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Review Article

Effect of Medications in Osseointegration

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ABSTRACT

Implants have been a modern solution for treating edentulism nowadays. But the effect of certain diseases as well as medications marks a question among the dental practitioners about the survivability of implants. This article aims to discuss the effect of certain medications and its effect in osseointegration.

Keywords: Dental implant; Osseointegration; Medications; Systemic; Literature review; Drugs

1 INTRODUCTION

An efficient masticatory system is essential for maintaining a good quality of physical, mental, and social life. Disturbance in the number of teeth not only affects the neighbouring teeth, but also the teeth segments opposing the edentulous area. Tooth loss which results due to decay, periodontal disease, wear, trauma or cancer leads to a sequelae of dental problems, nutritional changes, social and personal self -esteem issues. Even though, complete dentures, partial dentures and tooth borne prosthesis are available options for rehabilitating the missing teeth, patients' often demand a more advanced & integrated solution[(1)]. Today, implants have been a common procedure for replacing missing tooth as well as for craniofacial rehabilitation.

Successful bone to implant interaction is achieved by osseointegration. A perfect osseointegration usually occurs within 3 – 6 months. During this time, certain cellular & extracellular events occur at the bone-implant interface. Certain common medical conditions may affect the normal wound healing, bone metabolism & osseointegration compromising the long-term survivability of an implant. Occurrence of such conditions alters the normal healing cascade leading to failure of osseointegration.

2 CYCLOSPORINE

Cyclosporine A (CsA) are immunosuppressants used to prevent rejections in transplant cases and to treat immune borne diseases. These drugs are meant to have anti-anabolic effects on osteoblasts and hinders the participation of T-lymphocytes in bone remodelling[(1)]. Some studies show an increased incidence of osteoporosis with these drugs[(2)]. Patients undergoing immunosuppressive medications may not be ideal candidates for implant surgery because of compromised health. The intake of this medication must be carefully evaluated while planning an implant surgery, as it is closely connected to the bone density around the implant.[(3)]

3 GLUCOCORTICOIDS

These drugs that are used to reduce inflammation in diseases, such as asthma, rheumatoid arthritis, autoimmune disorders etc.[4] Bone loss is one of the accepted side effects associated with prolonged dosage of glucocorticoids which may negatively affect osseointegration.[5] Some studies reveals the effect of glucocorticoids in reducing bone formation and increasing the resorption of bone.[6] Several other studies have also reported the loss of osseointegration associated with the chronic use of glucocorticoids.[7,8] They also have detrimental effects on bone remodelling, as they enhance apoptosis of osteoblast and promotes the transformation of bone marrow cells into adipocytes.[5]

4 ALCOHOL

Alcohol inhibits osteoclast activity, reduces bone quality, and delays fracture repairs.[9,10] Alcohol consumption is a risk factor for osteoporosis with reductions in cortical bone area and trabecular volume reported in alcoholic animal models.[11,12] Patients with excessive alcohol intake are usually at higher risk for implant failure due to delayed healing as a result of alcohol-induced deficiencies in the complement system, suppression of T-lymphocytes and impairment in the mobility, adhesion and phagocytic capabilities of the innate immune system.[13]

5 SELECTIVE SEROTONIN RE-UPTAKE INHIBITORS (SSRIS)

Low measures of serotonin in the brain have been implicated as the cause of depression and, in the last 3 decades, selective serotonin re-uptake inhibitors (SSRIs) have been used successfully to treat depression which acts by blocking the re- uptake of serotonin (5-HT) into the neurons.[14] This frees up levels of serotonin which improves electrical transmission between neurons. Several 5-HT receptors (5-HTT, 5-HTR1B, 5-HTR2A, 5-HTR 2B) are present on osteoblastic cells and helps in regulation of pathways leading to early stage cell proliferation, which gets interfered by SSRIs.[15] Studies reveal the effect of SSRIs in reducing the density of bone and the risks associated with fracture of bone. Compared with patients with no medical history, patients who used 2 or multiple SSRIs had significantly greater risk for failure of implants. Another clinically relevant effect of SSRIs related to dental implant, or any other oral surgical procedures is the risk of bleeding which can arise from combination of SSRIs with NSAIDs.[15] Clinicians serving patients under SSRI medication must consider the deleterious effects on bone and the increased risk for bleeding.

6 NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

These are commonly used for managing pain and various inflammatory conditions following dental implant surgery. NSAIDs focus on preventing the conversion of arachidonic acid to prostaglandins who primarily interferes with normal bone healing, bone formation and angiogenesis.[16] There are many studies which shows the altered healing patterns of bony fractures along the usage of NSAIDs.[17,18]

7 BISPHOSPHONATES

These are anti-resorptive agents which inhibits the osteoclast activity. These are commonly used for maintaining the bone density. They are mostly administered in intravenous forms, for treating bone diseases such as osteopenia and osteoporosis.[19] There are many clinical situations that reveal the direct relationship between bisphosphonates and osteonecrosis of the jaw (ONJ), especially in cancer patients who are receiving high medicinal doses.[20] Grant et al., in his study revealed that there is insignificant difference between patients with and without oral bisphosphonates during implant surgery in developing osteoradionecrosis.[21] Madrid and Sanz found that it is relatively safe to perform implant surgery for patients receiving bisphosphonates in oral form for a time period less than 5 years.[22] Therefore, clinicians placing implants in these patients must be aware of the risks involved.

8 CHEMOTHERAPEUTIC AGENTS

They are drugs that act on cells with rapid growth and normal cells including bone marrow, hair follicles and gastrointestinal tract.[23] These agents also affect patient's nutrition, which impairs osseointegration & wound healing of the bones.[24] Kovacs found that osseointegration can be fortunately achieved in patients when implant surgery were done at a time period of 6 months post chemotherapy.[25] There are also several other case studies conducted which shows the detrimental effects of chemotherapy on implant survival.[26,27] Hyperbaric oxygen therapy in adjunct with radiotherapy should be given if the radiation dosage exceeds 50Gy in order to reduce risk of osteoradionecrosis, fibrosis and avascular necrosis.[28]

9 PROTON PUMP INHIBITORS (PPIS)

Chronic usage of PPI's leads to chronic acid suppression and adversely affects the absorption of certain nutrients and vitamins such as Vitamin B12, Fe, Calcium and Mg. Long term usage of PPIs leads to decreased intestinal absorption of calcium (negative calcium balance), increased osteoporosis, development of secondary hyperparathyroidism and increased bone fractures leading to poor osseointegration of implants. Increase in homocysteine due to deficiency

in Vitamin B12 due to chronic usage of PPIs is a common reason for the breakdown of bone. The inhibition of phosphoetanol amine/phosphocholine phosphatase and tissue nonspecific alkaline phosphatase in the bone matrix vesicles has been found to decrease osteoblastic matrix mineralization.[29] Elevation of serum Parathyroid hormone levels and hypomagnesemia also exerts certain effects on impaired bone metabolism.[29]

10 ANTIHYPERTENSIVE MEDICATION

Antihypertensive drug plays a positive role in formation and remodelling of the bones and shows decreased chances of bone fractures, thereby enhancing osseointegration. The effects of statins (atorvastatin, fuvastatin, lovastatin, rosuvastatin, or simvastatin) on osseointegration has been evaluated by Shabnam et al., in an animal study and was found that local application of fluvastatin around titanium implants improved the osseointegration by favouring osteogenesis, calcification of peri-implant bone and improved bone-to-implant contact.[30] Statins interfere with osteoclastogenesis, expresses BMP-2, favours osteoblastic activity and reduces the matrix metalloproteinases (MMPs) thereby enhancing osteogenesis and wound healing respectively.[30]

11 CONCLUSION

Rehabilitation of a partial or completely edentulous ridges by means of dental implants is a common treatment option nowadays. For an implant therapy to be successful, proper osseointegration is demanded. Proper healing cascade at an early stage is essential for successful osseointegration. Implant therapy should be available for all patients including those who take medications for certain diseases. The biochemical interaction of these drugs with osseointegration must be properly understood by the clinician; so that long term survivability of the implant would be successful. When treating patients under medications which questions the survivability and the healing potentials, it is important to consider modifiable risk elements like smoking, poor oral hygiene, premature loading, para functional habits etc., and adopt a stricter follow-up regimen. Therefore, patient compliance along with the proper skill and thorough knowledge on effect of medications enhances the success and durability of implants.

12 CONFLICT OF INTEREST

Nil

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