BÖLÜM
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PRİMER HİPERPARATİROİDİ VE D VİTAMİNİ

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Giriş

Primer hiperparatiroidi (PHPT) en sık görülen endokrinolojik bozukluklardan biridir ve hiperkalsemilerin en sık nedenidir. PHPT'li hastalarda D vitamini yetersizliği (25(OH)D, 20–29 ng/mL) veya eksikliği (25(OH)D, <20 ng/mL) oldukça sık görülür(1). PHPT'li hastaların ortalama D vitamini düzeylerinin genel topluma göre daha düşük olduğu gösterilmiştir(2,3). PHPT'li hastalarda D vitamini eksikliği gelişmesinin nedenleri tam ortaya konulmamakla beraber öne sürülen bazı mekanizmalar bulunmaktadır(4-6). PHPT'li hastalarda D vitamini eksikliği tedavi edilmelidir.

D vitamini PTH ilişkisi

D vitamini ve PTH arasındaki etkileşim kalsiyum ve fosfor homeostaz sağlanmasında çok önemlidir (7). D vitaminin 25 OH derivesi dolaşımdaki D vitamininin primer formudur ve D vitamini eksikliğinin en önemli göstergesidir. Serum 25 OH D vitamini düzeyi aynı zamanda ultravioleye bağlı endojen D vitamini üretiminin ve diyet yoluyla ekzojen alınan D vitaminin de göstergesidir (8-10).

Vitamin D3'ün normalde biyolojik etkisi yoktur. Önce karaciğerde 25(OH) formuna sonrasında da böbrekte 1,25$(OH)_2$D vitamin D [1,25$(OH)_2$D] aktif formuna dönüşür (2). 1,25$(OH)_2$D formu D vitamini reseptörüne (VDR) bağlanarak hücre içinde gen transkripsiyonunu ve etkilerini düzenler. PHPT'li hastalarda 25(OH)D vitamini düzeyi gerçek D vitamini durumunu göstermeyebilir. Çünkü 1,25$(OH)_2$D vitamini düzeyindeki değişim 25(OH)D vitamini düzeyinden farklı olabilir. Prohormon/hormon yani 1,25$(OH)_2$D/25(OH)D] oranı D vitamini durumunu daha iyi yansıtabilir (11,12). Genetik ve ırksal faktörler de D vitamini düzeyini etkileyebilirler. İkiz ve aile çalışmaları genetik faktörlerin D vitamini düzeyindeki değişkenliğe etkisinin %53'e kadar çıkabileceğini göstermektedir (13).

PHPT hastalarında D vitamini düzeyi için spesifik bir eşik değer yoktur. Ancak pek çok kılavuzda PHPT hastalarında D vitamini düzeyinin 20 ng/ml'in üstünde tutulması önerilmektedir (14,15).

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Kaynaklar

1. Bilezikian JP Primary hyperparathyroidism. *J Clin Endocrinol Metab*, 2018:103(11):3993–4004. https://doi.org/10.1210/jc. 2018-01225
2. Moosgaard B, Vestergaard P, Heickendorff L, Melsen F, Christiansen P, Mosekilde L. Vitamin D status, seasonal variations, parathyroid adenoma weight and bone mineral density in primary hyperparathyroidism. *Clin Endocrinol (Oxf)*, 2005;63:506–513. [PubMed: 16268801]
3. Boudou P, Ibrahim F, Cormier C, Sarfati E, Souberbielle JC. A very high incidence of low 25 hydroxy-vitamin D serum concentration in a French population of patients with primary hyperparathyroidism. *J Endocrinol Invest*, 2006;29:511–515. [PubMed: 16840828]
4. Meng L, Su C, Shapses SA, Wang X. Total and free vitamin D metabolites in patients with primary hyperparathyroidism. *J Endocrinol Invest*, 2022; Feb;45(2):301-307. doi: 10.1007/s40618-021-01633-1. Epub 2021 Jul 19. PMID: 34282553.
5. Wang X, Sheng Z, Meng L, Su C, Trooskin S, Shapses SA .25-hydroxyvitamin D and vitamin D binding protein levels in patients with primary hyperparathyroidism before and after parathyroidectomy. *Front Endocrinol* 2019; 10:171. https://doi.org/ 10.3389/ fendo. 2019.00171
6. Bikle DD, Schwartz J Vitamin D binding protein, total and free vitamin D levels in different physiological and pathophysi- ological conditions. Front Endocrinol, 2019; 10:317. https://doi.org/10. 3389/fendo.2019.00317
7. Cipriani C, Pepe J, Colangelo L, Minisola S. Vitamin D and Secondary Hyperparathyroid States. *Front Horm Res,* 2018;50:138-148. doi: 10.1159/000486077. Epub 2018 Mar 29. PMID: 29597237.
8. A. Hossein-Nezhad, M.F. Holick, Vitamin D for health: a global perspective. *Mayo Clin. Proc,* 2013;88, 720–755.
9. M.F. Holick, N.C. Binkley, H.A. Bischoff-Ferrari, C.M. Gordon, D.A. Hanley, R.P. Heaney, M.H. Murad, C.M. Weaver, Guidelines for preventing and treating vitamin D deficiency and insufficiency revisited. *J. Clin. Endocrinol. Metab*, 2012; 97, 1153–1158.
10. J. Ahn, K. Yu, R. Stolzenberg-Solomon, K.C. Simon, M.L. McCullough, L. Gallicchio, E.J. Jacobs, A. Ascherio, K. Helzlsouer, K.B. Jacobs, Q. Li, S.J. Weinstein, M. Purdue, J. Virtamo, R. Horst, W. Wheeler, S. Chanock, D.J. Hunter, R.B. Hayes, P. Kraft, D. Albanes, Genome-wide association study of circulating vitamin D levels. *Hum Mol Genet*, 2010;19, 2739–2745.
11. Thomas RL, Jiang L, Adams JS, Xu ZZ, Shen J, Janssen S et al Vitamin D metabolites and the gut microbiome in older men. *Nat Commun,* 2020; 11(1):5997. https://doi.org/10.1038/ s41467-020-19793-8
12. Pasquali M, Tartaglione L, Rotondi S, Muci ML, Mandanici G, Farcomeni A et al. Calcitriol/calcifediol ratio: an indicator of vitamin D hydroxylation efficiency? *BBA Clin,* 2015; 3:251–256. https://doi.org/10.1016/j.bbacli.2015.03.004
13. Battista C, Guarnieri V, Carnevale V, Baorda F, Pileri M, Garrubba M, Salcuni AS, Chiodini I, Minisola S, Romagnoli E, Eller-Vainicher C, Santini SA, Parisi S, Frusciante V, Fontana A, Copetti M, Hendy GN, Scillitani A, Cole DE. Vitamin D status in primary hyperparathyroidism: effect of genetic background. *Endocrine,* 2017; Jan;55(1):266-272. doi: 10.1007/s12020-016-0974-x. PMID: 27154872.
14. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab,* 2011; 96:53–8. [PubMed: 21118827]
15. Eastell R, Brandi ML, Costa AG, D'Amour P, Shoback DM, Thakker RV. Diagnosis of asymptomatic primary hyperparathyroidism: proceedings of the Fourth International Workshop. *J Clin Endocrinol Metab,* 2014; 99:3570–9. [PubMed: 25162666]
16. Rao DS, Agarwal G, Talpos GB, et al. Role of vitamin D and calcium nutrition in disease expression and parathyroid tumor growth in primary hyperparathyroidism: a global perspective. *J Bone Miner Res*, 2002;17(suppl 2):N75–N80. [PubMed: 12412781]
17. Rao DS, Honasoge M, Divine GW, et al. Effect of vitamin D nutrition on parathyroid adenoma weight: pathogenetic and clinical implications. *J Clin Endocrinol Metab*, 2000; 85:1054–1058. [PubMed: 10720039]
18. Moosgaard B, Vestergaard P, Heickendorff L, Melsen F, Christiansen P, Mosekilde L. Plasma 25-hydroxyvitamin D and not 1,25-dihydroxyvitamin D is associated with parathyroid adenoma secretion in primary hyperparathyroidism: a cross-sectional study. *Eur J Endocrinol*, 2006;155:237–244. [PubMed: 16868136]
19. Ozbey N, Erbil Y, Ademoglu E, Ozarmagan S, Barbaros U, Bozbora A. Correlations between vitamin D status and biochemical/clinical and pathological parameters in primary hyperparathyroidism. *World J Surg*, 2006;30:321–326. [PubMed: 16467981]
20. Moosgaard B, Christensen SE, Vestergaard P, Heickendorff L, Christiansen P, Mosekilde L. Vitamin D metabolites and skeletal consequences in primary hyperparathyroidism. *Clin Endocrinol (Oxf)*, 2008;68:707–715. [PubMed: 17980013]
21. Inoue Y, Kaji H, Hisa I, et al. Vitamin D status affects osteopenia in postmenopausal patients with primary hyperparathyroidism. *Endocr J*, 2008;55:57–65. [PubMed: 18187872]
22. Nordenström E, Westerdahl J, Lindergård B, Lindblom P, Bergenfelz A. Multifactorial risk profile for bone fractures in primary hyperparathyroidism. *World J Surg*, 2002;26:1463–1467. [PubMed: 12297914]
23. Rao SD, Miragaya J, Parikh N, Honasoge M, Springer K, Van Harn M, Divine GW. Effect of vitamin D nutrition on disease indices in patients with primary hyperparathyroidism. *J Steroid Biochem Mol Biol,* 2020; Jul;201:105695. doi: 10.1016/j.jsbmb.2020.105695.

Epub 2020 May 12. PMID: 32407867.
24. Rao, D.S., Agarwal, G., Talpos, G.B. et al. Role of vitamin D and calcium nutrition in disease expression and parathyroid tumor growth in primary hyperparathyroidism: a global perspec tive. *Journal of Bone and Mineral Research*, 2002; 17(Suppl 2), N75–N80.
25. Palmér M, Adami HO, Bergström R, Akerström G, Ljunghall S. Mortality after surgery for primary hyperparathyroidism: a follow-up of 441 patients operated on from 1956 to 1979. *Surgery*, 1987;102:1–7.
26. Söreide JA, van Heerden JA, Grant CS, Yau Lo C, Schleck C, Ilstrup DM. Survival after surgical treatment for primary hyperparathyroidism. *Surgery*, 1997; 122:1117–23.
27. Lundgren E, Ljunghall S, Akerström G, Hetta J, Mallmin H, Rastad J. Case-control study on symptoms and signs of "asymptomatic" primary hyperparathyroidism. *Surgery*, 1998; 124:980–5.
28. Hagström E, Lundgren E, Lithell H, Berglund L, Ljunghall S, Hellman P, et al. Normalized dyslipidaemia after parathyroidectomy in mild pri- mary hyperparathyroidism: population-based study over five years. *Clin Endocrinol*, 2002;56:253–60.
29. Rubin MR, Maurer MS, McMahon DJ, Bilezikian JP, Silverberg SJ. Arterial stiffness in mild primary hyperparathyroidism. *J Clin Endocrinol Metab*, 2005;90:3326–30.
30. Ahlstrom T, Hagström E, Larsson A, Rudberg C, Lind L, Hellman P. Cor- relation between plasma calcium, parathyroid hormone (PTH) and the metabolic syndrome (MetS) in a community-based cohort of men and women. *Clin Endocrinol*, 2009;71:673–8.
31. Chiu KC, Chuang LM, Lee NP, Ryu JM, McGullam JL, Tsai GP, et al. Insulin sensitivity is inversely correlated with plasma intact parathyroid hormone level. *Metabolism*, 2000; 49:1501–5.
32. Taylor WH, Khaleeli AA. Coincident diabetes mellitus and primary hyperparathyroidism. *Diabetes Metab Res Rev,* 2001;17:175–80.
33. Bilezikian JP, Meng X, Shi Y, Silverberg SJ. Primary hyperparathyroidism in women: a tale of two cities--New York and Beijing. *Int J Fertil Womens Med,* 2000; 45:158–65. [PubMed: 10831185]
34. Liu JM, Cusano NE, Silva BC, et al. Primary Hyperparathyroidism: A Tale of Two Cities Revisited - New York and Shanghai. *Bone research,* 2013; 1:162–9. [PubMed: 26273500]
35. Clements MR, Davies M, Hayes ME, et al. The role of 1,25-dihydroxyvitamin D in the mechanism of acquired vitamin D deficiency. *Clin Endocrinol (Oxf),* 1992; 37:17–27. [PubMed: 1424188]
36. Clements MR, Davies M, Fraser DR, Lumb GA, Mawer EB, Adams PH. Metabolic inactivation of vitamin D is enhanced in primary hyperparathyroidism. *Clin Sci (Lond)*, 1987; 73:659–64. [PubMed: 3690980]
37. Silverberg SJ, Shane E, Dempster DW, Bilezikian JP. The effects of vitamin D insufficiency in patients with primary hyperparathyroidism. *Am J Med,* 1999;107:561–7.
38. Lind L, Wengle B, Sørensen OH, Wide L, Akerström G, Ljunghall S. Treatment with active vitamin D (alphacalcidol) in patients with mild primary hyperparathyroidism. *Acta Endocrinol (Copenh)*, 1989;120: 250–6.
39. Shah VN, Shah CS, Bhadada SK, Rao DS. Effect of 25 (OH) D replace- ments in patients with primary hyperparathyroidism (PHPT) and coexistent vitamin D deficiency on serum 25(OH) D, calcium and PTH levels: a meta- analysis and review of literature. *Clin Endocrinol (Oxf)*, 2014;80:797–803 [ID 709670].
40. Kantorovich V, Gacad MA, Seeger LL, Adams JS. Bone mineral density increases with vitamin D repletion in patients with coexistent vitamin D insufficiency and primary hyperparathyroidism. *J Clin Endocrinol Metab*, 2000;85:3541–3.
41. Shah VN, Shah CS, Bhadada SK, Rao DS. Effect of 25 (OH) D replacements in patients with primary hyperparathyroidism (PHPT) and coexistent vitamin D deficiency on serum 25(OH) D, calcium and PTH levels: a meta-analysis and review of literature. *Clin Endocrinol (Oxf),* 2014 Jun;80(6):797-803. doi: 10.1111/cen.12398. Epub 2014 Jan 28. PMID: 24382124.
42. Bergman C, Gray-Scott D, Chen JJ, Meacham S. What is next for the dietary reference intakes for bone metabolism related nutrients beyond calcium: phosphorus, magnesium, vitamin D, and fluoride? *Crit Rev Food Sci Nutr*, 2009;49:136–44.
43. Eastell R, Arnold A, Brandi ML, et al. Diagnosis of asymptomatic primary hyperparathyroidism: proceedings of the Third International Workshop. *J Clin Endocrinol Metab*, 2009;94:340–350. [PubMed: 19193909]