

Effect of Vitamin D supplement on Gingivitis and Salivary Parameters in Patients with Vitamin D deficiency

Dr.Hussain Owaid Muhammed

Department of Periodontics, College of dentistry, Al-Mustansyria University.
: drhussain720@gmail.com

Abstract:

Background : Vitamin D, play a role in maintain oral health through it is effect on bone and mineral metabolism as well as it is effect on innate immunity. In addition most recent studies confirmed it is antimicrobial and anti-inflammatory effect.

Aims: To evaluate the effect of Vitamin D supplement on gingival index, salivary Immnoglobuline A (SIgA) secretion rate,salivary flow rate(SFR) and salivary PH. As antimicrobial and anti-inflmmtory effect.

Subjects and methods: Out of 132 patients, 28 with vit.D deficiency and gingivitis currently on initial supplement with vit.D was chosen to participate in this study. Patients who take the medication regularly throughout the study were considered as patients group and who did not take the medication due to any reason were assigned as control group. Gingival index ,Salivary Immunoglobuline A (SIgA),Salivary flow rate (SFR) and salivary PH were assessed pre and post administration of vitamin D.

Results:- The result of current study revealed that the gingival index was significantly reduced post supplement of vit.D in patients who were taken the medication regularly (pre=2.7, post 1.8, p=0.01) while nonsignificant difference was seen in control group (pre=2.9, post 2.6, p=0.6).The salivary IgA, SFR and salivary PH was significantly increased(p≤0.05) after supplement of vit.D with patients who were taken the medication regularly (pre=434.3, post=687.7)(pre=0.9, post=1.8)(pre=6.7, post=7.1) respectively while nonsignificant difference(p≥0.05) was reported with control group (pre=424.3, post=467.7)9pre=0.8, post=1.1)(pre=6.5, post=6.8) respectively.

Conclusion :- According to results inthis study, we conclude that, the using of Vitamin D supplement lead to asignificant anti-inflammatory effect and also and also patient with gingivitis to be screened for Vit. D deficiency.

الخلاصة:

خلفية البحث:- فيتامين (د) له دور في ادامة صحة الفم من خلال تأثيره على ايض العظام والاملاح وتأثيره على الجهاز المناعي بالاضافه لذلك فقد اثبت معظم الدراسات الحديثه فعاليته كمضاد للمايكروبات ومضاد للالتهابات. هدف الدراسة:- لاستكشاف فيما اذا كان هناك دور لفيتامين (د) على مؤشر اللثة،افراز الامينوكولوبين اللعابي ،معدل تدفق اللعاب وكذلك حموضيه اللعاب.

طريقةالدراسة :- من مجموع 132 مريضاً ممن يعانون من نقص فيتامين دي تم شمول 28 مريضاً ممن لديهم التهاب اللثة في الدراسة. وقد تم اعتبار (17) مريضاً ممن التزموا بالعلاج لنهاية فترة الدراسة كمجموعه مرضيه واعتبار (11) مريضاً ممن لم يأخذوا فيتامين (د) لاي سبب كان كمجموعة مراقبة.تم قياس مؤشر اللثة،امينوكولوبولين اللعاب،افرازية اللعاب وحموضته قبل وبعد اعطاء فيتامين(د) في المجموعتين.

نتائج الدراسة:- لقد اثبتت النتائج وجود فرق معنوي في مستوى مؤشر اللثة في المجموعة المرضية(17) مريضاً، الذين التزموا باخذ فيتامين(د) بصوره منتظمه قبل وبعد اخذ العلاج، وقد كان قبل العلاج =2.7 اما بعد العلاج =1.8 ولم يلاحظ وجود فرق معنوي في مؤشر اللثة في مجموعة المراقبة(11) مريضاً الذين لم يأخذوا فيتامين(د)، وكذلك اثبت النتائج وجود فرق معنوي في مستوى الامينوكولوبولين في اللعاب نوع اي ومستوى افراز اللعاب وحموضة اللعاب قبل وبعد اعطاء فيتامين(د) في المجموعة المرضية ولم يلاحظ وجود فرق معنوي في مجموعة المراقبة.

الاستنتاجات : من خلال نتائج البحث الذي قمنا به ان فيتامين(د) يلعب دور مهم كمضاد لالتهاب اللثة ونوصي بان يتم التحري عن نقص فيتامين(د) في المرضى الذين يشكون من التهاب اللثة .

Introduction:

Vitamin D is a fat-soluble vitamin derived either from endogenous or exogenous (dietary) source^[1]. There are two forms of vitamin D can be obtained from dietary sources; vitamin D₃ which obtained from diet of animal origin and vitamin D₂ which present in some plants and fungi^[2]. The diet derived vitamin D₂, D₃ and endogenously synthesized vitamin D₃ hydroxylated firstly in the liver into 25-hydroxy vitamin D(25OH)D then converted to biologically active form 1,25 dihydroxy vitamin D(1,25(OH)₂D) by 1- α -hydroxylase in the renal or non-renal compartments such as cells of the immune systems^[3].

The level of ≥ 75 nmol/L of serum 25(OH)D was recommended by some distinguished research groups but the recommendations given by the US National Institutes of Health state that a level of ≥ 50 nmol/L is adequate for bone and overall health. At the same time, many experts would define serum levels of < 50 nmol/L as Vitamin D deficiency and levels between (50 – 70) nmol/L as insufficiency^[4].

In 2010, the Institute of Medicine in USA released new recommendations for dietary intake of vitamin D: 400 IU/d (0–12 mo of age); 600 IU/d (1–70 years of age); and 800 IU/d for older adults (> 70 years of age)^[5]. Several experts feel that although these Institute of Medicine levels may prevent clinical vitamin D insufficiency (typically reported as < 30 ng/mL) and deficiency (< 20 ng/mL), they are significantly lower than the dose required to achieve optimal vitamin D status regulated through autocrine mechanisms^[6].

Vitamin D plays an important role in various physiological processes such as calcium homeostasis, cellular growth and differentiation, immunity modulation and cardio vascular function^[3]. Recent evidence suggests there is a protective role for the adequate serum levels of vitamin D metabolites against cardiovascular disease, diabetes, hypertension and cancer,

probably through the regulation of inflammatory pathways^[7]. In addition to anti-inflammatory role of vitamin D, many studies support the conception that Vitamin D has an anti-infective properties^[8].

The available evidence from the past ten years suggests that low levels of the two forms of Vitamin D (25(OH)D and 1,25(OH)₂D) are associated with a wide range of inflammatory/infectious conditions^[9]. The author Bikle D *et al*^[10] reported that the vitamin D enhancing the antimicrobial properties of immune cells as a vital mediator of innate immune response,

while Liu, P. T^[11] stated that the vitamin D has a vital role in up-regulating the production of antimicrobial proteins (AMPs), such as cathelicidin and β -defensin after activation the Toll-like receptor signaling cascade in the presence of microbes. These AMPs have a broad range of activities against microorganisms and may be involved in the direct inactivation of viruses through membrane destabilization.

The gingivitis and periodontitis are considered the most common disease of the periodontium; in gingivitis the inflammation involved epithelium and connective tissue while in periodontitis associated loss of periodontal connective tissue and tooth-supporting bone occurs. Previously the etiologies of gingivitis and periodontitis were limited to microbial cause but this notion is being updated and expanded today^[12]. Cannell JJ *et al*^[13] reported that the innate and adaptive immune response to microbial antigen in gingivitis and periodontitis modulated partly by active form of vitamin D. Stein SH *et al*^[14] demonstrated that the vitamin D have a positive impact on oral health through its anti-inflammatory properties and its capacity to stimulate the production of antimicrobial peptides, such as defensins and cathelicidin. A study carried out by He C S *et al*^[15] demonstrated that the administration of vitamin D to athletes

who were presented with low level of vitamin D result in significantly raising the level of cathelicidin and increased the S.IgA secretion rate in comparison to placebo group and such finding reflects in part the role of vitamin D in maintaining of the local defense mechanism in the oral cavity and maintaining the oral health.

This study was designed to evaluate the effect of vitamin D3 supplementation on the gingival index, concentrations of salivary IgA, SFR and salivary PH. throughout two months.

Subject and method:-

From Jan.-Dec.2016, Out of 132 patients with vitamin D deficiency screened on initial treatment at Medical City Teaching Hospital and many private clinics for presence of gingivitis, 28 patients who have had gingivitis were selected and enrolled in this study. Patient that has nutrients deficient other than vit.D was excluded.

Patients who were taken vit D tab.(500-2000) IU(international unit) aday,according to vit.D deficiency, the medication regularly throughout the study were considered as patients group and who did not take the medication due to any reason were assigned as control group. Gingival index, Salivary Immunoglobuline A, Salivary flow rate(SFR) and PH for each patient was measured pre and after two months of vitamin D supplement in patients and control groups.

Estimation of SIgA by(ELISA) test procedure,and salivary flow rate (SFR) ml/min was estimated by dividing the total collected saliva volume (ml)by collecting

time (min) that was measured by sample collection:

SFR ml/min = saliva sample volume (ml)/ collection time (min).

Salivary pH was measured with a digital pH-meter (Hanna Instruments, USA) 30 to 60 minutes after saliva samples were collected, and pH was considered as a quantative variable.

Ethical issue:-

Approval was obtained from concerned authorities, patients name were kept hidden.

Statistical analysis.

Statistical Package for the Social Sciences(SPSS) version 20 was used for data entry and analysis, mean and slandered deviation was used to represent the continuous data. Paired sample T test was used for data analysis. P-value \leq 0.05 considered significant.

Results:-

The results showed that the mean age of the patients was 32.3 \pm 2.1 SD and 68.3% was male. Eleven patients who were not take medication for any reason were considered as control and the remaining patients (17) who were taken the vitamin D regularly were considered as patient group. The results demonstrated that the mean of gingival index(GI) was significantly reduced from 2.7 to 1.8 after two months of vitamin D supplement with mean difference of 0.9,no significant difference was reported with control group (p=0.6) as shown in table.1 and Figure-1.

Table-1: The mean of Gingivitis index (GI)pre and post vit D supplement.

Study Groups	Time of treatment of vitamin D	Mean	Std. Deviation	Mean difference	p-value
Patients group N=17	Pre	2.7	0.8	0.9	0.01
	Post	1.8	0.7		
Control group N=11	Pre	2.9	0.9	0.3	0.6
	Post	2.6	0.6		

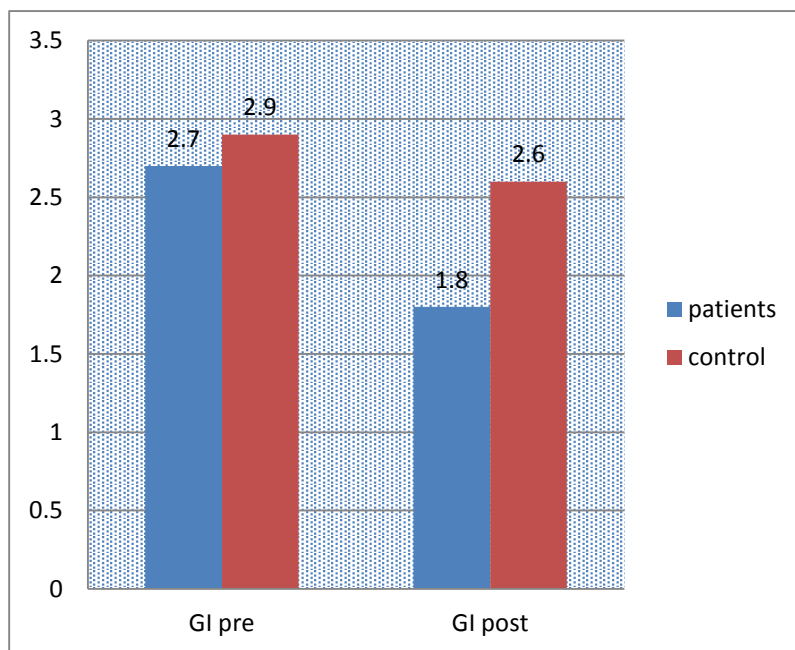


Figure-1 Gingivitis index (GI) pre and post vit.D supplement

The finding of current study revealed that the S.IgA significantly increased (P=0.02) after two months of vitamin D supplement with mean difference of 253.4, while non-

significant difference was reported regarding the control group as seen in table-2 and Figure-2.

Table-2 : The mean of SIgA pre and post vit. D supplement .

Study groups	Time of treatment of vit.D	S.IgA Mean mg/L	Std. Deviation	Mean difference	p-value
Patients group N=17	Pre	434.3	23.2	253.4	0.02
	Post	687.7	26.7		
Control group N=11	Pre	424.3	21.1	43.4	0.4
	Post	467.7	22.4		

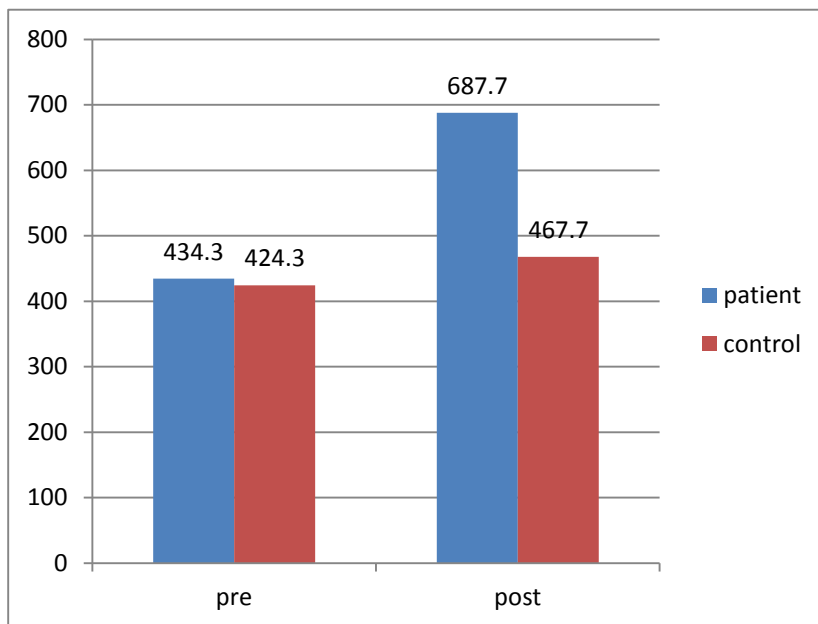


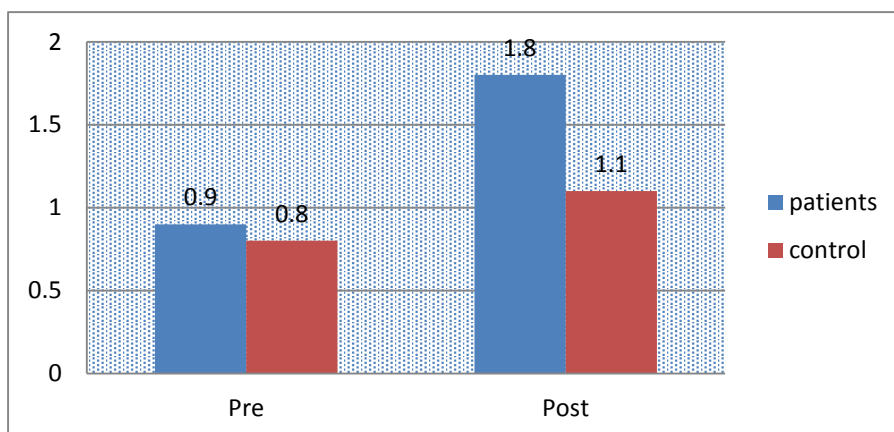
Figure -2: The mean of Salivary (IgA) pre and post vit. D supplement

The salivary flow rate was increased from 0.9 to 1.8 $\mu\text{L}/\text{min}$ after two months of follow up and this difference was reached

the significant level ($P=0.03$), no difference was observed with control group as shown in table-3 and Figure-3.

Table-3: The mean level of SFR in pre and post vit.D supplement

Study groups	Time of treatment	SFR Mean $\mu\text{L}/\text{min}$	Std. Deviation	Mean difference	p-value
Patients group N=17	Pre	0.9	0.2	0.8	0.03
	Post	1.8	0.2		
Control group N=11	Pre	0.8	0.1	0.2	0.3
	Post	1.1	0.3		



Figure(3) SFR level pre and post vit.D supplement

The mean value of salivary PH was significantly increased at the end of two months of supplement with vitamin D from

6.7 to 7.1,difference with control group did not reach the significant level (p=0.7) as shown in table-4 and Figure-4.

Table-4: The salivary PH level in pre and post Vit.D supplement

Study groups	Time of treatment	PH Mean	Std. Deviation	Mean difference	p-value
Patients group N=17	pre	6.7	0.3	0.4	0.02
	post	7.1	0.4		
Control group N=11	pre	6.5	0.1	0.3	0.7
	post	6.8	0.3		

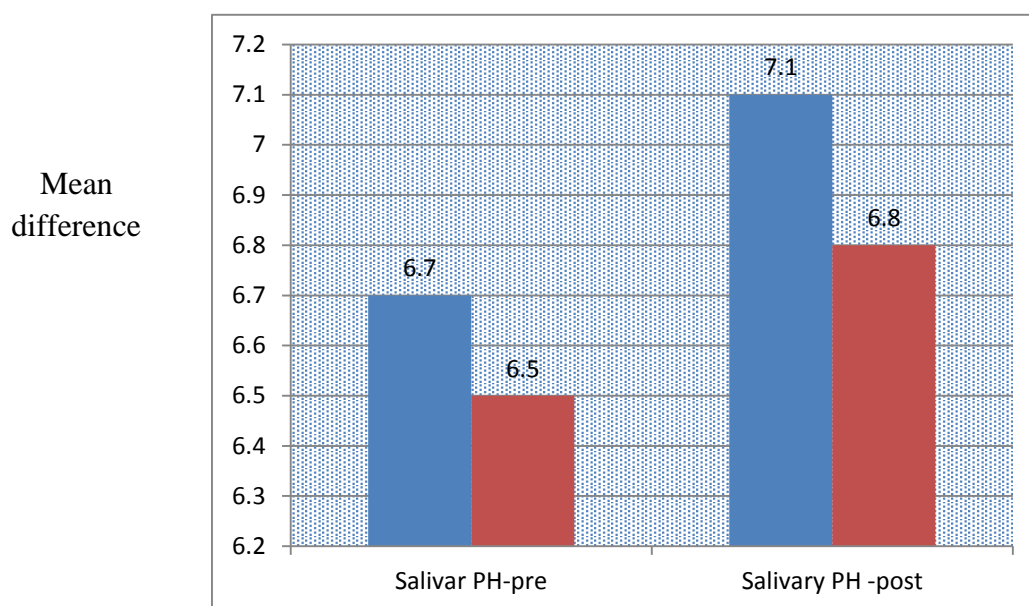


Figure-4: The salivary PH pre and post vit.D supplement

Discussion:

The vitamin D plays an essential role in maintaining bone health through regulating calcium concentrations in the body. The development of vitamin D deficiency is associated with deteriorating bone health and in severe cases, hypocalcaemia, rickets, and osteomalacia in children and adults^[16]. Early vit. D deficiency has been associated with adverse long-term effects on dental health, including delayed dentation, enamel defects, increased risk of caries and gingival inflammation^[17]. Dietrich *et al.* (2005)^[18] found an increased risk of periodontal disease and caries in children with vit. D deficiency.

In this study we observed that the gingival index was significantly decreased after supplementation of vit. D and this may reflect the anti-inflammatory role of vit.D, this finding partly in harmony with the results of study was conducted by Hiremath *et al*^[19], where they studied the anti-inflammatory effects of Vit.D in 88 patients initially diagnosed with gingivitis, after Vit.D supplementation for a period of 3 months with a different dosage for each of the 4 groups, authors demonstrated an anti-inflammatory effect for vitamin D but they concluded that the anti-inflammatory of vitamin D is dose dependent where that patients who were on 2000IU of Vit.D showed reduction of gingivitis faster than the patients who were on the 500IU as well

as the stated that the serum Vit.D concentration of >30-35 ng/ml was the level over which Vit.D exerts its anti-inflammatory action. In another study, Dietrich *et al* ^[18] examined the association between serum 25(OH) D concentration and gingival inflammation. They found an inverse association between serum concentrations of 25(OH) D3 and prevalence of bleeding on probing (BOP) after correction for a number of confounding variables. This association was attributed to the anti-inflammatory effect of vitamin D and the authors suggested that the higher serum 25(OH) D levels may be beneficial in regards to gingival health. The author Garcia M *et al* ^[20] has found that periodontal maintenance in patients taking calcium and vitamin D supplements had lower gingival index values compared with those who did not and this finding reflect the anti-inflammatory role of vit.D. The author Gombart A F ^[21] was reported that adequate vitamin D status is necessary for adequate innate immunity, particularly expression of antimicrobial peptides such as cathelicidin which promotes oral health. The finding of current study showed there was significant difference in the level of salivary IgA, SFR and salivary PH and this findings are in line with finding of a study was carried out by Cheng-Shiun *et al* ^[22] has found that the resting salivary SIgA secretion rates significantly increased over time in the vitamin D3 group in compare to placebo group and they attributed this significant difference to the elevated salivary flow rates after vitamin D3 supplementation where they reports that the salivary flow rates significantly increased over time in the vitaminD3 group, also they reported there are several animal studies have demonstrated that vitamin D receptors are present in the parotid, submandibular and sublingual salivary glands, which suggest a possible role for vitamin D in the regulation of salivary secretion.

With regard to anti-inflammatory effect of vitamin D, the authors Zhang *et al* ^[23] satiated that the 1, 25(OH)₂D inhibit the production of pro-inflammatory cytokines (Interleukin-1 α , Interleukin-6 and tumor necrosis factor TNF- α) in lipopolysaccharide stimulated monocytes.

Conclusion :

From the study we conclude that Vitamin D has as an anti-inflammatory effect and enhancing the rate of salivary IgA secretion. Further studies with larger sample size are needed to investigate the beneficial effect of vit. Supplementation on patients suffering gingival inflammations.

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