relative deficiency of insulin. It affects most parts of human body including the oral cavity. The review describes the effect of diabetes in the process of osseointegration of implants in oral cavity.

Key words: Diabetes in Osseointegration, implants, oral cavity.

INTRODUCTION

Diabetes Mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. This results in disturbances in carbohydrate, fat and protein metabolism due to insulin secretion, insulin action or both. Several pathogenetic processes are involved in the development of diabetes. These include processes which destroy the beta cells of the pancreas with consequent insulin deficiency, and others that result in resistance to insulin action. Contributing factors include genetics, obesity, physical inactivity and advancing age. Diabetes affects most parts of the human body including the oral cavity.

Definition of osseointegration

Branemark defined Osseointegration as a direct structural and functional connection between ordered living bone and the surface of a load-carrying implant⁴.

Later he redefined the definition of osseointegration as "A continuing structural and

functional coexistence, possibly in a symbolic manner, between differentiated, adequately remodeling, biologic tissues and strictly defined and controlled synthetic components providing lasting specific clinical functions without initiating rejection mechanism" in 1990.⁽⁴⁾

Biology of osseointegration

Osseointegration is an ongoing procedure representing process of bone formation and adaptation to function and repair, which takes place due to Osteoblastic and Osteoclastic activity of bone⁴.

Osteoblasts (bone forming cells) are of mesenchymal origin & they govern the activity of osteoclasts (bone resorbing cells) by secreting Osteoprotegerin (OPG), which inhibits osteoclastic bone resorption. Osteoclasts function in conjunction with Osteoblasts. This process is known as coupling⁴.

Osteocytes communicate with other bone cells through numerous cellular membrane protrusions that lie in tunnels, known as Canaliculi which participates in bone resorption and sense mechanical load on bone.

As soon as the implant is placed in the prepared site, within nanoseconds there is formation of water molecule layer around it. This layer facilitates protein and other molecules to adsorb on the implant surface. In the 2nd stage, within 30 seconds to hours after implantation, the implant surface is covered by a layer of extracellular matrix proteins. These proteins come from blood and tissue fluids at the wound site and later from the cellular activity in the periprosthetic region.

In the 3rd stage, interaction of cells with implant surface via adsorbed protein layer takes place, initiating cellular adhesion, migration and differentiation, which occurs from few hours to several days. This stage is enormously and tightly regulated by ECM proteins, cell surface-bound and cytoskeletal proteins, chemical characteristics, implant topographies and chemical ions released by the surface.

ECM is the mode through which transfer of information takes place via a no of proteins in which most of the ECM functions as cell attachment mediators, some signaling and cell-cell and cell-protein interactions.

Cell attachment takes place with the help of Integrins, Focal Adhesion and Filopodia(4).

Focal adhesion are integrin based molecular compositions of cells participating in adhesion dependent signaling and link ECM to cell.

Filopodia are Actin rich cell extensions through which cell adherence takes place on rough surface. Filopodia scan substrate's surface structures and stabilize the cell.

Bone formation occurs in 2 directions, from implant surface towards bone and from bone towards implant surface also known as contact osteogenesis and distance osteogenesis⁴.

In contact osteogenesis, the implant surface has to be colonized with bone cells before bone matrix formation can begin. In Contact osteogenesis, bone forms at a 30% faster rate than that of in distance osteogenesis⁴.

In distance osteogenesis, new bone is not formed at the implant surface, but implant gets surrounded by bone⁴.

Effects of diabetes on osseointegration of implants

Only experimental studies with animals have shown the effect of diabetes and insulin therapy on the osseointegration of implants.

Results of osseointegration of implants in experimental models of diabetes

The analysis of the effect of diabetes on implants has revealed an alteration in bone remodelling processes and deficient mineralization, leading to less osseointegration. Although the amount of bone formed is similar when comparing diabetes-induced animals with controls, there is a reduction in the bone-implant contact in diabetics. The rate of new bone formation in the periosteal region is comparatively higher than that occurs in endosteum & medullary canals. The reduction in the levels of bone-implant contact confirms that diabetes inhibits osseointegration¹. This situation may be reversed by treating the hyperglycaemia and maintaining near-normal glucose levels. The implants will integrate in areas predominated by cortical bone in a higher rate.

Effect of insulin on bone and osseointegration of implants in experimental models

Constant hyperglycaemia delays the healing of the bone around the implants. Osteopenia associated with diabetes induced in animals can be reversed when treatment with insulin is applied. When implants are placed in the tibia of diabetic rats, a reduction of 50% is observed in the bone formation area and on the bone - implant contact surface. If insulin is used, the ultra-structural characteristics of the bone-implant interface become similar to those in the control group. These results suggest that metabolic control is essential for osseointegration to take place. Although the insulin therapy allows regulation of bone formation around the implants and increases the amount of neoformed bone, it was not possible to equal the bone-implant contact when compared with non-diabetic groups¹.

Implants in patients with diabetes mellitus

Diabetes is currently classified as a relative contraindication for implant treatment. Compared with the general population, a higher failure rate has been seen in diabetic patients with adequate metabolic control. Reviewing the literature published, most of the studies shows a higher index of failures during the first year after placing the implants. Microvascular involvement is one of the factors implicated in implant failures in diabetic patients. The microvascularization alteration associated with diabetes leads to a diminished immune response and a reduction in bone remodelling processes. Most of the articles revised conclude that, despite the higher risk of failure in diabetic patients, maintaining adequate blood glucose levels along with other measures improves the implant survival rates in these patients.

Special considerations for the placement of implants in diabetic patients**Healing and risk of post-operative infection**

The repercussions of diabetes on the healing of soft tissue will depend on the degree of glycaemic control in the peri-operative period and the existence of chronic vascular complications. Patients with poor metabolic control have their immune defences impaired: granulocytes have altered functionality with modifications in their movement towards the infection site and a deterioration in their microbicide activity, with greater predisposition to infection of the wound. In addition, the high concentration of blood-glucose and in body fluids encourages the growth of mycotic pathogens such as *Candida*. The microangiopathy arising as a complication of diabetes may compromise the vascularization of the flap, thus delaying healing and acting as a gateway for the infection of soft tissue.

Good glycaemic control:

Although diabetes is considered as a contraindication for implant placement, the surgery can be performed when the patient is maintaining his glycaemic condition in a near normal level. The glycaemic level can be considered as near normal if the patient is having the all the below mentioned criterias

- ˘ HbA1c < 7%
- ˘ pre-prandial glycaemia (mg/dL): 80 - 110

- ˘ Maximum post-prandial level of glycaemia (mg/dL): < 180

- ˘ Pre-operative antibiotic therapy

- ˘ 0.12% chlorhexidine mouthwash

Effect of diabetes on bone and osteointegration

The persistent hyperglycemia in diabetic individuals, inhibit osteoblastic activity and alters the response of parathyroid hormone which in turn decreases collagen formation during callus formation, induces apoptosis in lining cells of bone and increases osteoclastic activity due to persistent inflammatory response. It also induces deleterious effect on bone matrix and diminishes growth and accumulation of extracellular matrix. The consequent result is diminished bone formation during healing(2).

Type -1 diabetes causes decreased bone mineral density, as well as reduced bone formation and higher bone resorption whereas Type -2 diabetes produces normal or greater bone mineral density in some patients. It has been observed that insulin not only reduces the deleterious effect of hyperglycemia by controlling it but also stimulates osteoblastic activity. Hence, bone matrix formation in insulin treated experimental models is similar to control ones. Most of the studies have been performed in streptozotocin/alloxan induced diabetic experimental models (rat/rabbit) to observe osseointegration of implants. Histochemical/histomorphologic/planimetric/ biomechanical torque/manometric analysis showed that bone volume formed in diabetic animals was similar to non-diabetic animals. Bone implant contact (BIC) in diabetic animals was lesser compared to non-diabetics(2). The rate of mineral apposition in newly formed bone and bone density around implant was significantly less in uncontrolled diabetic animals. The bone volume and bone density around implant in insulin controlled diabetic animals was observed similar or greater to non-diabetic but BIC was found significantly less(Even in insulin controlled diabetic animals).

Only few case studies for histological observation of dental implant osseointegration in human being have been reported. In one report, an implant was placed and intended to support an overdenture in 65-year-old diabetic women was

retrieved after 2 months due to prosthetically unfavorable condition. In histological analysis, no symptoms of implant failure recognized with 80% bone implant contact ratio. A case of diabetes mellitus type-2 having implant failure within 6 months, was reported by Park JB with conclusion that osseointegration was not affected by diabetes mellitus as there was no sign and symptoms of failure before loading.

Success/failure of dental implants in diabetic patients

Most of the studies observed slightly high percentage of early failure of implants in diabetics compared to late failure. Some reports indicated increased failure rate within first year of placement of implant². The success rate of implants in diabetic patients ranges from 85.5 -100%(2). Most of the studies were of opinion that success rate in well/fairly controlled diabetics was either equal or insignificantly lower than normal individuals.

However, it is noteworthy that number of patients and implants placed (4 implants in 3 patients) in uncontrolled diabetics was quite low and all the patients selected were free of micro and macro-vascular complications. Only two studies reported significantly high failure of implant in diabetic patients even when glucose level was adequately under control. One of these studies retrospectively included early, as well as late failures of implants over the period of 10 years but did not specify the glycemic control over that period. While other study, prospective in nature, observed significantly high early failures with probable reason that placement of multiple adjoining implants in diabetic patients increased the failure rates due to large wound, delayed healing and greater force posed over implants².

Most of the studies observed slightly high percentage of early failure of implants in diabetics².

Late onset complications of diabetes²

Microvascular complications	Macrovascular complications
Retinopathy	Cardiovascular disease
Nephropathy	Cerebrovascular diseases
Peripheral and autonomic Neuropathy	Peripheral arterial disease
Foot disease	

Observation shows high early failure in diabetic patients as such patients experienced low implant stability quotient (ISQ) in period of 2-12 weeks and lower the level of glycemic control, higher the amount of ISQ reduction and longer the duration of recovery in ISQ at base level was required. However, most of implants attained base level of stability within 4 months even in uncontrolled diabetic patients, if the patients were refrained with micro- and macro-vascular complications².

Duration of diabetes significantly affected the success of dental implant, observed in one study while another did not demonstrate significantly higher late implant failures in diabetic patients even with longer duration. Overall lower success of implant in patients with diabetes of longer duration may be due to higher chance of micro-vascular

complications which consequently lead to delayed healing around implants and hence higher early failure(2).

Few studies, demonstrated significantly higher failure of implant in type-1 diabetic patients than patients with type-2 diabetes patients. While one study did not find any significant difference in late failure of dental implant in type-1 and type-2 diabetic patients.

Higher failure rate of implants in diabetic patients may be due to depletion of insulin in tissues² whereas presence of insulin in tissues of type-2 diabetic individuals may reduce deleterious effect of hyperglycemia.

Immediate loading did not significantly affect the survival of dental implant in diabetic

patients provided their plasma glucose level were under normal range. The controlled mechanical stimuli over implant can be beneficial for osseointegration and implant survival.

Reports of some study suggests that implant survival is good in females compared to males in general population².

Measures for improving success of dental implant in diabetics

Good glycemic control, preoperative and post-operative, is required to achieve improved osseointegration in diabetic patients & use of 0.12% chlorhexidine further improves the success rate⁽²⁾. Certain factors like implant surface characteristics (implant coated with bioactive material) and higher implant length and width has been shown to improve success rate of implant in diabetic patients. In few studies, it was observed that systemic administration of aminoguanidine reduced the deleterious effect of diabetes on osseointegration². A recent hypothesis was made by Bai et al that adiponectin, an insulin sensitive adipokine may improve osseointegration in diabetic patients by infusing it systemically or using locally as it has shown potent anti-inflammatory properties and increased bone density by enhancing osteoblast and inhibiting osteoclast formation².

DISCUSSION

Most of the experimental studies have been indicated that the bone matrix formation and bone mineralization was almost equal in controlled diabetic and non-diabetic animals but BIC was lower even in controlled diabetic subjects. Number of studies has proposed and explained mechanism of deleterious effect of diabetes over wound healing and true association (osseointegration) of bone to implant surface. However studies, performed in humans specifically with diabetes type-2, observed insignificant effect over BIC and consequently good osseointegration of dental implant in controlled diabetic patients⁽²⁾. The difference in developing diabetes (alloxan or streptozotocin destruct beta cells of Langerhans consequently induces diabetes) in experimental animals and human being (type-2 diabetes develop due to glucose

resistance at cellular level and higher level of glucose in tissue consequently suppress the function of beta cells of Langerhans in long duration) maybe one reason for the difference in BIC⁽²⁾.

Most of clinical studies reported success of dental implant in diabetic individual as good as normal peoples. The reason may appear to be the inclusion of controlled diabetics in the almost all studies. The persistent hyperglycemia is responsible for development of micro-vascular complication and consequently the early or late implant failure⁽²⁾. Hence the uncontrolled level of diabetes, reflected through measurement of glycated hemoglobin HbA_{1c} (indicate average glucose level over preceding 2-3 months period, level 6 to 8 shows well controlled, 8.1 to 10 moderately controlled and more than 10 shows poorly controlled diabetes)⁽²⁾, persistent for longer duration with sign of micro-vascular complication may affect the success of dental implant significantly. Even the fairly or moderately controlled diabetes persisting for very longer duration (more than 10 years) may produce complications and diminish the health of tissues. The compromised condition along with some unfavorable restorative factors may bargain the success of dental implants. Therefore, numerous factors associated with rehabilitation and diabetes itself, affect the survival of dental implant in diabetic subjects. Cautious consideration of the mentioned factors during rehabilitation improves the success of implants in diabetic patients.

CONCLUSIONS

- Improperly controlled diabetes leads to significant reduction of contact between bone and implant.
- Insulin therapy helps in regulating bone formation around the implant.
- Use of mouth disinfectant solutions in pre-operative and postoperative stages decreases the inflammatory complications rate during wound healing and even improves survival in the first few weeks;
- Pre and post-operative antibiotic therapy is a protective factor against the primary disorders of wound healing in the treatment of diabetic patients with implants.

- Aggravating factors associated with age, sex, tobacco, periodontal disease, and influence of dispensary program of patients should be considered
- Correct adjustment of diabetes before, during and after surgery by the patient's doctor, so that HbA1c be <7% and a blood glucose <120 mg / dl
- Antibiotic therapy should be initiated one hour before surgery and continued until the completion of the healing process
- Mouthwash before and after surgery with an oral solution of 0.12% chlorhexidine gluconate
- Patient should undergo strict dispensary and professional cleaning for diagnosing periimplant infections if any present.

REFERENCES

1. Ana Mellado Valero(1), Juan Carlos Ferrer García (2),(3), Agustín Herrera Ballester (2),(3), Carlos Labaig Rueda(1); { (1)Department of Prosthodontics and Occlusion, School of Dentistry, Valencia University; (2) Diabetes and Endocrinology Unit, Department of Internal Medicine, Valencia University General Hospital Consortium; (3) Department of Medicine, School of Medicine, Valencia University; Effects of diabetes on the osseointegration of dental implants; year 2006
2. Rajendra Kumar Dubey, Deepesh Kumar Gupta, Amit Kumar Singh; review article on Dental implant survival in diabetic patients; review and recommendations in national journal of maxillofacial surgery – in the year 2013
3. Talib Amin Naqash, Resident, Department of Prosthodontics, Sunil Jangral, Popinder Singh, Nusrat Nazir, Sheema Bashir, Samrina Gulzar, House Surgeons, Government Dental College, Srinagar, J&K, India in International Journal of Clinical Cases and Investigations(2013); review article on Diabetes Mellitus: A concern for Prosthodontic care
4. Dr. Sagrika Shukla, Dr. Ashi Chug, Dr. Lanka Mahesh, Dr. Sanjay Jadwani. Osseointegration – molecular events at the bone-implant interface- a review .
5. Christian Marmandiu¹, Christos Giannarachis¹, Vlad Gabriel Vasilescu¹, Ion Patrascu¹, Elisabeta Vasilescu² (2013); osteointegration of dental implants a chance for diabetic patients - systematic review of the literature