

1. Giriş

Amputasyonlar travma, tümör, damar hastalıkları ve enfeksiyon gibi nedenlerden dolayı meydana gelmektedir. Amputasyondan sonra güdük ağrısı ve fantom ağrısı olmak üzere iki tür ağrı gelişebilmektedir. Fantom ağrısı, artık var olmayan uzuvdaki künt ağrı, karıncalanma, zonklama, keskin veya iğnelenme tarzındaki şikayetler olarak tariflenmektedir. Güdük ağrısı ise ampute uzvun gerçek bölgesinden kaynaklanan ağrı olmakla birlikte, genellikle enfeksiyon, sinir sıkışması, nöroma, iskemi veya cerrahi travmayla ilişkilidir, amputasyon sonrası erken dönemde görülür, yara iyileşmesi ile düzelme eğilimindedir. Fantom ağrısı, ise amputasyondan hemen veya yıllar sonra ortaya çıkabilmektedir ve ampute hastaların %60-85'inde değişen şiddetlerde deneyimlenmektedir. Fantom ağrısı hastaların yaşam kalitesinde kötüleşmeye neden olmaktadır (1).

Fantom ağrısının gelişmesindeki risk faktörleri, amputasyon öncesi dönemde ağrı varlığı, diyabetik nedenli amputasyonlar, bilateral amputasyonlar, proksimal amputasyonlar, güdük ağrısı, fantom hissi, amputasyon sonrası uyku bozukluğu ve depresyon varlığı, pasif baş etme stratejilerini kullanma ve katastrofizasyon varlığı

olarak bildirilmiştir. Öte yandan yaş, cinsiyet ve peroperatif gabapentinoid tedavisi ile fantom ağrısının ilişkisinin olmadığını gösteren sonuçlar vardır (2).

2. Patofizyoloji

Fantom ağrısının patofizyoloji periferik ve santral mekanizmalarla açıklanmaya çalışılmaktadır. Periferik değişiklikler amputasyon alanından kaynaklanmaktadır. Amputasyon sırasında sinirlerdeki ve çevre dokulardaki travma nedeniyle afferent ve efferent sinyallerin bozulmasıyla ve filizlenen nöromalarla sodyum kanallarında artış gelişir. Periferdeki sodyum kanallarındaki bu artış, spontan deşarjlara neden olmaktadır. Omurilikte ise sinirsel aktivitenin arttığı, nöronal alıcı alanın genişlediği ve sinirlerin aşırı duyarlı hale geldiği santral sensitizasyon gelişmektedir. Bu değişikliklerin nedeni, omuriliğin dorsal boyundaki N-Metil-D-Aspartat (NMDA) reseptörleri sayısı veya aktivitesindeki artıştır. Bu yeniden yapılanma sonucunda inen inhibitör lifler hedef bölgelerini kaybeder. Nosiseptif sinyallerdeki aktivitenin artmasının yanı sıra supraspinal merkezlerden gelen inhibitör aktivitedeki azalmanın, fantom ağrısının gelişmesinde önemli olduğu düşünülmektedir (3).

¹ Uzm. Dr., Sağlık Bilimleri Üniversitesi Konya Şehir Hastanesi, Algoloji Kliniği selinaa01@yahoo.com

rinin plaseboya üstün olduğu gösterilmiştir. Ağrılı tetik noktalara botulinum toksin enjeksiyonu, fonksiyonel protez kullanımı, kontralateral TENS uygulaması, transkraniyal direk akım tedavisi, ayna tedavisi, basamaklı motor imgeleme, sanal gerçeklik, duyuusal ayırt etme tedavisi, psikoterapiler (göz hareketleriyle duyarsızlaştırma ve yeniden işleme, hipnoz terapisi), nöroaksiyel infüzyon tedavisi, pleksus ve periferik sinir infüzyonları, dorsal root gangliyon radyofrekans tedavisi, spinal kord stimülatörü uygulaması, derin beyin stimülasyonu, motor korteks stimülasyonu ve DREZ lezyonu ile fantom ağrısının kontrolünde başarılı klinik sonuçlar elde etmek mümkündür.

KAYNAKLAR

- Hsu E, Cohen SP. Postamputation pain: epidemiology, mechanisms, and treatment. *Journal of Pain Research*. 2013;6:121.
- Limakatso K, Bedwell GJ, Madden VJ, et al. The prevalence and risk factors for phantom limb pain in people with amputations: a systematic review and meta-analysis. *PloS One*. 2020;15(10):e0240431.
- Knotkova H, Cruciani RA, Tronnier VM, et al. Current and future options for the management of phantom-limb pain. *Journal of Pain Research*. 2012;5:39.
- Jutzeler C, Curt A, Kramer J. Relationship between chronic pain and brain reorganization after deafferentation: A systematic review of functional MRI findings. *NeuroImage: Clinical*. 2015;9:599-606.
- Fuchs X, Flor H, Bekrater-Bodmann R. Psychological factors associated with phantom limb pain: A review of recent findings. *Pain Research Management*. 2018.
- Borghi B, D'Addabbo M, Borghi R. Can neural blocks prevent phantom limb pain? *Pain Management Nursing*. 2014;4(4):261-266.
- Jahangiri M, Jayatunga A, Bradley J, et al. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. *Annals of the Royal College of Surgeons of England*. 1994;76(5):324.
- Nikolajsen L, Ilkjaer S, Christensen JH, et al. Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. *The Lancet*. 1997;350(9088):1353-1357.
- Karanikolas M, Aretha D, Tsolakis I, et al. Optimized perioperative analgesia reduces chronic phantom limb pain intensity, prevalence, and frequency: a prospective, randomized, clinical trial. *The Journal of the American Society of Anesthesiologists*. 2011;114(5):1144-1154.
- Dahm PO, Nurescu PV, Appelgren LK, et al. Long-term intrathecal infusion of opioid and/or bupivacaine in the prophylaxis and treatment of phantom limb pain. *Neuromodulation: Technology at the Neural Interface*. 1998;1(3):111-128.
- Alviar MJM, Hale T, Lim-Dungca M. Pharmacologic interventions for treating phantom limb pain. *Cochrane database of systematic reviews*. 2016(10).
- Huse E, Larbig W, Flor H, et al. The effect of opioids on phantom limb pain and cortical reorganization. *Pain*. 2001;90(1-2):47-55.
- Wu CL, Tella P, Staats PS, et al. Analgesic effects of intravenous lidocaine and morphine on post-amputation pain: a randomized double-blind, active placebo-controlled, crossover trial. 2002;96(4):841-848.
- Abraham RB, Marouani N, Weinbroum AA. Dextromethorphan mitigates phantom pain in cancer amputees. *Annals of Surgical Oncology*. 2003;10(3):268-274.
- Eichenberger U, Neff F, Sveticic G, et al. Chronic phantom limb pain: the effects of calcitonin, ketamine, and their combination on pain and sensory thresholds. *Anesthesia Analgesia*. 2008;106(4):1265-1273.
- Bone M, Critchley P, Buggy DJ. Gabapentin in postamputation phantom limb pain: a randomized, double-blind, placebo-controlled, crossover study. *Regional Anesthesia Pain Medicine*. 2002;27(5):481-486.
- Smith DG, Ehde DM, Hanley MA, et al. Efficacy of gabapentin in treating chronic phantom limb and residual limb pain. *Journal of Rehabilitation Research Development*. 2005;42(5):645.
- Robinson LR, Czerniecki JM, Ehde DM, et al. Trial of amitriptyline for relief of pain in amputees: results of a randomized controlled study. *Archives of Physical Medicine Rehabilitation*. 2004;85(1):1-6.
- Jaeger H, Maier C. Calcitonin in phantom limb pain: a double-blind study. *Pain*. 1992;48(1):21-27.
- Wu CL, Tella P, Staats PS, et al. Analgesic effects of intravenous lidocaine and morphine on postamputation pain: a randomized double-blind, active placebo-controlled, crossover trial. *The Journal of the American Society of Anesthesiologists*. 2002;96(4):841-848.

21. Lang AM. Focused review: Botulinum toxin type A therapy in chronic pain disorders. *Archives of Physical Medicine Rehabilitation*. 2003;84:S69-S73.
22. Kern U, Martin C, Scheicher S, et al. Treatment of phantom pain with botulinum-toxin A. A pilot study. *Schmerz*. 2003;17(2):117-124.
23. Kern U, Martin C, Scheicher S, et al. Long-term treatment of phantom-and stump pain with Botulinum toxin type A over 12 months. A first clinical observation. *Der Nervenarzt*. 2004;75(4):336-340.
24. Kollwe K, Jin L, Krampfl K, et al. Treatment of phantom limb pain with botulinum toxin type A. *Pain Medicine*. 2009;10(2):300-303.
25. Charrow A, DiFazio M, Foster L, et al. Intradermal botulinum toxin type A injection effectively reduces residual limb hyperhidrosis in amputees: a case series. *Archives of Physical Medicine Rehabilitation*. 2008;89(7):1407-1409.
26. Lotze M, Grodd W, Birbaumer N, et al. Does use of a myoelectric prosthesis prevent cortical reorganization and phantom limb pain? *Nature Neuroscience*. 1999;2(6):501-502.
27. Weiss T, Miltner WH, Adler T, et al. Decrease in phantom limb pain associated with prosthesis-induced increased use of an amputation stump in humans. *Neuroscience Letters*. 1999;272(2):131-134.
28. Dietrich C, Walter-Walsh K, Preißler S, et al. Sensory feedback prosthesis reduces phantom limb pain: proof of a principle. *Neuroscience Letters*. 2012;507(2):97-100.
29. Dietrich C, Nehrlich S, Seifert S, et al. Leg prosthesis with somatosensory feedback reduces phantom limb pain and increases functionality. *Frontiers in Neurology*. 2018;9:270.
30. Ramachandran VS, Rogers-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. *Proceedings of the Royal Society of London Series B: Biological Sciences*. 1996;263(1369):377-386.
31. Weeks SR, Anderson-Barnes VC, Tsao JW. Phantom limb pain: theories and therapies. *The Neurologist*. 2010;16(5):277-286.
32. Campo-Prieto P, Rodríguez-Fuentes G. Effectiveness of mirror therapy in phantom limb pain: A literature review. *Neurología*. 2020.
33. Darnall BD, Li H. Home-based self-delivered mirror therapy for phantom pain: a pilot study. *Journal of Rehabilitation Medicine*. 2012;44(3):254.
34. Xie H-M, Zhang K-X, Wang S, et al. Effectiveness of Mirror Therapy for Phantom Limb Pain: A Systematic Review and Meta-analysis. *Archives of Physical Medicine Rehabilitation*. 2021.
35. Moseley GL. Graded motor imagery for pathologic pain: a randomized controlled trial. *Neurology*. 2006;67(12):2129-2134.
36. Limakatso K, Madden VJ, Manie S, et al. The effectiveness of graded motor imagery for reducing phantom limb pain in amputees: a randomised controlled trial. *Physiotherapy*. 2020;109:65-74.
37. Flor H, Denke C, Schaefer M, et al. Effect of sensory discrimination training on cortical reorganisation and phantom limb pain. *The Lancet*. 2001;357(9270):1763-1764.
38. Wakolbinger R, Diers M, Hruby LA, et al. Home-based tactile discrimination training reduces phantom limb pain. *Pain Practice*. 2018;18(6):709-715.
39. Eze U, Adeyi A, Ojieabu W. A Systematic Review of Studies on Virtual Reality Use in Management of Pain. *Nigerian Journal of Pharmaceutical Research*. 2021;17(2):131-155.
40. Mercier C, Sirigu A. Training with virtual visual feedback to alleviate phantom limb pain. *Neurorehabilitation Neural Repair*. 2009;23(6):587-594.
41. Giuffrida O, Simpson L, Halligan PW. Contralateral stimulation, using TENS, of phantom limb pain: two confirmatory cases. *Pain Medicine*. 2010;11(1):133-141.
42. Katz J, France C, Melzack R. An association between phantom limb sensations and stump skin conductance during transcutaneous electrical nerve stimulation (TENS) applied to the contralateral leg: a case study. *Pain*. 1989;36(3):367-377.
43. Vathakul J, Kessava N, Pooliam J, et al. The Analgesic Effect of Transcutaneous Electrical Nerve Stimulation (TENS) on the Opposite Side for Phantom Limb Pain. 2022;74(4):239-244.
44. Tilak M, Isaac SA, Fletcher J, et al. Mirror therapy and transcutaneous electrical nerve stimulation for management of phantom limb pain in amputees—a single blinded randomized controlled trial. 2016;21(2):109-115.
45. Tilak M, Isaac SA, Fletcher J, et al. Mirror therapy and transcutaneous electrical nerve stimulation for management of phantom limb pain in amputees—a single blinded randomized controlled trial. *Physiotherapy Research International*. 2016;21(2):109-115.
46. Melzack R. Phantom limbs and the concept of a neuromatrix. *Trends in Neurosciences*. 1990;13(3):88-92.
47. Vathakul J, Kessava N, Pooliam J, et al. The Analgesic Effect of Transcutaneous Electrical Nerve Stimulation (TENS) on the Opposite Side for Phantom Limb Pain. *Siriraj Medical Journal*. 2022;74(4):239-244.

48. Katz J, Melzack R. Auricular transcutaneous electrical nerve stimulation (TENS) reduces phantom limb pain. *Journal of Pain Symptom Management*. 1991;6(2):73-83.
49. Damercheli S, Ramne M, Ortiz-Catalan M. transcranial Direct Current Stimulation (tDCS) for the treatment and investigation of Phantom Limb Pain (PLP). *Psychoradiology*. 2022;2(1):23-31.
50. Bocci T, De Carolis G, Ferrucci R, et al. Cerebellar transcranial direct current stimulation (ctDCS) ameliorates phantom limb pain and non-painful phantom limb sensations. *The Cerebellum*. 2019;18(3):527-535.
51. Ferreira CM, De Carvalho CD, Gomes R, et al. Transcranial direct current stimulation and mirror therapy for neuropathic pain after brachial plexus avulsion: a randomized, double-blind, controlled pilot study. *Frontiers in Neurology*. 2020;11:568261.
52. Liebetanz D, Nitsche MA, Tergau F, et al. Pharmacological approach to the mechanisms of transcranial DC-stimulation-induced after-effects of human motor cortex excitability. *Brain*. 2002;125(10):2238-2247.
53. Stagg CJ, Antal A, Nitsche MA. Physiology of transcranial direct current stimulation. *The Journal of ECT*. 2018;34(3):144-152.
54. Kikkert S, Mezue M, O'Shea J, et al. Neural basis of induced phantom limb pain relief. *Annals of Neurology*. 2019;85(1):59-73.
55. Fitzgerald PB, Fountain S, Daskalakis ZJ. A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. *Clinical Neurophysiology*. 2006;117(12):2584-2596.
56. Schwenkreis P, Witscher K, Janssen F, et al. Changes of cortical excitability in patients with upper limb amputation. *Neuroscience Letters*. 2000;293(2):143-146.
57. Schwenkreis P, Witscher K, Janssen F, et al. Changes of cortical excitability in patients with upper limb amputation. 2000;293(2):143-146.
58. Schwenkreis P, Maier C, Pleger B, et al. NMDA-mediated mechanisms in cortical excitability changes after limb amputation. *Acta Neurologica Scandinavica*. 2003;108(3):179-184.
59. Karl A, Birbaumer N, Lutzenberger W, et al. Reorganization of motor and somatosensory cortex in upper extremity amputees with phantom limb pain. *Journal of Neuroscience*. 2001;21(10):3609-3618.
60. Malavera A, Silva FA, Fregni F, et al. Repetitive transcranial magnetic stimulation for phantom limb pain in land mine victims: a double-blinded, randomized, sham-controlled trial. *The Journal of Pain*. 2016;17(8):911-918.
61. Ahmed MA, Mohamed SA, Sayed DJN. Long-term antalgic effects of repetitive transcranial magnetic stimulation of motor cortex and serum beta-endorphin in patients with phantom pain. 2011;33(9):953-958.
62. Ahmed MA, Mohamed SA, Sayed D. Long-term antalgic effects of repetitive transcranial magnetic stimulation of motor cortex and serum beta-endorphin in patients with phantom pain. *Neurological Research*. 2011;33(9):953-958.
63. Oakley DA, Whitman LG, Halligan PW. Hypnotic imagery as a treatment for phantom limb pain: two case reports and a review. *Clinical Rehabilitation*. 2002;16(4):368-377.
64. Wei J, editor Psychotherapy for Phantom Limb Pain. 2021 International Conference on Social Development and Media Communication (SDMC 2021); 2022: Atlantis Press.
65. Schneider J, Hofmann A, Rost C, et al. EMDR in the treatment of chronic phantom limb pain. *Pain Medicine*. 2008;9(1):76-82.
66. Rostaminejad A, Behnammoghadam M, Rostaminejad M, et al. Efficacy of eye movement desensitization and reprocessing on the phantom limb pain of patients with amputations within a 24-month follow-up. *International Journal of Rehabilitation Research*. 2017;40(3):209-214.
67. Carvajal G, Rocha A, Dupoirion D. Multimodal intrathecal therapy for phantom limb pain: a report of 2 cases. *Colombian Journal of Anesthesiology*. 2019;47(3):198-201.
68. Birbaumer N, Lutzenberger W, Montoya P, et al. Effects of regional anesthesia on phantom limb pain are mirrored in changes in cortical reorganization. *Journal of Neuroscience*. 1997;17(14):5503-5508.
69. Preißler S, Dietrich C, Meissner W, et al. Brachial plexus block in phantom limb pain: a case report. *Pain Medicine*. 2011;12(11):1649-1654.
70. Kiefer RT, Wiech K, Töpfner S, et al. Continuous brachial plexus analgesia and NMDA-receptor blockade in early phantom limb pain: a report of two cases. *Pain Medicine*. 2002;3(2):156-160.
71. Ilfeld BM, Moeller-Bertram T, Hanling SR, et al. Treating intractable phantom limb pain with ambulatory continuous peripheral nerve blocks: a pilot study. *Pain Medicine*. 2013;14(6):935-942.
72. Kapural L, Mekhail N. Radiofrequency ablation for chronic pain control. *Current Pain Headache Reports*. 2001;5(6):517-525.
73. Wilkes D, Ganceres N, Solanki D, et al. Pulsed radiofrequency treatment of lower extremity phantom limb pain. *The Clinical Journal of Pain*. 2008;24(8):736-739.

74. Meiling JB, Raum GM, Barndt BS, et al. Radiofrequency Techniques for the Alleviation of Post-amputation Phantom Limb Pain: a Systematic Review. 2021;1-8.
75. Meiling JB, Raum GM, Barndt BS, et al. Radiofrequency Techniques for the Alleviation of Post-amputation Phantom Limb Pain: a Systematic Review. *Current Physical Medicine Rehabilitation Reports*. 2021;1-8.
76. Aiyer R, Barkin RL, Bhatia A, et al. A systematic review on the treatment of phantom limb pain with spinal cord stimulation. *Pain Management Nursing*. 2017;7(1):59-69.
77. Eldabe S, Burger K, Moser H, et al. Dorsal root ganglion (DRG) stimulation in the treatment of phantom limb pain (PLP). *Neuromodulation: Technology at the Neural Interface*. 2015;18(7):610-617.
78. Nielson KD, Adams JE, Hosobuchi Y. Phantom limb pain: treatment with dorsal column stimulation. *Journal of Neurosurgery*. 1975;42(3):301-307.
79. Guan Y. Spinal cord stimulation: neurophysiological and neurochemical mechanisms of action. *Current Pain Headache Reports*. 2012;16(3):217-225.
80. Krainick J-U, Thoden U, Riechert T. Pain reduction in amputees by long-term spinal cord stimulation: long-term follow-up study over 5 years. *Journal of Neurosurgery*. 1980;52(3):346-350.
81. Mekhail NA, Mathews M, Nageeb F, et al. Retrospective review of 707 cases of spinal cord stimulation: indications and complications. *Pain Practice*. 2011;11(2):148-153.
82. Bittar RG, Otero S, Carter H, et al. Deep brain stimulation for phantom limb pain. *Journal of Clinical Neuroscience*. 2005;12(4):399-404.
83. Katayama Y, Yamamoto T, Kobayashi K, et al. Motor cortex stimulation for phantom limb pain: comprehensive therapy with spinal cord and thalamic stimulation. *Stereotactic Functional Neurosurgery*. 2001;77(1-4):159-162.
84. Sindou M, Jeanmonod D. Microsurgical DREZotomy for the treatment of spasticity and pain in the lower limbs. *Neurosurgery*. 1989;24(5):655-670.
85. Young RF. Clinical experience with radiofrequency and laser DREZ lesions. *Journal of Neurosurgery*. 1990;72(5):715-720.
86. Gadgil N, Viswanathan A. DREZotomy in the treatment of cancer pain: a review. *Stereotactic Functional Neurosurgery*. 2012;90(6):356-360.
87. Mongardi L, Visani J, Mantovani G, et al. Long term results of Dorsal Root Entry Zone (DREZ) lesions for the treatment of intractable pain: A systematic review of the literature on 1242 cases. *Clinical Neurology Neurosurgery*. 2021;210:107004.