

Effect of Hypertension and Anti-Hypertensive Drugs on Dental Implants: A Review Article

Manisha Verma¹, Mohammad Abdurrahman Khan²,
Anjani Kumar Pathak³, Nand Lal⁴

How to cite this article:

Manisha Verma, Mohammad Abdurrahman Khan, Anjani Kumar Pathak, *et al.*/Effect of Hypertension and Anti-Hypertensive Drugs on Dental Implants: A Review Article/Indian J Dent Educ. 2023;16(3):137-145.

Abstract

Dental implant surgery has developed into a widely used procedure for dental rehabilitation and is a secure and predictable procedure. Local and systemic factors can result in higher failure rates. Hypertension is a chronic disease that goes in with atherosclerosis, and coronary artery disease which causes multifarious side effects. Hypertension as a relative contraindication for implant surgery is controversially discussed. Because the number of patients suffering from hypertension increases, therefore more hypertensive patients demanding implant procedures. We also conclude that patients with poorly controlled blood pressure suffer from impaired osseointegration, elevated risk of peri-implantitis, and a higher level of implant failure. The influence of the disease is not fully clear. The supportive administration of antibiotics and chlorohexidine seems to improve implant success. When hypertension is under well control, implant procedures are safe and predictable with a complication rate similar to that of healthy patients.

Keywords: Hypertension; Dental implants failure; Osseointegrated implant survival; Antihypertensive Drugs.

Author's Affiliation: ¹Senior Resident, ³Junior Grade, ⁴Professor and Head, Department of Periodontology, King George's Medical University, Lucknow 226003, Uttar Pradesh, India, ²Assistant Professor, Department of Forensic Medicine and Toxicology, Hind Institute of Medical Science, Barabanki, Uttar Pradesh 225003, India.

Corresponding Author: Mohammad Abdurrahman Khan, Assistant Professor, Department of Forensic Medicine & Toxicology, Hind Institute of Medical Science, Barabanki, Uttar Pradesh 225003, India.

E-mail: drmak2005@gmail.com

Received on: 06-05-2023

Accepted on: 03-06-2023

INTRODUCTION

Dental implants are one of the most common recent advances for the replacement of missing teeth. It is not necessary that only osseointegrated dental implants showed a successful result. There are also many secondary reasons for the failure of osseointegrated dental implants due to the presence of some overloaded infection and certain systemic conditions are also responsible like type-2 Diabetes Mellitus, Hypertension etc.¹ Also, it has been evaluated that the main predictors for implant

success are the quantity and quality of bone, the patient's age, the dentist's experience, location of implant placement, length of the implant, axial loading, and oral hygiene maintenance. Some patients want to receive dental implant prostheses, they often suffered from physical and mental stress after undergoing the surgical procedure. In some situations, we can reduce such kinds of problems by giving them an appropriate amount of anesthesia. Physical stress and mental problems are also the situations that cause an elevation in the blood pressure of a patient because of an increase in the level of uneasiness and a lot of fear when surgical procedures are carried out.^{2,3} The problem of patients' "white coat" response of higher in office blood pressure readings than ambulatory (out-of-office) readings is common. The "white coat" effect can lead to dentists referring patients for possible hypertension and to their physicians treating them for high blood pressure.^{4,5} The success and survival rate of dental implants were limited in medically compromised patients.⁷ Carrying out dental procedures on patients with cardiovascular disease can lead to difficulties. The potential problems that a dental practitioner is likely to encounter will be considered under the following headings⁸: Hypertension, Ischaemic heart disease, Valvular heart disease, Dysrhythmias and pacemakers, Anticoagulants, Congenital heart disease, Cardioactive drugs and vasoconstrictor therapy.

All these systemic conditions cause a negative influence on the osseointegrated implants and principally affect the treatment outcome.⁹ Mainly Primary predictors of implant failure are poor bone quality, chronic periodontitis, systemic diseases, smoking, unresolved caries or infection, advanced age, implant location, short implants, acentric loading, an inadequate number of implants, parafunctional habits, and absence/loss of implant integration with hard and soft tissues. Inappropriate prosthesis design also may contribute to implant failure. Some expertise groups have also elicited a strong correlation between hypertension and dental implant surgery.¹⁰ Also, it has been notified that endogenous adrenaline level increases in painful treatment conditions which causes a sharp rise in average systolic as well as diastolic blood pressure during painful dental implant treatment.^{11,12}

Some studies showed that if a patient is on antihypertensive medications it may be associated with an increase in the survival rate of Osseointegrated dental implants.¹³ Some other factors such as oral hygiene, age, smoking, quality of bone, systemic diseases, the persistence of infection,

and implant maintenance have been previously considered as the main determinant for the success or failure of implant.¹⁴ On the other hand, dentistry has also played an important role in the detection of patients with hypertension. Many patients found to have high blood pressure at or beyond defined levels should be referred for a medical diagnosis and indicated treatment. Once the hypertension condition is under control, oral and dental evaluation and treatment can be initiated. Beginning in 1976, the percentage of the general population in the united states with undetected hypertension declined steadily. However, this decline reversed, beginning in 1994. In addition, fewer than 50% of the patients who are aware of their hypertension have it medically under control. Thus, a significant number of patients with undetected high blood pressure or uncontrolled hypertension today are seeking dental treatment. These patients are at high risk for significant complications such as stroke, heart disease, kidney disease, and retinal disease. Those with very high blood pressure are at great risk for acute medical problems when receiving dental treatment. For those reasons, dentistry must continue to emphasize the detection and referral of patients with high blood pressure. In addition, an increased number of medically compromised patients are seeking dental treatment who should have their blood pressure monitored during the more stressful dental procedures, such as oral surgery, periodontal surgery, and placement of dental implants. This article reviews the recent advances in the dental and medical management of hypertension and its influence on dental implants.

Hypertension and Dental Implant Failure

Hypertension is a chronic medical condition in which the blood pressure in the arteries is elevated. The globally main cause of morbidity is cardiovascular diseases. Hypertension, atherosclerosis, and coronary artery disease are some common cardiovascular diseases.^{15,16} Cardiovascular diseases result in decreased blood flow which compromises the process of healing and osseointegration and leads to a reduction in the supply of oxygen and nutrients to tissues causing a reduction of fibroblast activity, capillary growth, collagen synthesis, and macrophages action promoting infections because of hypoxia, so normal healing of fractured bone appears as well.¹⁷ Diabetes mellitus and hypertension are common diseases that coexist in the community at a greater incidence rate.¹⁸ In several populations, hypertension is twice common in diabetic individuals as in those who

do not have diabetes.^{19,20} In the case of implant surgery, these two conditions might interfere with bone formation and also be deleterious to the survival of dental implants. Dental implants are the most significant alternative for the treatment of partial as well as complete edentulism.²¹ It has been proven that dental implants are widely used for rehabilitation procedures.^{22,23} Local and systemic factors both showed a greater impact on the osseointegration process. Hypertension is also one of the common serious situations for patients who are undergoing implant surgery.²⁴ At 60 years of age, the prevalence rate of hypertensive patient become 66% as more than half of them is taking antihypertensive medication.²⁵ Anti-hypertensive drugs play a significant role in bone remodeling and bone formation which is affiliated with decreased risk of bone breakage.²⁶ But those patients who are suffering from cardiac diseases having high blood pressure mostly leads to increased bone loss.²⁷ This may be because hypertension is associated with abnormal calcium metabolism, including an increase in urinary calcium excretion.²⁸ Moreover, even though history of periodontal disease has been associated with peri implant bone loss, still it has not been proven to be a risk factor of dental implant failure in literature. For osseointegration of dental implants, bone formation is very important because it is a physiological process that resembles bone fracture healing.²⁹ It has been approved that anti hypertensive drug shows a positive effect on bone, particularly in bone metabolism, and the formation of bone, promotes the healing process.³⁰ It sustains the alveolar bone microstructure and increases bone density and bone mass.³¹ Khadivi *et al*¹⁷ investigated on retrospective analysis in patients with cardiovascular disease involving 246 patients with initial osseointegration and 39 patient with an interest in cardiovascular disease. Their retrospective study demonstrated 13% failure in both the cardiovascular disease and control groups. Van Steenberg, *et al*³² researched and found no relation in patient with non-contributory cardiovascular disease, such as angina, heart valve anomalies, and arrhythmia and between early implant failure and cardiovascular disease. Studies with implants in function are needed, but it appears that cardiovascular disease does not diminish initial implant survival.

Anti-hypertensive Drug's and Survival of Osseointegrated Dental Implants

Antihypertensive drugs in general are beneficial for bone formation and remodelling, and are associated with lower risk of bone fractures.

The prevalence of hypertension is increasing in individuals older than 60 years in developed countries. Patients with hypertension also require dental implant therapy. Thus, the influence of anti hypertensive medications on peri implant tissue has been of great interest. Wu *et al.* conducted a retrospective cohort study on 728 patients that assessed the influence of antihypertensive medications on implant survival rates.¹³ As osseointegration is influenced by bone metabolism. Antihypertensive medications, such as beta-blockers, thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, and the angiotensin II receptor blockers (ARBs), are the most commonly prescribed drugs for people suffering from high blood pressure³³ Beta-blockers act by blocking the beta-2 receptor in the sympathetic nervous system resulting in a decrease in blood pressure³⁴; thiazide diuretics control hypertension by blocking the thiazide sensitive Na-Cl symporter and inhibiting reabsorption of sodium and chloride ions from the distal convoluted tubules in the kidneys³⁵; and ACE inhibitors and ARBs block the renin-angiotensin system to reduce blood pressure.³⁶ In addition to these effects, antihypertensive drugs also have an effect on bone, especially in bone formation, metabolism, and healing.^{33,37} Bone metabolism is regulated at three levels: by osteoblast osteoclast interaction, by the immune system, and by the central nervous system.³⁸ Osseointegrated medical devices, such as titanium implants, can create a firm and lasting connection with the recipient bone.³⁹ Treatment of edentulous patients with osseointegrated dental implants is a reliable choice and a routine treatment modality with long term success.⁴⁰ Bone formation is extremely important for osseointegrated dental implants because osseointegration follows a physiological process that resembles bone fracture healing, and is strongly influenced by bone metabolic activity.⁴¹ As anti hypertensive drugs affect bone formation and remodeling, our hypothesis was that anti hypertensive drugs might have an impact on implant osseointegration, and subsequently on implant survival rate.

Antihypertensive Drugs and Implant Failure

Many studies were confirmed that the present study showed the use of antihypertensive drugs was associated with a high survival rate of Osseointegrated dental implants. This can be explained by the relationship between antihypertensive drugs and bone metabolism.³⁷ Most antihypertensive drugs including beta-blockers, thiazide diuretics, ACE inhibitors, and

ARBs that was scheduled 1 week before implant placement and have positive effects on bone health.⁴² These drugs only represent 18% of the antihypertensive drugs prescription in the province of New Brunswick.⁴³

Beta-Blockers: Beta-blockers are among the most widely used for the treatment of hypertension. These drugs exert their effect on blood pressure by inhibiting the sympathetic beta-adrenergic receptors. The beta-adrenergic receptors, especially beta-2 receptors, are expressed in bone cells, and their activity induces bone resorption and decreases bone formation.⁴⁴ Therefore, beta-blockers have been shown to have beneficial effects on bone structure, metabolism, and healing.³⁷

Thiazide Diuretics: Thiazide diuretics inhibit the thiazide sensitive sodium chloride cotransporter (NCC) in the distal tubules of the kidney, reducing renal calcium excretion and subsequently enhancing calcium uptake.⁴⁵ Thiazide diuretics may have a direct positive effect on bone mineral density (BMD) by acting on the proliferation and the differentiation of osteoblasts.⁴⁶

ACE Inhibitors and ARBs: ACE inhibitors and ARBs are widely used antihypertensive drugs. They target the renin-angiotensin-aldosterone system (RAAS) which plays a crucial role in blood pressure control. RAAS operates systemically and locally in several tissues including bone.⁴⁷ ACE inhibitors and ARBs inhibit the activity of ACE and then affect bone metabolism.⁴⁸ Hypertensive medication that they receive has side effects such as xerostomia, consecutive fungal infections of the mouth (i.e., Candidiasis), calcium blockers also used as anti-hypertensive medication, produce gingival hyperplasia, erythema, and ulcers both in the natural dentition and around dental implants.⁴⁹

Dental management of patient who are unaware of their High Blood Pressure

The detection of the patient who is hypertensive is important from several aspects. Significant complications of hypertension can be avoided or minimized by early detection and treatment. From a dental standpoint, potential life-threatening complications can be prevented by not performing dental treatment for patients at risk because of severe uncontrolled hypertension. Data from 1976 to 1980 showed a 49% rate of patients unaware of their high blood pressure.⁵⁰ By 1988 to 1991 the number of individuals unaware of their high blood pressure was reduced to 27%. However, of great concern is that this reduction trend of the number of people unaware of their high blood pressure was

reversed from 1991 to 1994, showing that 32% of the people surveyed were unaware of their high blood pressure.⁵⁰ It is clear that much work remains to be done in the screening for hypertension and the education of the general population concerning the significance of high blood pressure and the importance of its treatment. With about one third of all adult patients with hypertension being unaware of their condition, we must continue to screen our dental patients for high blood pressure.

Recent Advances in High Blood Pressure Management

The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure⁵⁰ was published in 1997. This document provides guidelines for the management of hypertension developed by experts in the field.

*Alvarez et al*⁵¹ reported on the significance of selected risk factors in the development of high blood pressure over a short period in the Cienfuegos Global Project. It was shown that age, sex (male), and ethnicity (black race) were major risk factors for the development of high blood pressure over 2 years.

*Beilin et al*⁵² found that various lifestyle factors are critical determinants of blood pressure levels operating against a background of genetic susceptibility.

*Chrysant et al*⁵³ conclude their review by stating, "Whether dietary sodium reduction should be recommended for the general population remains questionable because of marginal benefit and the suggestion of possible deleterious effects on cardiovascular outcomes independent of blood pressure." The most recent studies have shown only modest decreases in blood pressure with sodium reduction. However, clinical evidence shows that sodium is related to target organ damage, such as left ventricular hypertrophy and renal disease.

*Rahn et al*⁵⁴ reviewed the role of the sympathetic nervous system in essential hypertension. They concluded that the available data show that sympathetic activation is a specific feature of essential hypertension and that it may play a pathogenic role in this disease.

Various Reviews on the Success Rate of Dental implants

The purpose of this review was to evaluate the impact of systemic disease i.e., hypertension or medications used to treat it, on the success of dental

implant therapy. The high prevalence of cardiac disease in the population, particularly ischaemic heart disease, makes it the most common medical problem encountered in dental practice.⁵⁵ In the present study, dental implant insertion, an oral surgical procedure, was used to evaluate the effect of anxiety on patients' ability to process relevant information under a stressful clinical situation.⁵⁶

Patients demonstrate physiological stress during dental implant surgery. Local anesthesia activates the adrenal cortex to produce cortisol. It is known that cortisol affects blood pressure during implant surgery. Osseointegration of dental implants has been largely improved during the last 50 years in a series of three breakthroughs. First, in the 1960s, the unique property of titanium for osseointegration was discovered⁵⁷; second, in the 1980s, it was found that surface treatment of implants had important benefits on dental implant osseointegration and survival⁵⁸; third, in the 1990s and 2000s, topical use of drugs and growth factors, such as BMP-2 (Bone morphogenetic proteins-2)⁵⁹ or melatonin,⁶⁰ was found to improve osseointegration. However, to our knowledge, this could be the first study showing that the systemic use of medication could also improve the survival rate of dental implants. This study might open the door for future systemic pharmacological treatments to improve implant success. According to Martin S Greenberg 2000⁶¹ detection of hypertensive patients is important from several aspects. Significant complications of hypertension can be avoided or minimized by early detection and treatment. From a dental standpoint, potentially life-threatening complications can be prevented by not performing dental treatment for patients at risk because of severe uncontrolled hypertension. Peacock and Carson⁶² found that over half the patients attending a periodontal clinic had a significant medical history, with drug allergies and cardiovascular disorders being predominant. Dental implants are in the bone and do not have any effect on bone integration. However, blood pressure and medications are taken to manage harmful situations for patients who have not properly addressed their condition with their treating dentists. Vaishnavi Devi. B, Priyalochan Gajendran 2021⁶³ also constituted those cardiovascular diseases may compromise the osseointegration and healing process due to decreased blood flow which reduces the supply of nutrients and oxygen to the tissues causing a reduction of fibroblast activity, collagen synthesis, capillary growth, and macrophage actions favoring infections. Whereas on the other hand Debby Hwang, DMD, and Hom-Lay Wong in 2007⁶⁴

said that certain systemic conditions and habits such as hypertension, atherosclerosis, vascular stenosis, coronary artery diseases, and Congestive Heart Failure may impair the healing process, which depends on the oxygen supply delivered by normal blood flow, this impairment leads to tissue hypoxia and results in necrosis of bone due to which chances of infection increases. Some hypothesis about blood pressure was given by Moy Pk, Medina D, Shetty V, Aghalou TL 2005⁶⁵ proven high risk of failure in patients with uncontrolled blood pressure is related to the possibility that the impaired blood supply and the consequent hypoxia may negatively affect the healing process of bone around implants. Epinephrine used along with local anaesthesia have more intense effects on the heart when they are combined with non-selective beta-blockers can result in a rapid increase in blood pressure which was advocated by Chappuis *et al* 2018 and Silverstein LH *et al* 1995.⁶⁶ Wuxi, Abedella K *et al* 2016⁶⁷ introduced a cohort study that was associated with implant failure and hypertension. But C. Scully, J Hobkirk, and P.D Dios 2007⁶⁸ found no evidence that cardiac disorders of any kind are contraindicated for dental implants only, medical consent should be taken first if the patient is suffering from any associated disorders such as hypertension, cardiac failure, bleeding tendency, ischaemic heart diseases or any risk of infective endocarditis. Daisuke Ueno *et al* 2012⁶⁹ also favor it and have proven that I.V sedation using midazolam and propofol reduces hypertensive risk during implant surgery. Nevertheless, care should be taken especially in older hypertensive patients and in hypertensive patients on ARBs or ARB+CCBs. Taguchi I *et al* 2011⁷⁰ also suggested sedation with midazolam before implant surgery to better stabilize hemodynamics and reduce stress. Recent animal studies involving antihypertensive medications and implants have shown that the bone implant contact percentage and peri-implant bone tissue volume of rats are significantly increased by propranolol, a non-selective beta-blocker.⁷¹ On the other hand, also concluded in a cohort study that, the survival rate of dental implants in patients with antihypertensive therapy, was higher in comparison to non-users.⁷² A dental implant Procedure is a treatment of choice for missing teeth but Diabetes, hypothyroidism, CVS, etc., have a negative influence on the success of dental implants.⁷³

The implant procedure failure rates may tend to increase without proper metabolic control in diabetic patients. It has also been proved that the patients with controlled hypertension do not pose

a higher risk of implant failure and have similar success rates as that of non-hypertensive patients.⁷⁴ Although we could find no evidence, that cardiac disorders of any kind are a contraindication for dental implant therapy, it is important to consider problems that are associated with hypertension, cardiac failure, bleeding disorders, ischaemic heart disease, or any risk of infective endocarditis. Such patients with cardiac disorders may not be considered a good risk group, and medical advice should be taken first for undergoing any kind of surgical procedure.

CONCLUSION

Dental treatment mostly carried out under local anesthesia has excellent safety records with or without sedation. Many dental patients with undetected or poorly controlled hypertension will be benefitted greatly if their hypertension is detected and they are referred for diagnosis and effective medical treatment of their condition. Whereas, Cardiac diseases increasingly becoming the most common cause of morbidity and mortality in our elderly population. Preferably morning appointments are considered for dental treatment because we have more time to take effective measures if any peri-treatment problems occur and there is less time for the patient to become anxious. To alleviate anxiety and effective analgesia it is important to consider premedication for stress reduction. Every effort should be made to keep procedures time down to a minimum, and treatment should be terminated early if the patient becomes overly anxious. Local anesthetics are given the potential problems and impregnated gingival displacement cords should be avoided in those with hypertension and ischemic heart disease.

Good communication forms the basis of safe care. The influence of high blood pressure remains controversial for long-term dental implants. So, in future outcomes more investigations needed to be done for clarifying the role of high blood pressure on dental implant therapy and also it is important for the dentists to be aware of hypertension in relation to the practice of dentistry.

REFERENCES

- Jemt T (1993) Implant treatment in resorbed edentulous upper jaws. *Clin Oral Impl Res* 4(4): 187-194.
- Coulthard P (2002) Should be checking blood pressure. *Br Dent J* 193 (5). 3. Greenwood M, Jowry RJ (2002) Blood pressure measuring equipment in the dental surgery: Use or ornament? *Br Dent J* 193 (5): 273-275.
- Greenwood M, Jowry RJ (2002) Blood pressure measuring equipment in the dental surgery: Use or ornament *Br Dent J* 193 (5): 273-275.
- Halberg E, Delmore P, Finch M, Cornelissen G, Halberg F. Chronobiologic assessment of deviant human blood pressure: an invitation for improvements. *ProgClinBiol Res* 1990.
- Little JW, Halberg F. A new horizon in the prevention, diagnosis, and treatment of hypertension: what role should dentistry play *Gen Dent* 1991.
- MacDonald MB, Laing GP, Wilson MP, Wilson TW. Prevalence and predictors of white-coat response in patients with treated hypertension. *CMAJ* 1999.
- TrucThi Hoang Nguyen*, Mi Young Eo*, Yun Ju Cho, HoonMyoung, Soung Min Kim.
- British Dental Journal* Volume 189 no. 6 September 23 2000.
- C. Scully*, J. Hobkirk* & P. D DIOS†, *Journal of Oral Rehabilitation* 2007 34; 590-599.
- Schwartz AD, Bar TY, Ilana E (2007) Effect of on information processing in the dental implant surgery setting. *Clin Oral Impl Res* 18(1): 9-12.
- Brand HS, Gortzaak RA, Palmer BC, Abraham RE, Abraham IL (1995) Cardiovascular and neuroendocrine responses during acute stress induced by different types of dental treatment. *Int Dent J* 45(1): 45-48.
- Gortzak RA, Dosting J, Abraham IL (1992) Blood pressure response to routine restorative dental treatment without local anesthesia. Continuous non-invasive blood pressure registration with a finger manometer. *Oral Surg Oral Med Oral Pathol* 73(6): 677-681.
- Wu X, Abedalla K, Elmar H, Daniel NG, Nicolau B, *et al.* (2016) Antihypertensive medications and survival rate of osseointegrated dental implants: A cohort study. *Clin Implant Dent Relat Res* 18[6]: 1171-1182.
- Intro bad Wala. 7. Diego RG, Gomez-de Diego R, la Rosa MM, Romero-Perez MJ, Cutando-Soriano A, Lopez-Valverde-Centeno A. Indications and contraindications of dental implants in medically.
- Akay AS, Arisan V. Dental Implants in the Medically Compromised Patient Population [Internet]. *Clinical Trials in Vulnerable Populations*. 2018.
- Singh S, Shankar R, Singh GP. Prevalence and Associated Risk Factors of Hypertension: A Cross-Sectional Study in Urban Varanasi [Internet]. Vol. 2017, *International Journal of Hypertension*. 2017. p. 1-10.

17. Khadivi V, Anderson J, Zarb GA. Cardiovascular disease and treatment outcomes with osseointegration surgery [Internet]. Vol. 81, The Journal of Prosthetic Dentistry. 1999. p. 533–6.
18. Ferrannini E, Cushman WC. Diabetes and hypertension: the bad companions [Internet]. Vol. 380, The Lancet. 2012. p. 601–10.
19. Group H in DS, Hypertension in Diabetes Study Group. Hypertension in Diabetes Study III. Prospective Study of Therapy of Hypertension in Type 2 Diabetic Patients: Efficacy of ACE Inhibition and β -Blockade [Internet]. Vol. 11, Diabetic Medicine. 1994. p. 773–82.
20. Stamler J, Vaccaro O, Neaton JD, Wentworth D, The Multiple Risk Factor Intervention Trial Research Group. Diabetes, Other Risk Factors, and 12-Yr Cardiovascular Mortality for Men Screened in the Multiple Risk Factor Intervention Trial [Internet]. Vol. 16, Diabetes Care. 1993. p. 434–44.
21. Scheuber S, Hicklin S, Bragger U. Implants versus short-span fixed bridges: survival, complications, patients' benefits. A systematic review of economic aspects. Clin Implants Res. 2012 Oct;23 Suppl 6:50–62.
22. Ramesh A, Ravi S, Karthikeyan G. Comprehensive rehabilitation using dental implants in generalized aggressive periodontitis. J Indian Soc Periodontol. 2017 Mar;21(2):160–3.
23. Bragger U, Krenander P, Lang NP. Economic aspects of single-tooth replacement. Clin Oral Implants Res. 2005 Jun;16(3):335–41.
24. Mulinari-Santos G, de Souza Batista FR, Kirchweger F, Tang S, Gruber R, Okamoto R. Losartan reverses impaired osseointegration in spontaneously hypertensive rats [Internet]. Vol. 29, Clinical Oral Implants Research. 2018. p. 1126–34.
25. Ong KL, Cheung BMY, Man YB, Lau CP, Lam KSL. Prevalence, Awareness, Treatment, and Control of Hypertension Among United States Adults 1999–2004 [Internet]. Vol. 49, Hypertension. 2007. p. 69–75.
26. Nikolopoulou, Anestis Chrysostomidis. Hypertension and Dental Implants: A Review. Surg Med Open Access J.3(1).
27. Cappuccio FP, Meilahn E, Zmuda JM, Cauley JA. High blood pressure and bone-mineral loss in elderly white women: a prospective study [Internet]. Vol. 354, The Lancet. 1999. p. 971–5.
28. Strazzullo P, Nunziata V, Cirillo M, Giannattasio R, Ferrara LA, Mattioli PL, *et al.* Abnormalities of Calcium Metabolism in Essential Hypertension [Internet]. Vol. 65, Clinical Science. 1983. p. 137–41.
29. Puleo D. Understanding and controlling the bone-implant interface [Internet]. Vol. 20, Biomaterials. 1999. p. 2311–21.27. Asaba Y, Ito M, Fumoto T, Watanabe K, Fukuhara R, Takeshita S, *et al.* Activation of Renin-Angiotensin System Induces Osteoporosis Independently of Hypertension [Internet]. Vol. 24, Journal of Bone and Mineral Research. 2009. p. 241–50.
30. Asaba Y, Ito M, Fumoto T, Watanabe K, Fukuhara R, Takeshita S, *et al.* Activation of Renin-Angiotensin System Induces Osteoporosis Independently of Hypertension [Internet]. Vol. 24, Journal of Bone and Mineral Research.
31. Abuhashish HM, Ahmed MM, Sabry D, Khattab MM, Al-Rejaie SS. The ACE-2/Ang1-7/Mas cascade enhances bone structure and metabolism following angiotensin-II type 1 receptor blockade [Internet]. Vol. 807, European Journal of Pharmacology. 2017. p. 44–55.
32. Van Steenberghe D, Jacobs R, Desnyder M, *et al.* The relative impact of local and endogenous patient-related factors on implant failure up to the abutment stage. Clin Oral Implants Res. 2002;13: 617–622.
33. Perez-Castrillon JL, Justo I, Sanz-Cantalapiedra A, Pueyo C, Hernandez G, Duenas A. Effect of the antihypertensive treatment on the bone mineral density and osteoporotic fracture. CurrHypertens Rev 2005; 1:61–66.
34. Schlienger RG, Kraenzlin ME, Jick SS, Meier CR. Use of β -blockers and risk of fractures. JAMA 2004; 292: 1326–1332.
35. Duarte JD, Cooper-De Hoff RM. Mechanisms for blood pressure lowering and metabolic effects of thiazide and thiazide-like diuretics. Expert Rev Cardiovasc Ther 2010; 8:793–802.
36. Rejnmark L, Vestergaard P, Mosekilde L. Treatment with beta-blockers, ACE inhibitors, and calcium-channel blockers is associated with a reduced fracture risk: a nationwide case-control study. J Hypertens 2006; 24:581–589.
37. Pierroz DD, Bonnet N, Bianchi EN, *et al.* Deletion of adrenergic receptor 1, 2, or both leads to different bone phenotypes and response to mechanical stimulation. J Bone Miner Res 2012; 27:1252–1262.
38. Eleftheriou F, Ahn JD, Takeda S, *et al.* Leptin regulation of bone resorption by the sympathetic nervous system and CART. Nature 2005; 434:514–520.
39. Albrektsson T, Branemark P-I, Hansson H-A, Lindström J. Osseointegrated titanium implants: requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. ActaOrthop 1981; 52:155–170.
40. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants, (II). Etiopathogenesis. Eur J Oral Sci 1998; 106: 721–764.
41. Puleo D, Nanci A. Understanding and controlling the bone-implant interface. Biomaterials 1999; 20:2311–2321.
42. Ghosh M, Majumdar SR. Antihypertensive medications, bone mineral density, and fractures:

- a review of old cardiac drugs that provide new insights into osteoporosis. *Endocrine* 2014; 46:397-405.
43. Walker RL, Chen G, Campbell NR, *et al.* Canadian provincial trends in antihypertensive drug prescriptions between 1996 and 2006. *Can J Cardiol* 2011; 27:461-467.
 44. Moore RE, Smith CK, II, Bailey CS, Voelkel EF, Tashjian AH, Jr. Characterization of beta-adrenergic receptors on rat and human osteoblast-like cells and demonstration that beta-receptor agonists can stimulate bone resorption in organ culture. *Bone Miner* 1993; 23:301-315.
 45. Bazzini C, Vezzoli V, Sironi C, *et al.* Thiazide-sensitive NaCl-cotransporter in the intestine possible role of hydrochlorothiazide in the intestinal Ca²⁺ uptake. *J Biol Chem* 2005; 280:19902-19910.
 46. Aubin R, Menard P, Lajeunesse D. Selective effect of thiazides on the human osteoblast-like cell line MG-63. *Kidney Int* 1996; 50:1476-1482.
 47. Nakagami H, Osako MK, Morishita R. Potential effect of angiotensin II receptor blockade in adipose tissue and bone. *Curr Pharm Des* 2013; 19:3049-3053.
 48. Rejnmark L, Vestergaard P, Mosekilde L. Treatment with beta-blockers, ACE inhibitors, and calcium-channel blockers is associated with a reduced fracture risk: a nationwide case-control study. *J Hypertens* 2006; 24:581-589.
 49. Scully C, Hobkirk J, Dios PD (2007) Dental endosseous implants in the medically compromised patient. *J Oral Rehabil* 34[8]: 590-599.
 50. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Washington, DC: National Institutes of Health, National Heart, Lung, and Blood Institute; 1997.
 51. Alvarez Li FC, Espinosa Brito AD, Ordunez Garcia PO, Silva Aycaguer LC. Risk markers and high blood pressure. The Cienfuegos Global Project. Longitudinal study 1992-1994. *Rev Invest Clin* 1999.
 52. Beilin LJ, Puddey IB, Burke V. Lifestyle and hypertension. *Am J Hypertens* 1999.
 53. Chrysant GS, Bakir S, Oparil S. Dietary salt reduction in hypertension—what is the evidence and why is it still controversial? *Prog Cardiovasc Dis* 1999.
 54. Rahn KH, Barenbrock M, Hausberg M. The sympathetic nervous system in the pathogenesis of hypertension. *J Hypertens* 1999.
 55. N. I. Jowett, 1 and L. B. Cabot, 2 *British Dental Journal* Volume 189 No. 6 September 23 2000.
 56. Schwartz-Arad D, Bar-Tal Y, Eli I. Effect of stress on information processing in the dental implant surgery setting. *Clin. Oral Impl. Res.* 18, 2007; 9-12.
 57. Brañemark P-I, Breine U, Adell R, Hansson B, Lindström J, Ohlsson A. Intra-osseous anchorage of dental prostheses: I. Experimental studies. *Scand J Plast Reconstr Surg Hand Surg* 1969; 3:81-100.
 58. Albrektsson T, Brañemark P-I, Hansson H-A, Lindström J. Osseointegrated titanium implants: requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. *Acta Orthop* 1981; 52:155-170.
 59. Liu Y, Enggist L, Kuffer AF, Buser D, Hunziker EB. The influence of BMP-2 and its mode of delivery on the osteoconductivity of implant surfaces during the early phase of osseointegration. *Biomaterials* 2007; 28:2677- 2686.
 60. Cuando A, Gomez-Moreno G, Arana C, *et al.* Melatonin stimulates osteointegration of dental implants. *J Pineal Res* 2008; 45:174-179.
 61. James W. Little, DMD, MSA Minneapolis, Minn University of Minnesota, (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:591-9.
 62. Peacock M E, Carson R E. Frequency of self-reported medical conditions in periodontal patients. *J Periodontal* 1995; 66: 1004-1007.
 63. Vaishnavi Devi. B, Priyalochana Gajendran, Delphine Priscilla Antony.S, *European journal of research and clinical medicine.* ISSN 2515-8260 volume 08- ISSUE 03, 2021.
 64. Debby Hwang, DMD, * and Hom-Lay Wang, DDS, MSD. *Implant Dentistry / Volume 16, Number 1 2007.*
 65. Moy PK, Medina D, Shetty V, Aghaloo TL (2005) Dental implant failure rates and associated risk factors. *The Int J Oral Maxillofacial Impl* 20(4): 569-577.
 66. Silverstein LH, Koch JP Lefkove MD, *et al.* (1995) Nifedipine-induced gingival enlargement around dental implants: A clinical report. *J Oral Implantol* 21(2): 116-120.
 67. Wu X, Abedalla K, Elmar H, Daniel NG, Nicolaus B, *et al.* (2016) Antihypertensive medications and survival rate of osseointegrated dental implants: A cohort study. *Clin Implant Dent Relat Res* 18[6]: 1171-1182.
 68. Scully C, Hobkirk J, Dios PD (2007) Dental endosseous implants in the medically compromised patient. *J Oral Rehabilitation* 34[8]: 590-599.
 69. Daisuke Ueno, Junichi Sato, Jun Nejima, Keisuke Maruyama, Mariko Kobayashi, Toshikazu Iketani, Rei Sekiguchi, Hiroshi Kawahara *Int J Oral Maxillofacial Implants* Nov-Dec 2012;27(6):1520-6.
 70. Taguchi I, Fukuda K, Sekine H, Kakizawa T (2011) Intravenous sedation and hemodynamic

- changes during dental implant surgery. *Int J Oral Maxillofacial Impl* 26(6): 1303-1308.
71. Al-Subaie AE, Laurenti M, Abdallah MN, Tamimi I, Yaghoubi F, Eimar H, et al. Propranolol enhances bone healing and implant osseointegration in rats' tibiae. *J Clin Periodontal*. 2016; 43:1160-70
72. Wu X, Al-Abdalla K, Eimar H, *et al.* Antihypertensive medications and the survival rate of osseointegrated dental implants: a cohort study. *Clin Implant Dent Relat Res*. 2016; 18:1171-82.
73. Parihar, Anuj Singh *et al.* "Assessment of failure rate of dental implants in medically compromised patients." *Journal of family medicine and primary care* vol. 9,2 883-885. 28 Feb. 2020.
74. Liddelow G, Klineberg I. Patient-related risk factors for implant therapy. A critique of pertinent literature [Internet]. Vol. 56, *Australian Dental Journal*. 2011.
-