

Bölüm 14

DİYABETİK NÖROPATİ

Bora UZUNER¹

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Diyabetik nöropati (DN), diabetes mellitus'un (DM) en sık görülen komplikasyonudur. Ciddi bir morbidite ve mortalite nedeni olup, DM tedavisinde büyük bir ekonomik yüke yol açar (1). Gelişmiş ülkelerde, nöropatinin en sık sebebi olup, tüm diğer diyabet komplikasyonlardan daha fazla hastane yatışına neden olur. Aynı zamanda, non-travmatik amputasyonların %50-75'inin nedenidir (2). Diyabetik hastalarda kardiovasküler mortalitenin artmış olduğu, hastaların yaklaşık yarısının stroke veya iskemik kalp hastalıklarından kaybedildiği bilinmektedir. Diyabetik nöropati, DM'nin mikrovasküler komplikasyonlarından biri olup, otonomik kardiovasküler değişikliklerden, diyabetik ayak ülserlerine kadar çok çeşitli problemlere yol açmaktadır. Diyabetik nöropatide ortaya çıkan nöropatik ağrı, uzun yıllar asemptomatik seyreden tip 2 diyabette, hastayı hekime getiren ilk semptomlardan biri olmaktadır.

Diyabetik bir hastada ortaya çıkan ve başka herhangi bir nedene bağlanamayan periferik sinir sistemi semptom ve bulgularına DN denir. DM'nin en sık görülen mikrovasküler komplikasyonu olmasına karşın çoğu hekim tarafından tanı kolaylıkla atlanabilir. Genellikle; non-spesifik bulgularla başlaması, yavaş progresyon göstermesi ve bir çok hastalığıdaki şikayetlere karışabilmesi nedeniyle diyabet tedavisiyle uğraşan hekimlerin üçte biri tarafından DN tanısı atlanabilmektedir (3). Tam prevalans bilinmemek ile birlikte yapılan araştırmalarda DM'li hastaların %10-90'ında DN görüldüğü tespit edilmiştir. Prevalanstaki bu büyük farkın sebebinin, DN tanısı için yapılan araştırmalarda belirlenen kriter ve metodlardaki farklılıktan kaynaklandığı düşünülmektedir (4,5). Diyabet kliniklerine başvuran hastaların %25'inde DN semptomları mevcutken bu hastalarda tanıya

¹ Uzman Doktor, SBÜ Samsun Eğitim ve Araştırma Hastanesi, Algoloji Kliniği, buzuner@hotmail.com,

ni, DM'de ortaya çıkan mikroanjyopatiler ve dolaşım yetmezliğidir (63). Yaralar, sonrasında ülser, enfeksiyon, gangren ve son aşamada ampütasyona neden olabilir. Her ne kadar DN'ye bağlı his kaybı oluşsa da, büyük yaralar ve enfeksiyon, çok şiddetli ağrıya neden olur. Bu hastalarda hem beslenmenin iyileşmesi hem de ağrının azaltılması için lomber sempatik blokaj etkili bir tedavidir.

Epidural kateter ve hasta kontrollü analjezi, şiddetli alt ekstremitte ağrısı olan DN'li hastalarda, kısa süreli rahatlatma amacıyla uygulanabilir, tercih edilebilir

Spinal Kord Stimülasyonu: Konuyla ilgili çok fazla prospektif, randomize kontrollü çalışma olmamakla birlikte, özellikle, mikrovasküler yetersizliği ve ağrısı olan DN'de etkinliği gösterilmiştir (64).

Diyabetik nöropatiye bağlı vücudun farklı yerlerinde de tutulumlar söz konusu olabilir. Tedavi semptomatiktir, tutulan bölgeye yönelik işlemler yapılır. Torakal nöropatide torasik paravertebral blok, interkostal blok, serratus anterior bloğu, lokal enjeksiyonlar uygulanabilir (65). Abdominal tutulumda oluşan ağrılar için çölyak pleksus bloğu başarıyla uygulanmıştır (66). Ayrıca üst ve alt ekstremitte periferik sinir blokları da DN'de ağrı kontrolü amacıyla kullanılabilirler. Elektrofizyolojik yanıtların bozulduğu bu hastalarda sinirleri görenek yapılan ultrason rehberliğinde bloklar uygulama kolaylığı açısından tercih edilebilir (67).

KAYNAKLAR

1. Vinik AI, Mitchell BD, Leichter SB, et al. Epidemiology of the complications of diabetes. In: Leslie RD, Robbins DC, editors. *Diabetes: clinical science in practice*. Cambridge (United Kingdom): Cambridge University Press; 1995. p. 221–87.
2. Holzer SE, Camerota A, Martens L, et al. Costs and duration of care for lower extremity ulcers in patients with diabetes. *Clin Ther* 1998;20:169–81.
3. Herman WH, Kennedy L. Underdiagnosis of peripheral neuropathy in type 2 diabetes. *Diabetes Care* 2005;28:1480–1.
4. Young MJ, Boulton AJ, MacLeod AF, et al. A multicenter study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. *Diabetologia* 1993;36:150–4.
5. Dyck PJ, Kratz KM, Karnes JL, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: The Rochester Diabetic Neuropathy Study. *Neurology* 1993;43:817–24.
6. Vinik A. Diabetic neuropathy: pathogenesis and therapy. *Am J Med* 1999; 107(2B):17S–26S.
7. Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system. The contribution of depth, infection, and ischemia to risk of amputation. *Diabetes Care* 1998;21:855–9.
8. Caputo GM, Cavanagh PR, Ulbrecht JS, et al. Assessment and management of foot disease in patients with diabetes. *N Engl J Med* 1994;331:854–60.
9. Vinik EJ, Hayes RP, Oglesby A, et al. The development and validation of the Norfolk QOL-DN, a new measure of patients' perception of the effects of diabetes and diabetic neuropathy. *Diabetes Technol Ther* 2005;7:497–508.
10. Levitt NS, Stansberry KB, Wychanck S, et al. Natural progression of autonomic neuropathy and autonomic function tests in a cohort of IDDM. *Diabetes Care* 1996;19:751–4.

11. Rathmann W, Ziegler D, Jahnke M, et al. Mortality in diabetic patients with cardiovascular autonomic neuropathy. *Diabet Med* 1993;10:820-4.
12. Vinik A, Lullal J, Parson HK, et al. Diabetic neuropathies: clinical manifestations and current treatment options. *Nat Clin Pract Endocrinol Metab* 2006; 2:269-81.
13. Sadosky A, McDermott AM, Brandenburg NA, et al. A review of the epidemiology of painful diabetic peripheral neuropathy, postherpetic neuralgia, 778 Vinik et al and less commonly studied neuropathic pain conditions. *Pain Pract* 2008;8: 45-56.
14. Tesfaye S, Boulton AJ, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care* 2010;33:2285-93.
15. Ziegler D. Painful diabetic neuropathy: treatment and future aspects. *Diabetes Metab Res Rev* 2008;24(Suppl 1):S52-7.
16. Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. *Circulation* 2007;115:387-97.
17. Vinik AI, Maser RE, Ziegler D. Autonomic imbalance: prophet of doom or scope for hope? *Diabet Med* 2011;28:643-51.
18. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047-1053.
19. Satman I, Yilmaz T, Sengu' l A, et al. Population-based study of diabetes and risk characteristics in Turkey: results of the Turkish Diabetes Epidemiology Study (TURDEP). *Diabetes Care*. 2002;25:1551-1556.
20. Erbas, T., Ertas, M., Yucel, A., Keskinaslan, A., & Senocak, M. (2011). Prevalence of Peripheral Neuropathy and Painful Peripheral Neuropathy in Turkish Diabetic Patients. *Journal of Clinical Neurophysiology*, 28(1), 51-55.
21. Thomas PK. Classification of the diabetic neuropathies. In: *Textbook of diabetic Neuropathy*. Gries FA, Cameron NE, Low PA, Ziegler D (Eds.), Thieme, Stuttgart, 2003;175-177.
22. Ziegler D. Treatment of diabetic neuropathy and neuropathic pain. How far have we come ? *Diabetes Care* 2008;31 (Suppl. 2): 255-261.
23. Vinik AI, Holland MT, LeBeau JM, et al. Diabetic neuropathies. *Diabetes Care* 1992;15:1926-75.
24. Vinik AI, Mehrabyan A. Diabetic neuropathies. *Med Clin N Am* 2004;88:947-99.
25. Ziegler D, Hidvegi T, Gurieva I, et al. Efficacy and safety of lacosamide in painful diabetic neuropathy. *Diabetes Care* 2010;33:839-41
26. Wilbourn AJ. Diabetic entrapment and compression neuropathies. In: *Dyck PJ, Thomas PK, editors. Diabetic neuropathy*. Toronto:WB Saunders; 1999. p. 481-508
27. Watanabe K, Hagura R, Akanuma Y, et al. Characteristics of cranial nerve palsies in diabetic patients. *Diabetes Res Clin Pract* 1990;10:19-27
28. Sinnreich M, Taylor BV, Dyck PJ. Diabetic neuropathies. Classification, clinical features, and pathophysiological basis. *Neurologist* 2005;11:63-79.
29. Pittenger GL, Ray M, Burcus NI, et al. Intraepidermal nerve fibers are indicators of small-fiber neuropathy in both diabetic and nondiabetic patients. *Diabetes Care* 2004;27:1974-9.
30. The Diabetes Control and Complications Trial Research Group. The effect of intensive diabetes therapy on the development and progression of neuropathy. *Ann Intern Med* 1995;122:561-568. Albers JW, Herman WH, Pop-Busui R, et al. Effect of prior intensive insulin treatment during the Diabetes Control and Complications Trial (DCCT) on peripheral neuropathy in type 1 diabetes during the Epidemiology of Diabetes Interventions and Complications (EDIC) Study. *Diabetes Care* 2010;33:1090-6
31. UK Prospective Diabetes Study (UKPDS) Group: Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complication in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352:837-853.
32. The ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Eng J Med* 2008;358:2560-72.
33. Sing r, Kishore I, Kaur N. Diabetic Peripheral Neuropathy: Current Perspective and Future

- Directions. *Pharmacolog res.* 2014;80:21–35.
34. Pittenger G, Vinik A. Nerve growth factor and diabetic neuropathy. *Exp Diabetes Res* 2003;4:271–85.
 35. Vinik AI. Treatment of diabetic polyneuropathy (DPN) with recombinant human nerve growth factor (rhNGF). *Diabetes* 1999;48(Suppl 1):A54–5
 36. Rivard A, Silver M, Chen D, et al. Rescue of diabetes-related impairment of angiogenesis by intramuscular gene therapy with adeno-VEGF. *Am J Pathol* 1999;154:355–63.
 37. Vinik AI, Anandacoomaraswamy D, Ullal J. Antibodies to neuronal structures: innocent bystanders or neurotoxins? *Diabetes Care* 2005;28:2067–72.
 38. Vinik A. The approach to the management of the patient with neuropathic pain. *J Clin Endocrinol Metab* 2010;95:4802–811; and
 39. Vinik, A. Management of the Patient with Neuropathic Pain. In: Wartofsky L, editor. *A clinical approach to endocrine and metabolic diseases, Vol 2.* Chevy Chase (MD): The Endocrine Society, 2012. p. 177–94; with permission.
 40. Finnerup NB, Sindrup SH, Jensen TS. The evidence for pharmacological treatment of neuropathic pain. *Pain* 2010;150:573–81.
 41. Hardy T, Sachson R, Shen S, et al. Does treatment with duloxetine for neuropathic pain impact glycemic control? *Diabetes Care* 2007;30:21–6.
 42. Simpson DA. Gabapentin and venlafaxine for the treatment of painful diabetic neuropathy. *J Clin Neuromuscul Dis* 2001;3:53–62.
 43. Backonja M, Beydoun A, Edwards KR, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. *JAMA* 1998;280:1831–6.
 44. Gilron I, Bailey JM, Tu D, et al. Morphine, gabapentin, or their combination for neuropathic pain. *N Engl J Med* 2005;352:1324–34.
 45. Lesser H, Sharma U, LaMoreaux L, et al. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology* 2004;63: 2104–10.
 46. Richter RW, Portenoy R, Sharma U, et al. Relief of painful diabetic peripheral neuropathy with pregabalin: a randomized, placebo-controlled trial. *J Pain* 2005;6:253–60.
 47. Rosenstock J, Tuchman M, LaMoreaux L, et al. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain* 2004;110:628–38
 48. Guglielmo R, Martinotti G, Clerici M, Janiri L. Pregabalin for alcohol dependence: a critical review of the literature. *Adv Ther* 2012; 29:947-957.
 49. Papazisis G, Tzachanis D. Pregabalin's abuse potential: a mini review focusing on the pharmacological profile. *Int J Clin Pharmacol Ther* 2014; 52:709-716.
 50. Bonnet, U., & Scherbaum, N. How addictive are gabapentin and pregabalin? A systematic review. *European Neuropsychopharmacology*, 2017; 27(12), 1185–1215.
 51. Kalso E. Sodium channel blockers in neuropathic pain. *Curr Pharm Des* 2005; 11:3005–11.
 52. Dogra S, Beydoun S, Mazzola J, et al. Oxcarbazepine in painful diabetic neuropathy: a randomized, placebo-controlled study. *Eur J Pain* 2005;9:543–54.
 53. Harati Y, Gooch C, Swenson M, et al. Maintenance of the long-term effectiveness of tramadol in treatment of the pain of diabetic neuropathy. *J Diabetes Complications* 2000;14:65–70.
 54. Watson CP, Moulin D, Watt-Watson J, et al. Controlled-release oxycodone relieves neuropathic pain: a randomized controlled trial in painful diabetic neuropathy. *Pain* 2003;105:71–8.
 55. Dworkin RH, O'Connor AB, Audette J, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc* 2010;85:S3–14.
 56. Vinik AI, Nevoret ML, Casellini C, Parson H. Diabetic Neuropathy. *Endocrinal Metab Clin N Am* 2013;42:747–87.
 57. Mason L, Moore RA, Derry S, et al. Systematic review of topical capsaicin for the treatment of chronic pain. *BMJ* 2004;328:991.
 58. Backonja M, Wallace MS, Blonsky ER, et al. NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia: a randomised, double-blind study. *Lancet Neurol*

- 2008;7:1106–12.
59. Baron R, Mayoral V, Leijon G, et al. Efficacy and safety of combination therapy with 5% lidocaine medicated plaster and pregabalin in post-herpetic neuralgia and diabetic polyneuropathy. *Curr Med Res Opin* 2009;25:1677–87.
 60. Jarvis B, Coukell AJ. Mexiletine. A review of its therapeutic use in painful diabetic neuropathy. *Drugs* 1998;56:691–707.
 61. Thakral G, Kim PJ, LaFontaine J, et al. Electrical stimulation as an adjunctive treatment of painful and sensory diabetic neuropathy. *Diabetes Sci Technol*. 2013 Sep 1; 7(5):1202-9.
 62. Dean S, Unity N, Trilce S, et al. Clinical Trial of Group Acupuncture for Painful Diabetic Neuropathy Among Diverse Safety Net Patients, *Pain Medicine*, 2019;0(0):1-11
 63. Cameron NE, Eaton SE, Cotter MA, et al. Vascular factors and metabolic interactions in the pathogenesis of diabetic neuropathy. *Diabetologia*. 2001 Nov; 44(11):1973-88.
 64. De Vos CC, Rajan V, Steenberg W, et al. Effect and safety of spinal cord stimulation for treatment of chronic pain caused by diabetic neuropathy. *Diabetes Complications*. 2009 Jan-Feb; 23(1):40-5.
 65. Sir E, Eksert S, Emin Ince M, et al. A Novel Technique: Ultrasound-Guided Serratus Anterior Plane Block for the Treatment of Post-Traumatic Intercostal Neuralgia. A Case Report. *Am J Phys Med Rehabil*. 2018 Dec 28.
 66. C Sun X, Xu J, Ni Y, et al. T-Guided Consecutive Neurolytic Celiac Plexus Block for the Management of Refractory Abdominal Neuralgia Caused by Diabetic Neuropathy. *J Vasc Interv Radiol*. 2018 Oct;29(10):1474-1476.
 67. Erdem Y, Sir E. The Efficacy of Ultrasound-Guided Pulsed Radiofrequency of Genicular Nerves in the Treatment of Chronic Knee Pain Due to Severe Degenerative Disease or Previous Total Knee Arthroplasty. *Med Sci Monit*. 2019 Mar 12;25:1857-1863.