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Vitamin D therapy's preventive effect in type 2 diabetes mellitus

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Abstract:

Diabetes type II (DM II) is becoming more common, and it is highly harmful to several bodily systems. It's critical to keep DM II under control in order to avoid consequences like diabetic nephropathy, peripheral neuropathy, and damage to the retina. The fact that vitamin D lowers hemoglobin A1c (HbA1c) levels is just one of its many benefits. It boosts insulin's sensitivity and secretion. To find pertinent data, we thoroughly searched PubMed, a Medline, PMC, and Google Scholar. Following the application process of the inclusion and exclusion criteria, the studies' quality was assessed using the Cochrane bias analysis, the SANRA (Scale for the Testing of Narrative Review Articles) checklist, the AMSTAR (A Measuring Tool to Assess A Systematic Reviews) criteria, and the AMSTAR criteria. Data has been collected from 14 studies, of which 5 case reports, 3 general articles about DM II and vitamin D, 1 review of the literature, and 8 systematic reviews or meta-analyses.

Three were narrative reviews and three were randomized controlled studies. The clinical significance of vitamin D treatment in type 2 diabetes is also evaluated in this study from the perspectives of glucose metabolism and adverse effects such retinopathy, neurotoxicity, and proteinuria. In terms of hemoglobin A1c (HbA1c) reduction, the relief of diabetic neuropathy and nephropathy symptoms, and the reduction of oxidative stress brought on by hypoglycemia in the retinal cells, vitamin D improved glucose levels clinically.

One of the essential vitamins for diabetics is vitamin D..

Introduction .

Diabetes mellitus type II (DM II) is a complex metabolic disorder that affects developed as well as emerging countries. By the year 2035, there may be 592 million cases of DM II worldwide, predicts The World Diabetes Federation Forecast (Wild S. Roglic, 2004). The CDC estimates that 90 to 95 percent of the 34 million Americans who have diabetes mellitus have type II diabetes. Pancreatic beta (B) cell dysfunction and insulin receptor resistance are both of the main causes of type II diabetes (Leahy JL, 2005, 127). One of the frequent effects of DM II is peripheral neuropathy. You must keep this consideration because, if left untreated, it is the main contributor of diabetic foot troubles and subsequent physical

disadvantage. the human receptors for hormones gene promoter, which is home to the Vitamin D signaling pathway (Leal MA, 1995, 217), (Maestro B,2,2000,74). Through the activation of its transcription factor, it influences the fatty acid metabolism in cells that respond to insulin. Additionally, it acts as a barrier to prevent cytokine-induced apoptosis (Gysemans CA,2005,146). As a result, there is a link between vitamin D deficiencies and diabetes-related problems. For instance, studies on neuropathy found that the formation of transmitters synthetase and neurotrophic chemicals is influenced by the presence of sunlight receptors in neurons and glial cells.

I - Vitamins D's Impact on Glycemic Management.

Resistance to insulin at the receptor level, pancreatic B cell dysfunction, or both can contribute to an ongoing metabolic condition II that is experienced by diabetic patients who have had diabetes for a while. These disorders are well-understood due to chronic inflammation caused by a high concentration of cytokines that are proinflammatory and proteins from the acute phase (Kolb H, Mandrup-Poulsen,2005,48). These facilitators, which are the production of a generated by adipose tissue inflammation, are what cause insulin resistance and B cell dysfunction, according to Sung CC and Liao MT in 2012 and Christakos S in 2004. According to Hu Z, Chen J, and Sun X (2019,69), vitamin D has anti-inflammatory effects that inhibit the generation of cytokines, which in turn helps to decrease the persistent low-grade inflammation that is common in type II diabetes. By controlling the expression of the long-acting insulin receptor gene, which is responsible for directing the creation of an insulin-specific receptor, antioxidant vitamin D boosts the action of insulin.

1- Numerous varieties of cells include the protein known as the insulin receptor, which binds to the blood-circulating insulin (Maestro B,1994,46). This relates to the enhanced insulin hormone manufacturing from the person's insulin gene (Giulietti A, 2007, 77). The transcription of PPAR-delta (peroxisome proliferator-activated protein delta) is additionally impacted (Dunlop TW, 2005, 349).

2. The calcium input and outflow are two of the many complex mechanisms that help insulin secretion. The hormone vitamin D is the primary regulator of calcium, which indirectly controls insulin production. Pancreatic B cells include vitamin D receptors, which help vitamin D trigger insulin release in response to blood glucose levels. Its ability to activate vitamin D is brought to light by pancreatic B cells, which also produce the 1-alpha hydroxylase enzyme (Leal MA, Aller P, 1995, 217). The active component of vitamin D, calcitriol, can speed up the conversion of pro-insulin to insulin. It has been proposed that the presence of vitamin D receptors in skeletal muscle tissue facilitates the hemostasis of glucose in this tissue. The index of hemoglobin A1c (HbA1c) is

) It has been proposed to be the A separate investigation that compare DM II patients obtaining oral Vitamin D along with metformin to those receiving only metformin found that the group obtaining Vitamin D had lower HbA1c levels following a three-month follow-up (Jung SR, Reed BJ, 2009, 297). After reviewing the meta-analysis, we learned that vitamin D supplementation lowers insulin resistance. Similar improvements have been observed in insulin release (Hu Z, Chen J, 2019, 98). The L-type calcium channels in islets B cells that are accountable for generating insulin get triggered by vitamin D (Maestro B, 2005, 146). Vitamin D treatment lowers the resistance to insulin because the protein peroxisome proliferator-activated receptor delta (PPAR-) gene regulates fatty acid metabolism and is linked to insulin resistance (Maestro B, 2005, 47). Identifying resistance to insulin is contingent upon how much of it there is.

Depending on the person's race, taking vitamin D pills has different ramifications. Participants from the Middle East did better than Asians due to a polymorphism in the vitamin D interacting protein (Jung SR, Reed BJ, 2009, 297). The likelihood of vitamin D deficiency is higher in those who's clothing choices prevent them from getting enough sun exposure; vitamin D tablets work best to cure these people. The difficulty, nevertheless, is caused by the use of anti-diabetic drugs, restricted eating habits, and vitamin D insufficiency.

II- Vitamin D's effect on diabetes peripheral neuropathy.

T2DM neurological pain is a common nerve disease that seriously impacts the quality of life for patients. Neuropathy can either be completely painless or quite painful. It is the primary cause of diabetic foot, which can result in limb amputations. There is a bad correlation between the amount of vitamin D and the condition, according to several observations on research that show patients with painful nerve damage brought on by diabetes have lower levels of vitamins D than those who don't (Shillo P, Selvarajah D, 2019; 36). According to scientific studies that examined Vitamin D as a potent painkiller, pain can be substantially decreased by an injection of the vitamin (Basit A, the Basit KA, 2016;38).

Supplementation not only accelerates the healing of diabetic foot ulcers and sores but also significantly improves nerve function (Shehab D, Al-Jarallah K, 2015, 24). Because it controls neurotrophin levels and the equilibrium of neuronal calcium, vitamin D has a protective effect on the brain (Garcion E, 2002, 13). The molecules in question, which are protein chains, help neurons survive, grow, and operate.

An RCT analysis of 67 individuals with DM II with neuropathy who received 40,000 IU of sunlight weekly showed improvements in symptoms, a decline in proinflammatory cytokines (IL-6) and an increase in interleukin-10 (Riachy R, 2002, 143). Another study discovered that taking vitamin D supplements helped to lessen the discomfort caused by cutting back on or even stopping the use of semi-

synthetic opioids. An rise in 25-hydroxyvitamin D [25(OH)-D] levels of 1 ng/ml is associated with increased nerve activity.

However, 1. conductance frequency by 2.2% and 3.4% . Additional research displayed that when the serum 25(OH)-D level drops below 16 ng/ml, the severity of the signs and symptoms of peripheral nerve injury brought on by diabetes increases.(Sebastian P.) 2018;19 Increase in TNF-alpha, IL-6, and decreased levels of IL-10 have been linked to rising HbA1c (Colotta F, 2017, 85). Additionally, it has been shown that sunlight increases IL-10 through the immune system while decreasing TNF-alpha and IL-6 (Colotta F, 2017, 95). Individuals that got excessive doses of vitamin D experienced significant impacts (Colotta F, 2017, 110).

II- ocopheryl D's implications on renal dysfunction.

Despite the use of therapeutic medicines, the prevalence of chronic renal failure—defined as a persistent decline in Cgmp or an increase in urine albumin excretion by more than 25%—has been increasing along with the duration of diabetes (Afkarian M, 1988–2014. J, 10). Short-term supplementation with the active form of vitamin D3 significantly decreased urine albumin excretion when compared to placebo, but continued use had no effect on GFR, according to a meta-analysis. Large amounts of vitamin D are thought to protect the kidneys.

According to an RCT study by Aggarwal et al.126, additional hyperparathyroidism treated with an analog of 1, 25 dihydroxyergocalciferol induced a 50% decrease in urine albumin production in people who were not undergoing renal replacement therapy in CKD stages III and IV (Goodarzi MO, 2020).

The study included people with CKD from a variety of causes in addition to renal illness (Agarwal R, 2005, 68). When compared to a randomised cross-sectional research, patients with nephropathy brought on by diabetes and a high level of who received enough vitamin D3 daily for 12 weeks had significantly lower amounts of albumin in their urine. Identical results reported found in other RCT trial that was not impacted by a condition called hyper in which most of the individuals had GFRs more than 30 ml/min, and in which the subjects were not vitamin D deficient (Liyanage P 2018, 64). The active form of sunlight modulates the renin-angiotensin system by reducing renin release, according to a study by Li et al. (2010) 65. Therapy with vitamin D may also aid in lowering blood pressure. Parker and Hashmi, O.how nl)1-tocopheryl D affects retinopathy.

The considerable consumption of polyunsaturated fatty acids, high oxygen consumption, and rapid oxidation of glucose, which is unavoidably the primary cause of diabetes retinopathy, all put the retina at risk for oxidative damage. A state of imbalance involving the body's defenses against antioxidant and free radicals that can damage tissue is known as oxidative stress, also known as oxidative damage. Oxidative damage is brought on by diabetes both directly and indirectly.

During the breakdown of glucose, auto-oxidation has a direct impact (Brownlee M 2005, 54). As opposed to AGEs, which are advanced processes of end products and are accountable for collateral damage (Brownlee M 2005, 54). AGEs have an effect on the retinal blood vessels, making them less flexible and more stiff. further Centuries Oxygen nitride (NO) Polymer Kinase C (PKC) and NADPH, or the nicotinamide adenine oxidase, are both activated as a result of synthase activation, which creates reactive oxygen species (ROS) (Zhang WJ 2017, 24:10). Even though there is no way to reverse the oxidative stress brought on by diabetes, low levels of low molecular weight antioxidants like glutathione and inactivation of the antioxidant enzymes like catalase and superoxide dismutase, or SOD, serve a significant role in macular degeneration (King H, Aubert RE 1998, 21).

Three enzymes involved in the detoxification of ROS that can have their expression levels boosted by vitamin D are the enzymes glutathione reductase (GR), peroxidases (GPx), and Mda (Saedisomeolia A, 2013, 67). This promotes the production of reduced glutathione and GR (Saedisomeolia A, 2013, 93 A significant Superoxide dismutase 2 (SOD-2) is an additional enzyme that sunlight up-regulates and functions as a defense mechanism against the effects of oxidative stress (Saedisomeolia A, 2013, 110). It is critical to remember that in the DM II trials, it was found that there is an inverse association between vitamin D level but a positive correlation with the activity of the enzymes GPx and GR when compared to control. At larger concentrations of vitamin D, which boost the immune system and function as a protective antioxidant system, nuclear factor B cannot be stopped by gsh from escaping control units (ecus) (Alvarez JA 2014, 81). The vitamin D and vitamin D receptor (VDR) regulate mitochondrial respiration and guard against oxidative stress, respectively.

Organ systems, cellular activities, and tissues	**Tocopheryl D's impact**
Pancreas	**boosts insulin production and enhances the transformation of pro-insulin to glucose by promoting duodenal B cells.**
Fatty acids	**This increases the fatty acid oxidation process, reducing insulin sensitivity.**
Skeletal Muscles	**The presence of VDR in skeletal muscles has been proposed to be how VDR helps regulate sugar blood clotting.**
Kidney	**reduces albuminuria in the urine.**
Nervous system	**enables better nerve conduction. effective narcotic impact.**

Skin	**increases skin microcirculation, which aids in wound healing.**
Hemoglobin A1c (HbA1c)	**reduces Glycosylated hemoglobin.**
Retina	**resistant to osmotic damage.**

VDR, or the iodine D receptor, with HbA1c, or hemoglobin A1c, are related.

Conclusions.

The significance of vitamin D supplementation and their impact on glucose management and the most common challenges in people with type II diabetes mellitus have been evaluated in the current evaluation of the literature. It has been found that vitamin D interacts with many systems in a number of ways and has receptors in several organs. Numerous studies have been conducted to determine how vitamin D impacts the amount of hemoglobin A1c and DM II blood glucose levels. Both insulin sensitivity and secretion are increased. Vitamin D's anti-inflammatory effects on type II diabetes are essential for managing diabetic peripheral neuropathy. Vitamin D also improves brain connections in diabetics and speeds up wound healing.

Additionally, it has a potent analgesic effect. keeping under control D deficient.

References.

1. Wild S, Roglic G, Green A, Sicree R, King H: Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004, 27.
2. Leahy JL: Pathogenesis of type 2 diabetes mellitus. Arch Med Res. 2005, 36:197-209.
3. Ahmed LH, Butler AE, Dargham SR, et al.: Association of vitamin D2 and D3 with type 2 diabetes complications. BMC Endocr Disord. 2020, 20:65.
4. Takiishi T, Gysemans C, Bouillon R, Mathieu C: Vitamin D and diabetes. Rheum Dis Clin North Am. 2012, 38:179-206.
5. Johnson JA, Grande JP, Roche PC, Kumar R: Immunohistochemical localization of the 1,25(OH)2D3 receptor and calbindin D28k in human and rat pancreas. Am J Physiol. 1994, 267 .
6. Leal MA, Aller P, Mas A, Calle C: The effect of 1,25-dihydroxyvitamin D3 on insulin binding, insulin receptor mRNA levels, and isotype RNA pattern in U-937 human promonocytic cells. Exp Cell Res. 1995, 217:189-94.
7. Maestro B, Campión J, Dávila N, Calle C: Stimulation by 1,25-dihydroxyvitamin D3 of insulin receptor expression and insulin responsiveness for glucose transport in U-937 human promonocytic cells. Endocr J. 2000, 47.
8. Dunlop TW, Väisänen S, Frank C, Molnár F, Sinkkonen L, Carlberg C: The human peroxisome proliferator-activated receptor delta gene is a primary target of 1-alpha, 25-dihydroxyvitamin D3 and its nuclear receptor. J Mol Biol. 2005, 349:248.

9. Gysemans CA, Cardozo AK, Callewaert H, et al.: 1,25-Dihydroxyvitamin D3 modulates expression of chemokines and cytokines in pancreatic islets: implications for prevention of diabetes in nonobese diabetic mice. Endocrinology. 2005, 146:1956-64.
10. Riachy R, Vandewalle B, Kerr Conte J, et al.: 1,25-dihydroxyvitamin D3 protects RINm5F and human islet cells against cytokine-induced apoptosis: implication of the antiapoptotic protein A20. Endocrinology. 2002, 143.
11. lini M, Iagulli MP, Miconi V, et al. Serum 25-hydroxyvitamin D3 concentrations and prevalence of cardiovascular disease among type 2 diabetic patients. Diabetes Care. 2006;29:722–4.
12. Giulietti A, van Etten E, Overbergh L, Stoffels K, Bouillon R, Mathieu C: Monocytes from type 2 diabetic patients have a pro-inflammatory profile. 1,25-Dihydroxyvitamin D(3) works as anti-inflammatory. Diabetes Res Clin Pract. 2007, 77:47-57.
13. Garcion E, Wion-Barbot N, Montero-Menei CN, Berger F, Wion D: New clues about vitamin D functions in the nervous system. Trends Endocrinol Metab. 2002, 13:100-5.
14. Zhang J, Upala S, Sanguankeo A: Relationship between vitamin D deficiency and diabetic retinopathy: a meta-analysis. Can J Ophthalmol. 2017, 52:219-24 .
15. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009, 6:e1000097.
16. Kolb H, Mandrup-Poulsen T: An immune origin of type 2 diabetes?. Diabetologia. 2005, 48:1038-50.
17. Severino P, D'Amato A, Netti L, et al. Diabetes mellitus and ischemic heart disease: the role of ion channels. Int J Mol Sci. 2018;19.
18. Pittas AG, Joseph NA, Greenberg AS: Adipocytokines and insulin resistance. J Clin Endocrinol Metab. 2004, 89:447-52.
19. Sung CC, Liao MT, Lu KC, Wu CC: Role of vitamin D in insulin resistance. J Biomed Biotechnol. 2012, 2012:63 .
20. Goodarzi MO, Rotter JI. Genetics insights in the relationship between type 2 diabetes and coronary heart disease. Circ Res. 20. Goodarzi MO, 2020;126.
21. Christakos S, Liu Y: Biological actions and mechanism of action of calbindin in the process of apoptosis. J Steroid Biochem Mol Biol. 2004, 89-90 .
22. Hu Z, Chen J, Sun X, Wang L, Wang A: Efficacy of vitamin D supplementation on glycemic control in type 2 diabetes patients: a meta-analysis of interventional studies. Medicine (Baltimore).:e14970.
23. Khan DM, Jamil A, Randhawa FA, Butt NF, Malik U: Efficacy of oral vitamin D on glycated haemoglobin (HbA1c) in type 2 diabetics having vitamin D deficiency - a randomized controlled trial. J Pak Med Assoc. 2018, 68 .

24. Jung SR, Reed BJ, Sweet IR: A highly energetic process couples calcium influx through L-type calcium channels to insulin secretion in pancreatic beta-cells. Am J Physiol Endocrinol Metab. 2009, 297 -27.
25. Li X, Liu Y, Zheng Y, Wang P, Zhang Y: The effect of vitamin D supplementation on glycemic control in type 2 diabetes patients: a systematic review and meta-analysis. Nutrients. 2018, 10 .
26. Shillo P, Selvarajah D, Greig M, et al.: Reduced vitamin D levels in painful diabetic peripheral neuropathy. Diabet Med. 2019, 36 .
27. Basit A, Basit KA, Fawwad A, et al.: Vitamin D for the treatment of painful diabetic neuropathy. BMJ Open Diabetes Res Care. 2016, 4: .
28. Shehab D, Al-Jarallah K, Abdella N, Mojiminiyi OA, Al Mohamedy H: Prospective evaluation of the effect of short-term oral vitamin d supplementation on peripheral neuropathy in type 2 diabetes mellitus. Med Princ Pract. 2015, 24.
29. Karonova T, Stepanova A, Bystrova A, Jude EB: High-dose vitamin D supplementation improves microcirculation and reduces inflammation in diabetic neuropathy patients. Nutrients. 2020, 12:.
30. Alamdari A, Mozafari R, Tafakhori A, et al.: An inverse association between serum vitamin D levels with the presence and severity of impaired nerve conduction velocity and large fiber peripheral neuropathy in diabetic subjects. Neurol Sci. 2015, 36 .
31. Colotta F, Jansson B, Bonelli F: Modulation of inflammatory and immune responses by vitamin D. J Autoimmun. 2017, 85:78-97.
32. Zelnick LR, Weiss NS, Kestenbaum BR, et al.: Diabetes and CKD in the United States Population, 2009-2014. Clin J Am Soc Nephrol. 2017, 12 .
33. Afkarian M, Zelnick LR, Hall YN, Heagerty PJ, Tuttle K, Weiss NS, de Boer IH: Clinical manifestations of kidney disease among US adults with diabetes, 1988-2014. JAMA. 2016, 316:602-10. 10.
34. de Borst MH, Hajhosseiny R, Tamez H, Wenger J, Thadhani R, Goldsmith DJ: Active vitamin D treatment for reduction of residual proteinuria: a systematic review. J Am Soc Nephrol. 2013, 24:
35. Agarwal R, Acharya M, Tian J, et al.: Antiproteinuric effect of oral paricalcitol in chronic kidney disease. Kidney Int. 2005, 68:2823-8.
36. Joergensen C, Tarnow L, Goetze JP, Rossing P: Vitamin D analogue therapy, cardiovascular risk and kidney function in people with Type 1 diabetes mellitus and diabetic nephropathy: a randomized trial. Diabet Med. 2015, 32.
37. Liyanage P, Lekamwasam S, Weerarathna TP, Liyanage C: Effect of Vitamin D therapy on urinary albumin excretion, renal functions, and plasma renin among patients with diabetic nephropathy: a randomized, double-blind clinical trial. J Postgrad Med. 2018, 64.

38. Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP: 1,25-Dihydroxyvitamin D(3) is a negative endocrine regulator of the renin-angiotensin system. J Clin Invest. 2002, 110.
39. Anderson RE, Rapp LM, Wiegand RD: Lipid peroxidation and retinal degeneration. Curr Eye Res. 1984, 3:223-7.
40. Brownlee M: The pathobiology of diabetic complications: a unifying mechanism. Diabetes. 2005, 54: .
41. Zhang WJ, Li PX, Guo XH, Huang QB: Role of moesin, Src, and ROS in advanced glycation end product-induced vascular endothelial dysfunction. Microcirculation. 2017, 24.
42. King H, Aubert RE, Herman WH: Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998, 21.
43. Saedisomeolia A, Taheri E, Djalali M, Djazayeri A, Qorbani M, Rajab A, Larijani B: Vitamin D status and its association with antioxidant profiles in diabetic patients: A cross-sectional study in Iran. Indian J Med Sci. 2013, 67 .
44. Alvarez JA, Chowdhury R, Jones DP, et al.: Vitamin D status is independently associated with plasma glutathione and cysteine thiol/disulphide redox status in adults. Clin Endocrinol (Oxf). 2014, 81 .
45. Gupta R, Gaur K. Epidemiology of ischemic heart disease and diabetes in South Asia: an overview of the twin epidemic. Curr Diabetes Rev. 2021;17
46. Parker J, Hashmi O, Dutton D, et al. Levels of vitamin D and cardiometabolic disorders: systematic review and meta-analysis. Maturitas. 2010;65 .

التأثير الوقائي للعلاج بفيتامين د في داء السكري من النوع 2

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مستخلص البحث:
يؤثر انتشار مرض السكري من النوع 2 (DM II) بشكل خاص على العديد من أنظمة الجسم ، ويزداد بسرعة. من أجل منع المضاعفات ، مثل اعتلال الكلية السكري ، والاعتلال العصبي المحيطي وشبكية العين ، من الضروري التحكم بشكل صحيح في DM II. واحدة من العديد من مزايا فيتامين (د) هي تقليل مستوى الهيموغلوبين A1C (HBA1C). تحسين حساسية وإفراز الأنسولين. من أجل تحديد المعلومات ذات الصلة ، قمنا باستكشاف PubMed و Medline و PMC و Google Scholar على نطاق واسع. بعد تنفيذ معايير التضمين والاستبعاد ، استخدم معيار AMSTAR (الأدوات التي تم تقييمها بواسطة نظام التقييم) ، وتعليقات SANRA (مقالات المراجعة) ، ومعايير Cokreen و Northeern Sunder تقييم جودة البحث. تأتي البيانات من 14 مقالة ، 8 منها مراجعات منهجية أو تحليل تشويه. ثلاث مقالات عامة حول DM II و Vitamin D. 1 هي مراجعة للأدب. هناك 5 حالات من تقارير الحالة.
الكلمات المفتاحية : يعتبر فيتامين دي من الفيتامينات المهمة لمرضى السكري .