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The Effect of Common Local and Systemic Conditions on Dental Implant Osseointegration: A Review of Literature

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Abstract

Context: Although dental implant (DI) is an increasingly prevalent therapeutic approach in partial or complete edentulous patients, understanding the bone healing mechanisms and effective factors on it, is still necessary for us. The initial requirement in DI success rate is to achieve a proper wound healing, DI stability and desirable osseointegration, Thereby, assessment of all probable risk factors of DI treatment should be considered prior to a treatment plan.

Evidence Acquisition: Literature searching was performed through electronic search in three data bases of MEDLINE, Google scholar and SCOPUS, and also manual search on available performed studies up to June 2013.

Results: Though, there are multiple technique-related or patient-related local and systemic factors, which may interfere with proper osseointegration or compromise the long-term implant prognosis. There are just few absolute contraindications for DI therapy such as IV bisphosphonate therapy and severe renal failure.

Conclusions: There are few absolute contraindications for DI treatment. As a whole, correct patient selection, and applying standard rules of surgical procedure and DI loading would lead to a successful DI treatment.

Keywords: Dental Implants, Osseointegration, Contraindications

1. Context

Nowadays, dental implant (DI) placement is a desirable treatment approach in complete or partial edentulous patients and plays an important role in orofacial anatomic contour reconstruction, function, health, and esthetic (1, 2). The initial goal of this type of treatment is to ensure implant success in creating and keeping a tight connection between bone and DI. Histologically, osseointegration is described as a structural and functional direct connection between vital bone and loaded DI surface without soft tissue interference. Clinically, osseointegration is an asymptomatic permanent stability of the alloplastic material (DI) in a bone with occlusal force tolerance (3). However during early healing phase, DI may fail due to lack of osseointegration, breakage or infection of peri-implant tissues after implant function, which leads to loss of implant support (4). Local or systemic disease or some other contributing factors may affect long term outcomes of implant therapy. Therefore, it is proposed that some of these factors could be identified as contraindications to DI therapy (5-7). The present study is addressing the most common local and systemic factors affecting osseointegration and final treatment result.

2. Evidence Acquisition

Literature searching was performed through electronic search in three data bases of MEDLINE, Google scholar and SCOPUS, and also manual search among available performed studies up to June 2013.

3. Results

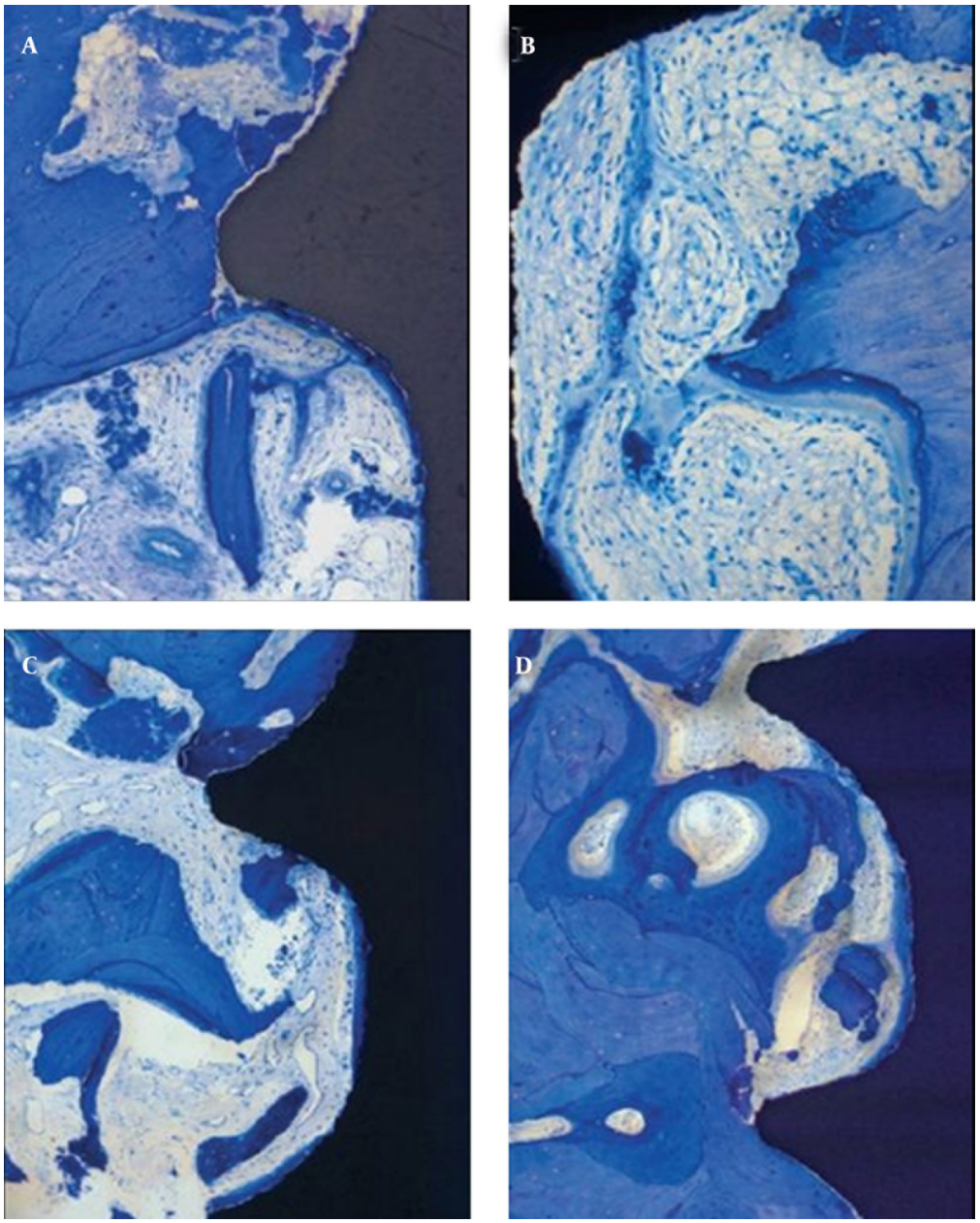
3.1. Cellular and Molecular Biology and Histology of Osseointegration

Different types of cells play the main role in osseointegration process. At all stages of this process, cells activity is controlled by typical genes activated by different cytokine types, small molecules (i.e. histamine and prostaglandins (PGs)) and molecules of extracellular matrix (8). Cytokines (i.e. interleukins and growth factors) and hormones (i.e. bradykinin, PGs and steroid hormones) are the most important groups of messenger molecules (9). Osseointegration stages are summarized in appendix (Table 1, Figure 1).

Table 1. Osseointegration Phases of Dental Implant (10)

Phases	Functions
Hemostasis phase	Proteins adsorption, soft tissue healing, platelet activation, clot formation
Inflammatory phase	Neutrophils and macrophages response, inflammatory mediators releasing (i.e. interleukins)
Proliferative phase	
Early stage	Angiogenesis, increase in the number of fibroblasts and osteoclasts.
Late stage	woven bone formation
Remodeling phase	
Early stage	Beginning of remodeling and reconstruction of woven bone by osteoclasts.
Late stage	immature woven bone replacement by mature lamellar bone

Figure 1. Osseointegration Stages



A, One-week human histology (toluidine blue), early proliferative phase with initial bone formation bone growing on the sandblasted large grit and acid etched surface towards the grooves bone debris; B, Two weeks human histology, proliferative phase with new bone starts to bridge between parent bone and implant, bone debris particles into immature new bone trabeculae; C, Four weeks human histology, transition to remodeling phase, parent bone has been degraded; D, Six weeks human histology, remodeling phase with formation of new primary and secondary osteons (4).

3.1.1. Homeostasis Phase

The first stage in osseointegration process is homeostasis, which begins as a result of surgical trauma of drilling and continues after DI insertion. This stage period may vary from a few minutes to several hours. Bone trauma leads to activation of extracellular matrix proteins and growth factors exist in bone matrix (11). Injured vessels bleeding would cause fibrinogen, polymerization and subsequently extracellular matrix formation in the bony defect (12). Following platelet activation, effective molecules such as thrombin, collagens, fibrinogen, and thrombospondin would aggregate in the area and cause clot formation (10).

3.1.2. Inflammatory Phase

The second stage of osseointegration process is inflammatory phase. This stage begins about 10 minutes after surgery and lasts for a few days. This stage starts with platelets degranulation. The growth factors such as transforming growth factor beta (TGEB), platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) are released from the platelets. Bradykinine released from platelets increases the permeability of blood vessels to fluids, serum proteins, and white blood cells (WBCs).

On the other hand, platelet-derived histamine causes the blood flow increase, velocity decline and also hyperemia (13). At this stage, molecular immune system (i.e. complementary system) and cellular immune system (i.e. polymorphonuclear cells and macrophages) are activated and secrete inflammatory cytokines like tumor necrosis factor- α (TNF- α) and interlukin-8 (IL-8). The immune system secretes angiocentric factors and fibrinogen growth factors (FGF) after purging the tissue debris and micro-organisms (13, 14).

3.1.3. Proliferative Phase

Proliferative phase is the third stage of osseointegration. This phase is determined by new extracellular matrix formation and angiogenesis. This recently constructed tissue is named granulation tissue. Angiogenesis is considered as an osteogenic initiating factor. Immature woven bone would be created through attachment of osteoprogenitor cells to the DI surface and then by initiating their secretory activity, they would be named osteoblasts (15).

3.1.4. Remodeling Phase

The fourth stage of osseointegration process is remodeling phase. The osteoclasts are the main players in this stage. It has been tried to remove woven bone and old bone surrounding DI to create a space for new bone formation. This phase may continue for some years until most of the primary woven bone and old bone are replaced by lamellar ones (16).

3.2. Implant Failure Factors

The long-term results of DI treatment are affected by multiple systemic and local factors. Despite abundant researches and advanced therapeutic approaches, a large number of treatment failures have been reported. Absence of osseointegration is generally identified by symptomatic mobility of DI and peri-implant radiolucency. In these cases, the implant is called "failed" (17, 18).

In addition, implant failure process may occur gradually and continuously. This situation is recognized by progressive marginal bone loss in addition to increased clinical probing depth, bleeding on probing and suppuration. Such DI is considered as "failing". However, late implant failure is due to pathologic process, which involves the osseointegration (18-20).

3.3. Local Factors Affecting Implant Failure

Generally, local factors are effective on success of all the stages of implant treatment (3). Lack of primary stability, surgical trauma and infection are the main reasons for early DI failure, while the most considerable factors related to late DI failure are occlusal overload and peri-implantitis (21). According to performed studies, four main causes are suggested for DI failure.

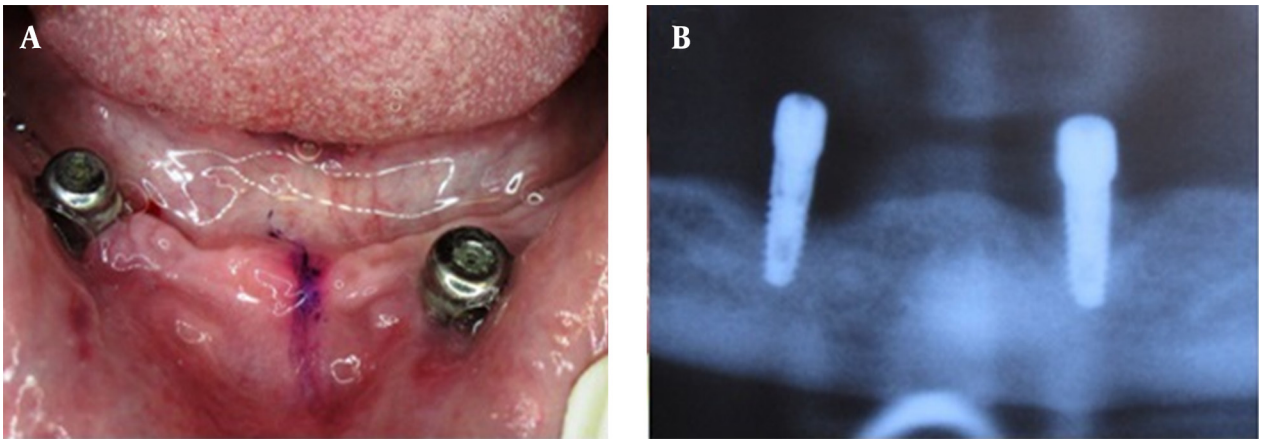
3.3.1. Infections and Advanced Periodontal Disease

Bacterial infections can lead to DI failure in each stage of treatment process (22). According to researches, mild inflammation increases bone repair, while moderate or severe inflammation prevents appropriate healing (3). The term peri-implant mucositis refers to reversible inflammation in the soft tissue circumscribing DI; whereas, the term peri-implantitis refers to inflammatory reaction of surrounding implant soft tissue with bone loss (23, 24).

Hence, sterile surgical procedure and mouth washing with chlorhexidine (about 1 to 2 minutes before the operation and after it) are very important and may result in bacterial loads reduction (3).

Implant therapy requires particular attention in patients with advanced periodontal disease. According to previous studies, 5 mm of probing depths or more, bleeding on probing and radiographic signs of marginal bone loss in patients with periodontal disease background are significantly more than others with no history of periodontal disease (25) (Figure 2). Based on investigations, peri-implantitis microflora in partially edentulous patients is equal to their natural teeth. This fact is due to transmission of periopathogens from the natural tooth pocket to the DI Surface. Thereby, patients' periodontal status impresses the peri-implantitis tissue condition. Infection control, oral hygiene observance, appropriate plaque control, extraction of hopeless teeth, and scaling root planning before and after DI treatment are particularly considerable. To reduce infections risk, prophylactic antibiotic therapy would be helpful (26). In patients with advanced bone loss, bone graft techniques and alveolar bone reconstruction could be applied to increase success rate (26).

Figure 2. A 61-Year-old Female With History of Full Mouth Tooth Loss as a Result of Advanced Chronic Periodontitis



A, Clinical photograph of implants 5 years over-denture placement. Implants are evidently mobile and painful (note buccally and asymmetric position of the patient's left implant); B, Panoramic radiograph of dental implants seen in A. (Photograph by: authors).

3.3.2. Reduced Salivary Flow

Reduced salivary flow is a local factor that can affect DI treatment result. Xerostomia could be attributed to some conditions such as autoimmune disease (i.e. Sjogren), systemic lupus erythematosus and diabetes mellitus), head and neck radiotherapy, salivary glands neoplasms, administration of some drugs (i.e. antihistamines, diuretics and tricyclic antidepressants) (27). However, reduction in antimicrobial activity and washing effect of saliva leads to increased plaque formation, fungal and bacterial overgrowth, dental caries and periodontal disease (1), but successful DI placement has been reported by numerous studies (28, 29). Anyway, it is needed to evaluate patients' medical status and severity of salivary flow reduction before treatment (28).

3.3.3. Impaired Healing

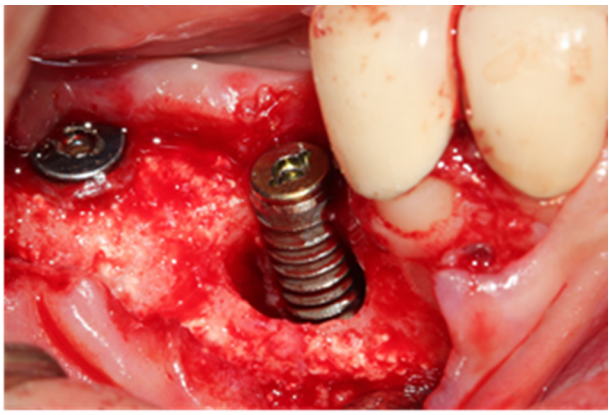
Peri-implant bone healing could be impaired by failure to observe the principles of surgery, surgical trauma and overheating attributed to lack of proper cooling. It is believed that adequate blood and oxygen supply are needed to have desirable bone healing (30). Lack of adequate oxygen supply may result in differentiation of primary stem cells to fibroblasts and subsequently fibrotic scar tissue formation, unfavorable osseointegration and finally treatment failure (3). In addition, overheating and over pressing of bone during cavity preparation and using excessive torque in DI insertion may lead to necrosis and sequester formation (Figure 3).

Therefore, bone preparation must be performed via intermittent drilling with moderate velocity and sharp drills accompanied by adequate irrigation (3).

3.3.4. Over Loading/Immediate Loading

According to performed investigations, micromotions over than 150 μm, impair osteoblast differentiation and consequently lead to formation of fibrotic scar tissue in bone-implant contact.

Figure 3. Implant Failure Three Months After Insertion With no Obvious Reason in a Generally Healthy Young Adult



It is likely that the failure is due to lack of observing surgical principles such as proper irrigation, which leaded to bone necrosis. (Note circumferential bone loss). (photograph by: authors).

Thus, DI loading should be postponed at least 2 months after insertion and prevention of inflicting excessive force and occlusal loading during initial phase of healing and osseointegration is necessary (3). However, in recent investigations, it is demonstrated that the reverse torque value in immediate loaded implants is influenced by multiple factors like surface roughness and topography, bone site quality, length and diameter of implants (31), thereby immediate loading does not appear to be a serious risk for implant stability quotient, bone-implant contact or osseointegration and survival rate of implants (32, 33). Unsuitable design and inappropriate prosthetic constructions are two responsible factors for DI troubles and failure (21). Para-functional habits (i.e. bruxism, clenching and grinding) are potential risk factors for peri-implantitis and DI failure (34). Bruxism is a masticatory disorder identified by teeth clenching and grinding in both sleep and wake (35, 36). The outbreak of this disorder is about

10% of population. Bruxism is affected by multiple factors such as occlusion, genetic, drugs, trauma and neurologic factors. Bruxism causes occlusal overload on implant and consequently alveolar bone loss around DI. Detection and elimination of the main bruxism reason is necessary before DI treatment (37). Essential principles of favorable DI osseointegration are summarized in Box 1 (3).

3.4. Effective Systemic Factors in DI Treatment

Regarding increased demand for DI as an alternative for lost teeth, medical consideration should be taken into account to have appropriate osseointegration. In the following, some of the factors involved in implant treatment are explained (38, 39) (Table 2).

Box 1. Essential Principles of Favorable DI Osseointegration

Principles for Favorable dental implant Osseointegration
1. Insertion of a tissue compatible and sterile fixture (such as titanium coated fixtures)
2. Preparation of bone under sterile condition
3. Preparation of bone by means of atraumatic surgical techniques. Avoiding overheating.
4. Providing proper primary stability of DI.
5. Avoiding DI load and preventing DI micro movements during osseointegration phase (about 2 - 4 or 4 - 6 months, depending on bone density and DI primary stability); considering favorable occlusal pattern.

Table 2. Dental Implant Treatment in Patients With Systemic Disorders

Condition	Treatment Success Rate Compared With Matched Healthy Control Group	How it Affects DI Osseointegration	How the Condition Could be Managed to Increase Success Rate
Osteoporosis	Equal or reduced	Reduced bone Density, possibility of osteonecrosis in patient using IV bisphosphonates	Increased primary healing time, adjunctive drugs and hormones. IV bisphosphonates: absolute contraindication
Corticosteroid therapy	Equal	Osteoporosis, immune deficiency and adrenal suppress	Antimicrobial therapy adrenal suppress consideration, adjunctive corticosteroid
Diabetes mellitus	Equal in metabolic controlled patients	Vascular disorders, impaired wound healing, immune deficiency	Glycemic control, antimicrobial therapy oral hygiene instruction (OHI), severe renal failure: absolute contraindication
Immune deficiency	Equal	Increased infection risk, impaired wound healing	Antimicrobial therapy, chlorhexidine mouth wash, OHI
Bleeding disorders	Equal	Increased risk of bleeding during and after operation	Evaluation of coagulation system function in elderly patients, anti-coagulant drugs alteration if needed, coagulative mechanisms, fibrinolysis inhibition
Neuron psychiatric disorders	equal	Malnutrition, behavioral problems, poor oral hygiene	OHI, long- term follow up
Oncology: chemotherapy and radiotherapy	Reduced (particularly after radiotherapy)	Chemotherapy: bone marrow suppression radiotherapy: reduced tissue healing potency, osteoradionecrosis	Preventing early loading, hyper baric oxygen, antimicrobial cover, OHI. Proper time for surgery: 21 days before and 9 months after radiotherapy.
Cardiovascular disease	Equal	Impaired tissue repair due to insufficient oxygen delivery in severe cases	Considering anticoagulant drugs used by patients, AB Prophylaxis, avoid general anesthesia
Alcoholism/Smoking	Equal or reduced	Tobacco use osteoporosis, bleeding tendency, immune deficiency, malnutrition, Behavioral problems	Stop smoking, a week before surgery till 8 weeks after it, OHI
Mucocutaneous diseases	Equal	Increased infection risk due to corticosteroid therapy, adrenal might be suppressed, xerostomia	Consider corticosteroid therapy, OHI
Hypothyroidism	Equal in medically controlled patients	Reduced osteogenesis	Use hormone replacement drugs

3.4.1. Aging

Over time, tendency to DI treatment in elderly patients, particularly in those with systemic disorders is increasing (40). According to several studies, long-term success rate for DI treatment in elderly patients and young patients has been approximately equal (41); although, in some aged patients with systemic disorders reduction in bone repair ability, immunodeficiency and xerostomia may decrease the success rate (40). Aging leads to alteration in mineral deposits, bone protein and collagen contents and derangement in bone and muscle adaptation. Delay in bone fractures healing and reduced tissue regeneration as a result of aging have been reported (7, 42). Decreased bone density related to aging has also been seen in men and women, particularly in postmenopausal women (43).

Prevalence of numerous systemic diseases such as osteoporosis, diabetes mellitus, immune disorders and also pharmaceutics products consumption would be increased by aging. Nevertheless, DI treatment in elderly patients with controlled systemic condition is not contraindicated (43). Generally, according to performed studies, aging does not affect the osseointegration lonely.

3.4.2. Osteoporosis

Osteoporosis is one of the most common bone disorders that may compromise implant osseointegration. Osteoporosis is described as generalized reduction in bone mass and bone density. Osteoporosis is categorized into primary and secondary types. Primary osteoporosis is considered as decreased bone density attributed to aging, postmenopausal condition and idiopathic osteoporosis. Secondary osteoporosis would occur in patients with predisposing factors such as other endocrinopathies and some drugs consumption (1, 44). In histopathologic evaluation of osteoporotic bone, decreased thickness, derangement in trabecular structure, reduced mineral contents and increased carbonate to phosphate ratio have been seen (45). Reduction of osteoid formation is probably due to absence or deficit of pre-osteoblasts differentiation to osteoblasts or reduction of osteoprogenitor cells number and defects in their proliferation and differentiation (46).

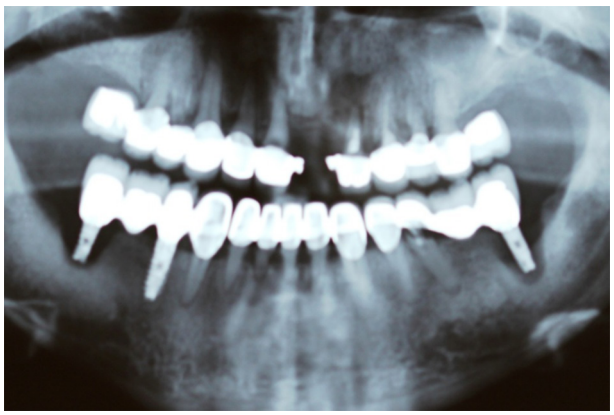
Considering performed studies about evaluation of DI treatment in osteoporotic patients, the most important putative complication in such cases is bisphosphonate-related osteonecrosis of jaws (BRONJ), which affects osseointegration. Bisphosphonates act through inhibiting osteoclasts and inducing apoptosis in them, increasing collagen synthesis and restraining osteoblasts proliferation (47-49).

A systematic review showed that insertion of DI in osteoporotic patients who used oral bisphosphonates for less than 5 years did not cause BRONJ, and most adverse effects related to intravenous (IV) administration of this drug (50). Results of DI treatment in osteoporotic patients are reported differently in various studies.

Anyway, osteoporosis is not considered as a definite contraindication for DI placement and by application of specific considerations, such as giving more time to primary healing and prescribing adjunctive medication (i.e. Calcium, multivitamins, vitamin D, fluoride, estrogen and calcitonin) successful DI treatment would be achieved. Furthermore, primary stability of implant is very important in these patients (51).

Fibrous dysplasia is another disorder with jaw involvement characterized by fibrous connective tissue proliferation and dysplastic abnormal trabecular bone formation (52, 53). Recently, successful placement of DI in affected jaws by fibrous dysplasia has been reported (54). It is found that direct bone-implant contact around titanium screws exists in both normal and dysplastic bone. Although bone healing in dysplastic bone occurs as well as normal bone without inflammatory reaction, the area in contact is wider in normal bone than dysplastic bone (55). More studies are needed about osseointegration in fibrous dysplastic jaws (Figure 4).

Figure 4. A 48-Year-Old Female Patient With Moderate to Severe Secondary Osteoporosis Due to Long-term Administration of Systemic Corticosteroids



Note two mandibular hopeless implants. (Photograph by: authors).

3.4.3. Corticosteroid Therapy

Systemic corticosteroid therapy is prescribed for different reasons, such as autoimmune disease and organ transplantations. Applying these drugs leads to reduced bone density (osteoporosis), increased epithelial fragility and immune suppression (56). Consequently, corticosteroid therapy may result in compromised osseointegration of DI (57). Negative effect of steroid application on DI osseointegration in mandible is less than skeletal bones (58). The failure rate in these cases is still questionable, and there is no definite evidence to affirm steroid therapy as a contraindication for DI placement (38).

In such patients, medical consideration and evaluation of adrenal gland suppression rate are necessary (56). Medical central agency also suggests to provide supple-

mentary dose of corticosteroids before and after the operation for patients with more than 3 weeks consumption of steroids, patients with stressful situations such as trauma, infection and surgery, and those with adrenal deficiency (38). In addition, patients who used less than 10 mg prednisolone a day do not need supplementary dose for surgery (59) (Figure 4).

3.4.4. Diabetes Mellitus

Diabetes mellitus is one of the most common systemic disorders categorized in types of insulin dependent (type I), insulin independent (type II), gestational diabetes and other specific types. Recently, the American diabetes association (60) has stated the new criteria for diabetes diagnosis including:

1) A1C hemoglobin $\geq$ 6.5%,

2) Fasting plasma glucose $\geq$ 126 mg/dL,

3) 2-hour plasma glucose after administration of 75g glucose $\geq$ 200 mg/dL,

4) Plasma random glucose in patients with hyperglycemic signs $\geq$ 200 mg/dL.

There are various systemic complications with this disorder, such as neuropathy, retinopathy, nephropathy, vascular disorders and wound healing deficiency. Immune deficiency and defect in macrophages chemotactic function are two other important complications (39). Increased risk of dental implant failure in patients with diabetes has been reported by some studies (61). Furthermore, a close relation between hyperglycemic condition and implant osseointegration has been indicated (62) (Figure 5). However, success rate is reported from 85.6% to 94.3% in different studies (63).

There are many systematic reviews and case series that support the similarity between success rate of dental implant in proper metabolic controlled diabetic patients and healthy group (61, 64). Some strategies are suggested to reduce failure rate of implant placement in these patients including systemic antibiotic (AB) therapy, blood sugar control (particularly during primary healing phase and after treatment period), smoking prevention and oral hygiene care (38, 39).

Renal failure, one of the most serious diabetic complications that necessitates dialyze, is an absolute contraindication for DI placement or every bone graft surgery (2).

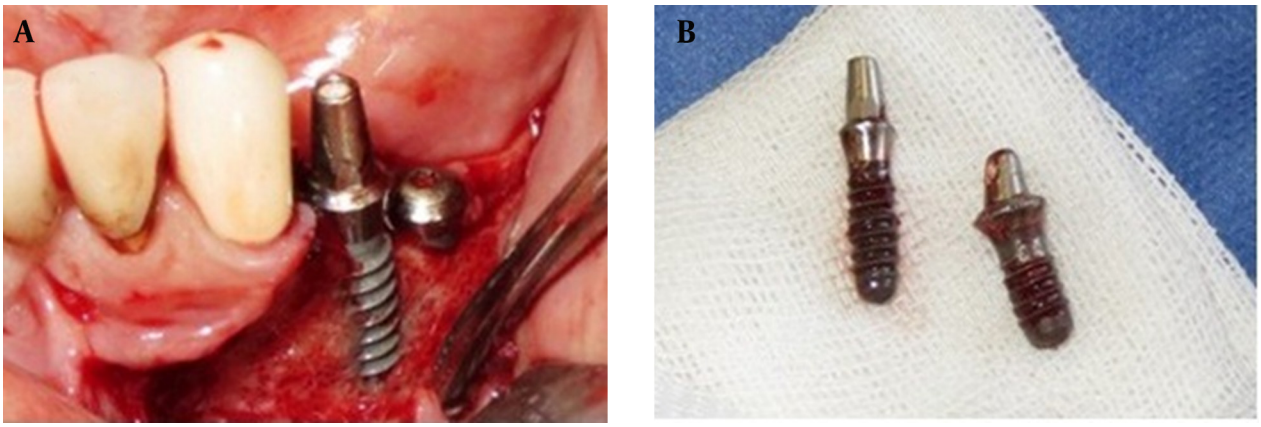
3.4.5. Immune Deficiency

Patients with immune deficiency are at increased risk of implant failure due to increased predisposition to infection and compromised tissue repair (65); however, dental implant placement is not contradicted for these patients. Thereby, medical considerations before DI surgery and adjunctive antimicrobial therapy are required for them (56). According to recent studies in patients with stable immune status, HIV positive cases with sufficient number of CD4+ cells and using antiviral drugs, DI placement has been performed successfully; However, long-term results are not clear yet (66, 67).

3.4.6. Bleeding Disorders

Platelet disorders, coagulant factors deficiency and using anticoagulant drugs (Aspirin, warfarin, etc.) are the most common reasons for uncontrolled hemorrhage (68). Regarding the fact that most applicants for dental implants are elderly patients consuming anticoagulant drugs, evaluating coagulation system function before the operation is very important. Patients with infection, idiopathic purpura, history of radiotherapy, bone marrow suppression and malignancies (i.e. leukemia), may have platelet deficiency. The most possibility of bleeding is accompanied by platelet deficiency to less than 50000/mm^3 (69), whereas the normal range of platelet count is 100000/mm^3 to 500000/mm^3. The most life threatening adverse effect of DI placement in these patients (which occurs rarely) is upper airway obstruction, secondary to severe hemorrhage of mouth floor (70).

Figure 5. A 59-Year-Old Female With Diabetes Mellitus Type II



A and B, Clinical photograph of mandibular first premolar implant failure. (Photograph by: authors).

The first mandibular premolar position is the riskiest area for DI placement, due to potency of lingual artery involvement secondary to lingual cortical plate or inferior alveolar canal perforation (71-73).

3.4.7. Neuropsychiatric Disorders

Patients with neuropsychiatric disorders such as several character disorders, brain lesions, dementia, severe anxiety, severe alcoholism and drug abuse require more attention for D.I placement. There are not sufficient evidences to support a definite association between DI failure and psychological disorders in these patients (73-75).

In some patients with bulimia such as those with mental retardation or Parkinson's disease, DI placement would be successfully performed provided that oral hygiene is observed, drug-induced xerostomia is controlled, and long-term follow up is performed (43, 76, 77). However, there are many reports of DI failure as a result of psychological problems in particular poor oral hygiene parafunctional habits and behavioral problems (74). According to performed studies this condition is not an absolute contraindication to DI placement (39). It is preferred not to place DI in patients who are unable to perceive and interpret dental treatment rationally (78).

3.4.8. Patients With History of Head and Neck Cancer and Treatments

Proper osseointegration in patients with cancer is still questionable due to active cancer therapy including radiotherapy, chemotherapy and surgery. Cancer treatment causes loss of osteocytes and consequently leads to osteoclast dependent or independent resorption (79). With radiotherapy, the scattered bone gets hypovascular, hypoxic and hypocellular; thereby, its healing potency would be reduced and the bone would be disposable to osteoradionecrosis.

Periodontal tissues are also susceptible to radiotherapy, due to their high turnover levels (49, 80). On the other hand, chemotherapeutic drugs cause bone marrow suppression and have adverse effects such as immune system deficiency, coagulative system deficiency, infection, hemorrhage, mucositis and mucosal pain (39).

However, cancer treatment is not considered as absolute contraindication for DI placement. Therefore, improved outcome could be achieved by additional oral hygiene and postponing DI placement till blood cells get normal (81). According to some studies, DI placement in elderly patients with head and neck cancer is less successful than young patients (82). To improve success rate in patients candidate for radiotherapy, following considerations are recommended (81):

- Implants should not be early loaded.
- The best time for DI placement is at least 21 days before and 9 months after radiation.
- If radiation used is more than 50 Gys, giving hyperbaric oxygen would be necessary.
- Postponing surgery if mucositis is observed.
- Avoiding surgery during radiotherapy phase.
- Prescribing antimicrobial drugs before and after surgery.

Recent studies approved that applying hyperbaric oxygen is beneficial for enhancing bone regeneration success (38).

3.4.9. Cardiovascular Disease

Variant types of cardiovascular disease (hypertension, atherosclerosis, congestive heart failure, etc.) could interfere with healing and osseointegration process, which is dependent on normal oxygen delivery (83). Sufficient oxygen delivery is required for fibroblast activity, macrophage function, collagen synthesis, angiogenesis, and prevention of wound infection (43). Hence in these patients reduced fibroblast activity, impaired macrophage function and decreased collagen synthesis inhibit appropriate osseointegration (83).

However, cardiovascular disease has not had significant influence on long-term success rate of DI treatment (7). Relevant considerations should be regarded in these patients (Table 2).

3.4.10. Alcoholism and Smoking Habit

Alcoholism alone is not a contraindication for DI treatment, but in alcoholic patients who have smoking habit, some disorders may be seen like osteoporosis, bleeding complications, immune deficiency, and malnutrition. Furthermore, proper osseointegration in these patients is hindered by liver disorders, impaired tissue healing as a result of nutritional deficiency, psychological disorders and inadequate oral hygiene (38).

Smoking habit may lead to delayed bone healing, decreased bone height, poor bone quality, increased periimplant inflammation as well as increased bone loss rate. More than 4000 bioactive chemical components (i.e. nitrosamines, aldehydes, carbon monoxide, carbon dioxide, ammonia and benzene) with potential detrimental impact exist in the cigarette (84, 85). As investigations demonstrate, smoking may affect the tissue healing by four essential mechanisms:

1) Carbon monoxide (Co) releasing increases hemoglobin (Hb) concentration and adhesion, which consequently leads to reduced oxygen delivery to healing tissues.

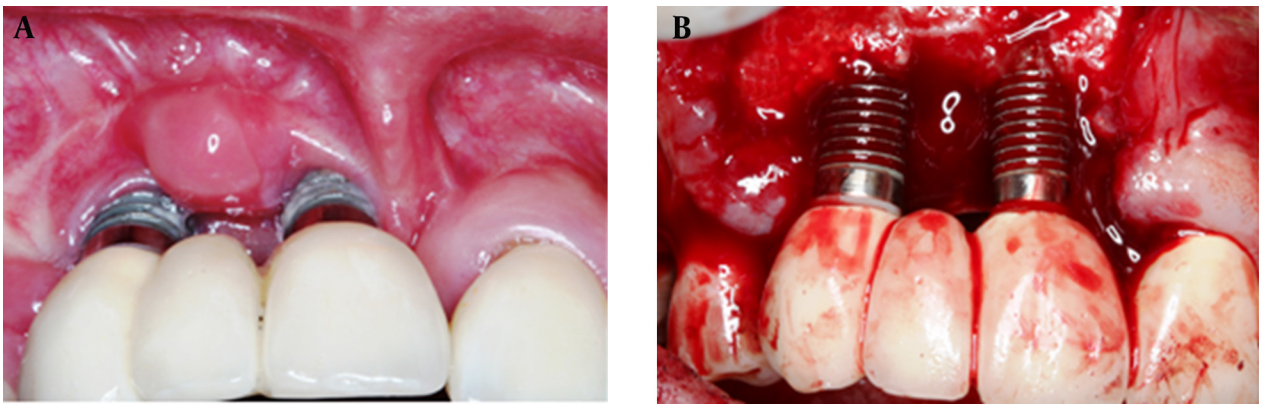
2) Nicotine causes vasoconstriction, which increases platelet aggregation and platelet adhesion, and finally results in blood flow reduction.

3) Nicotine affects osteoblasts activity and consequently causes reduced available collagen to form extracellular matrix.

4) Cytotoxic effects of tobacco on fibroblasts and polymorphonuclear cells (PMN) cause impaired tissue healing (86).

Since the fundament of osseointegration is tissue repair, tobacco consumption is considered as an important

Figure 6. Smoking Patient With Long-term Failure of Maxillary Central Incisor and Canine Implants



Patient used to smoke 2 packs of cigarettes per day for 6 years ; A, Clinical view; B, Crestal bone loss is obviously demonstrated after flap reflection. (Photograph by: authors).

risk factor for DI surgery (87, 88). However, there are several studies considering that isolated nicotine administration is not responsible for DI failure (89-91). Negative effects of smoking on dental implants are also notable after DI loading. Regarding reverse effects of tobacco on remained teeth periodontal status by continuing tobacco use after treatment, there is expectancy of catching advanced periodontal disease and subsequently delayed DI failure. As a result, in addition to smoking cessation before and immediately after DI surgery, it is recommended to stop or reduce smoking after DI loading (Figure 6, Table 2) (43).

3.4.11. Mucocutaneous Diseases

In patients with mucocutaneous disorders (i.e. ectodermal dysplasia, epidermolysis bullosa, systemic lupus erythematosus and lichen planus) infection risk is raised due to systemic corticosteroid therapy, immune-suppressive drugs administration, salivary glands involvement and failure in proper oral hygiene care (92).

The most common reported complication in these patients, especially in those with systemic lupus erythematosus, is bleeding blisters formation by trauma, particularly in contact areas with prosthesis. Furthermore, some cases of oral lichen planus-related oral squamous cell carcinoma have been reported. However, these complications do not interfere with normal osseointegration. Therefore, the extent and severity of underlying disease should be determined before dental implant placement. By applying a fixed full arch implant-supported prosthesis, implant success rate would be raised due to reduced mucosal contact surface (93).

3.4.12. Scleroderma

Scleroderma is a chronic disorder of connective tissue characterized in part by leatherlike and inflexible skin (94). These patients often have moderate-to-advanced periodontitis. According to our researches, we did not encounter any well controlled study on the effects of scleroderma on DI success rate, but some case reports reported successful DI placement in these patients, which had been survived for several years (95-97). However, regarding the high prevalence of moderate-advanced periodontitis in these patients, correlation of this condition with improper osseointegration and implant failure is probable (98). Clearly, more researches are needed in this field.

3.4.13. Hypothyroidism

Thyroid hormones are effective factors on natural bone metabolism. In patients with hypothyroidism, the bone cells maturation, recruitment and activity are decreased. Therefore, it may be concluded that hypothyroidism results in more failure rate of DI osseointegration. However, some studies do not agree with this subject (99, 100). Totally, thyroid disorders are not considered as absolute contraindications for DI placement. However, it is suggested to postpone the DI surgery until patient achieves good metabolic control (7).

4. Conclusions

Nowadays, dental implant is the treatment of choice in edentulous patients. Regarding the fact that DI candidates are often older population with various local and systemic disorders, DI treatment outcomes could be influenced adversely. There are few absolute contraindications for DI treatment. As a whole, correct patient selection, considering patients local and systemic status, determining cost-benefit analysis with patient's condition and applying standard rules of surgical procedure and DI loading would lead to a successful DI treatment. Thereby, it is better to check up patients for overall health before beginning the treatment process. Clinical, paraclinical and laboratorial evaluations should be performed, and in suspicious cases, consultation with other medical sectors would be necessary.

Footnote

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