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Is vitamin D and L-arginine deficiency associated with male erectile dysfunction?

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Vitamin D deficiency and male erectile dysfunction

Optimal blood concentrations of vitamin D are vital for a healthy sexual life in men [1]. Calcitriol (the active form of vitamin D) induced the production of nitric oxide (NO) in cultured endothelial cells, and NO is a potent vasodilator associated with penile erection [2]. The outcome of a meta-analysis conducted by Crafa et al. [3] suggests that hypovitaminosis D (serum concentrations of 25-hydroxyvitamin D < 20 ng/mL) is associated with male erectile dysfunction (ED). Men with 25-hydroxyvitamin D deficiency had a higher incidence of ED compared to those with serum levels at least 30 ng/mL [4]. Vitamin D deficiency may weaken erectile function by promoting endothelial dysfunction [5]. However, vitamin D supplementation improved erectile function which was complemented by an increase in serum testosterone levels in middle-aged men [6]. An optimal blood concentration of vitamin D may promote arterial blood supply to the cavernous bodies by improving endothelial vasodilation via mediating the bioavailability of NO, which is an effective endothelium vasodilator [7]. The intake of vitamin D supplement was significantly associated with increased chances of survival among patients with cardiovascular diseases and diabetes, most especially in patients who are vitamin D deficient [8]. The increase in the chances of survival among the patients was associated with improvements in endothelial function [8]. Normal levels of vitamin D [serum concentrations of 25-hydroxyvitamin D] range between 30 and 80 ng/mL [9]. Serum concentrations between 21 and 29 ng/mL are considered insufficient [9]. Serum concentrations of 25-hydroxyvitamin D < 20 ng/mL are considered deficient, and it increases the risk of ED; moreover, severe deficiency may be defined as serum concentrations < 10 ng/mL [9]. The incidence of ED declines when serum

concentrations of 25-hydroxyvitamin D are over 35 ng/mL [9]. Low serum concentrations of 25-hydroxyvitamin D are strong diagnostic criteria for ED in men with type 2 diabetes, because vitamin D deficiency affects endothelial function consequently increasing the risk of cardiovascular diseases [10]. A considerable percentage of men with ED had lower serum concentrations of 25-hydroxyvitamin D, and it is more prevalent among patients with arteriogenic etiology, which indicates that hypovitaminosis D may weaken erectile function by increasing endothelial dysfunction [10]. The recommended daily amount of vitamin D is 600 international units (IU) for adults aged 18–70 years and 800 IU for adults older than 70 years [7, 8]. Moreover, to sustain or improve endothelial and erectile function which is maintaining serum levels of 25-hydroxyvitamin D above 30 ng/mL, male adults need to take at least 1500–2000 IU/day of supplemental vitamin D [6–8].

L-arginine deficiency and male erectile dysfunction

NO is a soluble gas that is synthesized from L-arginine in the endothelial cells via the activity of calcium-calmodulin-dependent enzyme NO synthase [11]. Lower levels of plasma L-arginine may increase the risk of ED in men, because of the decrease in the concentration of NO [12]. The use of L-arginine supplements significantly improved the International Index of Erectile Function (IIEF) subdomain scores of sexual intercourse satisfaction, orgasmic function, and erectile function [13]. Erectile function improved in men after oral administration of high dose L-arginine [14, 15]. Moreover, the combination of L-arginine with a phosphodiesterase type 5 inhibitor (e.g., tadalafil) is more effective in improving erectile function in men [14, 15]. Daily intake of L-arginine with tadalafil significantly increased the IIEF 5-item questionnaire scores, and total testosterone levels compared to single dose of each medication in diabetic patients with ED [16]. The normal range of L-arginine plasma levels has been specified as 81.6

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± 7.3 mmol/L in young men and 113.7 ± 19.8 μ mol/L in elderly men [17]. The plasma levels of L-arginine are not substantially decreased in most disease conditions, except end-stage renal failure during hemodialysis treatment. Nevertheless, intravenous or dietary (oral) administration of reasonably high doses of L-arginine has been demonstrated to result in improved NO formation in individual with endothelial dysfunction [17]. Furthermore, L-arginine doses of 3–8 g/day seem to be safe and do not trigger acute pharmacologic reactions in humans [17].

Molinari et al. [18] found that the combination of Coenzyme Q10, L-arginine, and vitamin D3 was able to induce a NO production higher than the effects induced by the single doses in cardiac and endothelial cells. Increase in vasodilation was also confirmed in an in vivo model [18].

Conclusion

Vitamin D and L-arginine deficiency might be associated with male ED separately or equally, especially in individuals with underlying endothelial dysfunction. Moreover, the blood concentrations of vitamin D and L-arginine should be analyzed in men with symptoms of ED. However, further studies are needed to substantiate the role of hypovitaminosis D and L-arginine deficiency in male ED.

Abbreviations

ED: Erectile dysfunction; IIEF: International Index of Erectile Function; IU: International units; NO: Nitric oxide

Acknowledgements

Not applicable.

Author's contributions

CEO did the literature search, wrote the manuscript, drafted the manuscript, and revised the manuscript critically. The author read and approved the final manuscript.

Funding

There was no funding received for this study.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The author declares that he has no competing interests.

Received: 12 March 2021 Accepted: 12 April 2021

Published online: 20 April 2021

References

- Canguven O, Al Malki AH (2021) Vitamin D and male erectile function: an updated review. *World J Mens Health* 39(1):31–37. <https://doi.org/10.5534/wjmh.190151>
- Molinari C, Uberti F, Grossini E, Vacca G, Carda S, Invernizzi M et al (2011) 1 α ,25-dihydroxycholecalciferol induces nitric oxide production in cultured endothelial cells. *Cell Physiol Biochem* 27(6):661–668
- Crafa A, Cannarella R, Condorelli RA, La Vignera S, Calogero AE (2020) Is there an association between vitamin D deficiency and erectile dysfunction? A systematic review and meta-analysis. *Nutrients*. 12(5):1411. <https://doi.org/10.3390/nu12051411>
- Farag YM, Guallar E, Zhao D, Kalyani RR, Blaha MJ, Feldman D et al (2016) Vitamin D deficiency is independently associated with greater prevalence of erectile dysfunction: the National Health and Nutrition Examination Survey (NHANES) 2001–4. *Atherosclerosis*. 252:61–67. <https://doi.org/10.1016/j.atherosclerosis.2016.07.921>
- Barassi A, Pezzilli R, Colpi GM, Corsi Romanelli MM, Melzi d'Eril GV (2014) Vitamin D and erectile dysfunction. *J Sex Med* 11(11):2792–2800. <https://doi.org/10.1111/jsm.12661>
- Canguven O, Talib RA, El Ansari W, Yassin DJ, Al Naimi A (2017) Vitamin D treatment improves levels of sexual hormones, metabolic parameters and erectile function in middle-aged vitamin D deficient men. *Aging Male* 20(1): 9–16. <https://doi.org/10.1080/13685538.2016.1271783>
- Kim DH, Meza CA, Clarke H, Kim JS, Hickner RC (2020) Vitamin D and endothelial function. *Nutrients*. 12(2):575. <https://doi.org/10.3390/nu12020575>
- Vacek JL, Vanga SR, Good M, Lai SM, Lakkireddy D, Howard PA (2012) Vitamin D deficiency and supplementation and relation to cardiovascular health. *Am J Cardiol* 109(3):359–363. <https://doi.org/10.1016/j.amjcard.2011.09.020>
- Farag YM, Guallar E, Zhao D, Kalyani RR, Blaha MJ, Feldman DI et al (2016) Vitamin D deficiency is independently associated with greater prevalence of erectile dysfunction: The National Health and Nutrition Examination Survey (NHANES) 2001–2004. *Atherosclerosis* 252:61–67
- Krysiak B, Szwajkowski A, Okopień B (2018) The effect of low vitamin D status on sexual functioning and depressive symptoms in apparently healthy men: a pilot study. *Int J Impot Res* 30(5):224–229. <https://doi.org/10.1038/s41443-018-0041-7>
- Tousoulis D, Kampoli AM, Tentolouris C, Papageorgiou N, Stefanadis C (2012) The role of nitric oxide on endothelial function. *Curr Vasc Pharmacol* 10(1):4–18. <https://doi.org/10.2174/157016112798829760>
- Barassi A, Corsi Romanelli MM, Pezzilli R, Damele CAL, Vaccalluzzo L, Goi G, Papini N, Colpi GM, Massaccesi L, Melzi d'Eril GV (2017) Levels of L-arginine and L-citrulline in patients with erectile dysfunction of different etiology. *Andrology*. 5(2):256–261. <https://doi.org/10.1111/andr.12293>
- Rhim HC, Kim MS, Park YJ, Choi WS, Park HK, Kim HG, Kim A, Paick SH (2019) The potential role of arginine supplements on erectile dysfunction: a systemic review and meta-analysis. *J Sex Med* 16(2):223–234. <https://doi.org/10.1016/j.jsxm.2018.12.002>
- Gallo L, Pecoraro S, Sarnacchiaro P, Silvani M, Antonini G (2020) The daily therapy with L-arginine 2,500 mg and tadalafil 5 mg in combination and in monotherapy for the treatment of erectile dysfunction: a prospective, randomized multicentre study. *Sex Med* 8(2):178–185. <https://doi.org/10.1016/j.esxm.2020.02.003>
- Xu Z, Liu C, Liu S, Zhou Z (2021) Comparison of efficacy and safety of daily oral L-arginine and PDE5Is alone or combination in treating erectile dysfunction: a systematic review and meta-analysis of randomised controlled trials [published online ahead of print]. *Andrologia*. 53(4):e14007. <https://doi.org/10.1111/and.14007>
- El Taieb M, Hegazy E, Ibrahim A (2019) Daily oral L-arginine plus tadalafil in diabetic patients with erectile dysfunction: a double-blinded, randomized, controlled clinical trial. *J Sex Med* 16(9):1390–1397. <https://doi.org/10.1016/j.jsxm.2019.06.009>
- Böger RH (2007) The pharmacodynamics of L-arginine. *J Nutr* 137(6 Suppl 2):1650S–1655S. <https://doi.org/10.1093/jn/137.6.1650S>
- Molinari C, Morsanuto V, Polli S, Uberti F (2018) Cooperative effects of Q10, vitamin D3, and L-arginine on cardiac and endothelial cells. *J Vasc Res* 55(1): 47–60. <https://doi.org/10.1159/000484928>

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