

Bölüm 5

REJENERATİF ENDODONTİK TEDAVİDE TEMEL ESASLAR

Esma SARİÇAM¹

GİRİŞ

Diş yapısı mineralize ve mineralize olmayan dokulardan oluşmaktadır. Mine, dentin ve cement mineralize diş dokularıdır. Pulpa mineralize olmayan gevşek bağ dokusu yapısında olup, dişin merkezinde lokalizedir. Dentin ile çevrili pulpa dokusu, apikal foramen aracılığıyla dişin canlılığını sağlayan temel faktörleri temin eder (Morotomi, Washio, & Kitamura, 2019).

Endodontik tedavi, çürük veya travma nedeniyle etkilenmiş pulpa dokusunun uzaklaştırılması ve kök kanallarının inert bir materyalle doldurulması işlemidir. Endodontik tedavi uzun yillardır pratikte uygulanmakta olup, güvenilir ve başarısı öngörelebilir bir tedavi seçenekidir (C. Jung, & ark., 2019). Ancak nekrotik pulpali ve apikal periodontitis bulunan immatur dişlerde rutin kök kanal tedavisi yöntemleri ile başarı elde edilmesi güçtür (Trope, 2010). Buna gerekçe olarak ise şu faktörler gösterilmiştir: (I) standart dezenfeksiyon yöntemleri ile kök kanallarının dezenfeksiyonun güçlüğü, (II) geniş apikal açıklık nedeniyle kanal dolumu için gerekli olan apikal daralımın elde edilememesi, (III) ince kök kanallarının kırılmaya yatkın oluşu. Tüm bu problemlerin kök kanallarını inceltmeye sebebiyet vermemek amacıyla minimal kök kanal enstrümantasyonu temelli, sert doku bariyeri veya apikal daralım oluşumuyla kök kanallarının kalınlaşmasını stimüle edici bir protokol ile aşılabileceği düşünülmüştür (Trope, 2010).

Rejeneratif endodonti tedavi (RET) nekrotik pulpali immatur dişler için tavsiye edilen bir yöntemdir (Almutairi, Yassen, Aminoshariae, Williams, & Mickel, 2019). Bu tedavi yöntemi biyolojik temelli olup, nekrotik dişlerde pulpa-dentin kompleksinin rejenerasyonu ile dentin ve kök kanal sistemi yapıları gibi zarar görmüş dokuların tamiri ve yerine konmasını hedefler (Nosrat, Seifi, & Asgary, 2011). Başarılı bir RET' nin bulguları klinik semptomların ve periapikal radyolüsensinin kaybolması, dentin kalınlığı ve kök boyunun artması ile dişin vitalite testlerine yanıtının yeniden kazanmasıdır (Kim, Malek, Sigurdsson, Lin, & Kahler, 2018).

¹ Doktor Öğretim Üyesi, Ankara Yıldırım Beyazıt Üniversitesi Diş Hekimliği Fakültesi, Endodonti ABD. dt.esmasaricam@gmail.com

sıklıkla ulaşılabilirliği raporlanmıştır (Chen, Jovani-Sancho Mdel, & Sheth, 2015). RET sonrası dişte meydana gelebilecek doku tipleri şu şekilde sınıflandırılmıştır (Andreasen & Bakland, 2012) 1. Dentin formasyonu 2. Periodontal ligament ve sement oluşumu, 3. Periodontal ligament, sement ve kemik oluşumu, 4. Kemik ve kemik iliği oluşumu. Bunların arasından hedeflenen, dentin formasyonu ile iyileşmedir. Ancak RET sonrası kök gelişiminin (kanal duvarlarının kalınlaşması ve / veya apikal kapanma) tamamlandığını net olarak tespit etmek güçtür (Kim & ark., 2018). RET ile gerçek pulpa-dentin kompleksi rejenerasyonunun sağlanamadığı, oluşan dokunun pulpa benzeri doku olduğu bilinmektedir (Duncan, Cooper, & Smith, 2019).

KAYNAKLAR

1. Ajay Sharma L, Sharma A, & Dias GJ. (2015). Advances in regeneration of dental pulp -a literature review. *Journal of Investigative and Clinical Dentistry*, 6(2), 85-98. doi:10.1111/jicd.12064
2. Alkahtani A, Alkahtany SM, & Anil S. (2014). An in vitro evaluation of the cytotoxicity of varying concentrations of sodium hypochlorite on human mesenchymal stem cells. *The Journal of Contemporary Dental Practice*, 15(4), 473-481.
3. Almutairi W, Yassen GH, Aminoshariae A, et al. (2019). Regenerative Endodontics: A Systematic Analysis of the Failed Cases. *Journal of Endodontics*, 45(5), 567-577. doi:10.1016/j.joen.2019.02.004
4. AlSaeed T, Nosrat A, Melo MA, et al. (2018). Antibacterial Efficacy and Discoloration Potential of Endodontic Topical Antibiotics. *Journal of Endodontics*, 44(7), 1110-1114. doi:10.1016/j.joen.2018.03.001
5. Andreasen JO, & Bakland LK. (2012). Pulp regeneration after non-infected and infected necrosis, what type of tissue do we want? A review. *Dental Traumatology*, 28(1), 13-18.
6. Bakhtiar H, Esmaeili S, Fakhr Tabatabayi S, et al. (2017). Second-generation Platelet Concentrate (Platelet-rich Fibrin) as a Scaffold in Regenerative Endodontics: A Case Series. *Journal of Endodontics*, 43(3), 401-408. doi:10.1016/j.joen.2016.10.016
7. Bakopoulou A, Leyhausen G, Volk J, et al. (2011). Comparative analysis of in vitro osteo/odontogenic differentiation potential of human dental pulp stem cells (DPSCs) and stem cells from the apical papilla (SCAP). *Archives of Oral Biology*, 56(7), 709-721. doi:10.1016/j.archoralbio.2010.12.008
8. Banchs E, & Trope M. (2004). Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? *Journal of Endodontics*, 30(4), 196-200. doi:10.1097/00004770-200404000-00003
9. Barrientos S, Stojadinovic O, Golinko MS, et al. (2008). Growth factors and cytokines in wound healing. *Wound Repair and Regeneration*, 16(5), 585-601. doi:10.1111/j.1524-475X.2008.00410.x
10. Becerra P, Ricucci D, Loghin S, et al. (2014). Histologic study of a human immature permanent premolar with chronic apical abscess after revascularization/revitalization. *Journal of Endodontics*, 40(1), 133-139. doi:10.1016/j.joen.2013.07.017
11. Bezgin T, Yilmaz AD, Celik BN, et al. (2015). Efficacy of platelet-rich plasma as a scaffold in regenerative endodontic treatment. *Journal of Endodontics*, 41(1), 36-44. doi:10.1016/j.joen.2014.10.004
12. Bezgin T, Yilmaz AD, Celik BN, et al. (2014). Concentrated platelet-rich plasma used in root canal revascularization: 2 case reports. *International Endodontic Journal*, 47(1), 41-49. doi:10.1111/iej.12144
13. Chan G, & Mooney DJ. (2008). New materials for tissue engineering: towards greater control over the biological response. *Trends in Biotechnology*, 26(7), 382-392. doi:10.1016/j.tibtech.2008.03.011

14. Chen YP, Jovani-Sancho Mdel M, & Sheth CC. (2015). Is revascularization of immature permanent teeth an effective and reproducible technique? *Dental Traumatology*, 31(6), 429-436. doi:10.1111/edt.12214
15. Dhillon H, Kaushik M, & Sharma R. (2016). Regenerative endodontics-Creating new horizons. *Journal of Biomedical Materials Research*, 104(4), 676-685. doi:10.1002/jbm.b.33587
16. Dubey N, Xu J, Zhang Z, et al. (2019). Comparative Evaluation of the Cytotoxic and Angiogenic Effects of Minocycline and Clindamycin: An In Vitro Study. *Journal of Endodontics*, 45(7), 882-889. doi:10.1016/j.joen.2019.04.007
17. Duncan HF, Cooper PR, & Smith AJ. (2019). Dissecting dentine-pulp injury and wound healing responses: consequences for regenerative endodontics. *International Endodontic Journal*, 52(3), 261-266. doi:10.1111/iej.13064
18. Egusa H, Sonoyama W, Nishimura M, et al. (2012). Stem cells in dentistry--part I: stem cell sources. *Journal of Prosthodontic Research*, 56(3), 151-165. doi:10.1016/j.jpor.2012.06.001
19. Fundaooglu Kucukkenceli F, Cakici F, & Kucukkenceli AS. (2019). Spectrophotometric analysis of discoloration and internal bleaching after use of different antibiotic pastes. *Clinical Oral Investigations*, 23(1), 161-167. doi:10.1007/s00784-018-2422-1
20. Galler KM. (2016). Clinical procedures for revitalization: current knowledge and considerations. *International Endodontic Journal*, 49(10), 926-936. doi:10.1111/iej.12606
21. Galler KM, Buchalla W, Hiller KA, et al. (2015). Influence of root canal disinfectants on growth factor release from dentin. *Journal of Endodontics*, 41(3), 363-368. doi:10.1016/j.joen.2014.11.021
22. Galler KM, Krastl G, Simon S, et al. (2016). European Society of Endodontontology position statement: Revitalization procedures. *International Endodontic Journal*, 49(8), 717-723. doi:10.1111/iej.12629
23. Gathani KM., & Raghavendra SS. (2016). Scaffolds in regenerative endodontics: A review. *Dental Research Journal*, 13(5), 379-386.
24. Goldberg M, & Smith AJ. (2004). Cells and Extracellular Matrices of Dentin and Pulp: A Biological Basis for Repair and Tissue Engineering. *Critical Reviews in Oral Biology & Medicine*, 15(1), 13-27.
25. Guo W, He Y, Zhang X, et al. (2009). The use of dentin matrix scaffold and dental follicle cells for dentin regeneration. *Biomaterials*, 30(35), 6708-6723. doi:10.1016/j.biomaterials.2009.08.034
26. Hargreaves KM, Diogenes A, & Teixeira FB. (2013). Treatment options: biological basis of regenerative endodontic procedures. *Journal of Endodontics*, 39(3 Suppl), S30-43. doi:10.1016/j.joen.2012.11.025
27. Hoshino E, Kurihara-Ando N, Sato I, et al. (1996). In-vitro antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. *International Endodontic Journal*, 29(2), 125-130.
28. Hotwani K, & Sharma K. (2014). Platelet rich fibrin - a novel acumen into regenerative endodontic therapy. *Restorative Dentistry & Endodontics*, 39(1), 1-6. doi:10.5395/rde.2014.39.1.1
29. Iwaya SI, Ikawa M, & Kubota M. (2001). Revascularization of an immature permanent tooth with apical periodontitis and sinus tract. *Dental Traumatology*, 17(4), 185-187.
30. Jadhav G, Shah N, & Logani A. (2012). Revascularization with and without platelet-rich plasma in nonvital, immature, anterior teeth: a pilot clinical study. *Journal of Endodontics*, 38(12), 1581-1587. doi:10.1016/j.joen.2012.09.010
31. Jadhav GR, Shah N, & Logani A. (2013). Comparative outcome of revascularization in bilateral, non-vital, immature maxillary anterior teeth supplemented with or without platelet rich plasma: A case series. *Journal of Conservative Dentistry*, 16(6), 568-572. doi:10.4103/0972-0707.120932
32. Jin Q, Yuan K, Lin W, et al. (2019). Comparative characterization of mesenchymal stem cells from human dental pulp and adipose tissue for bone regeneration potential. *Artificial Cells, Nanomedicine, and Biotechnology*, 47(1), 1577-1584. doi:10.1080/21691401.2019.1594861

33. Jung C, Kim S, Sun T, et al. (2019). Pulp-dentin regeneration: current approaches and challenges. *Journal of Tissue Engineering*, 10, 2041731418819263. doi:10.1177/2041731418819263
34. Jung IY, Lee SJ, & Hargreaves KM. (2008). Biologically based treatment of immature permanent teeth with pulpal necrosis: a case series. *Journal of Endodontics*, 34(7), 876-887. doi:10.1016/j.joen.2008.03.023
35. Kahler B, Mistry S, Moule A, et al. (2014). Revascularization outcomes: a prospective analysis of 16 consecutive cases. *Journal of Endodontics*, 40(3), 333-338. doi:10.1016/j.joen.2013.10.032
36. Karczewski A, Feitosa SA, Hamer EI, et al. (2018). Clindamycin-modified Triple Antibiotic Nanofibers: A Stain-free Antimicrobial Intracanal Drug Delivery System. *Journal of Endodontics*, 44(1), 155-162. doi:10.1016/j.joen.2017.08.024
37. Kim SG, Malek M, Sigurdsson A, et al. (2018). Regenerative endodontics: a comprehensive review. *International Endodontic Journal*, 51(12), 1367-1388. doi:10.1111/iej.12954
38. Kim SG, Zhou J, Solomon C, et al. (2012). Effects of growth factors on dental stem/progenitor cells. *Dental Clinics of North America*, 56(3), 563-575. doi:10.1016/j.cden.2012.05.001
39. Krampera M, Franchini M, Pizzolo G, et al. (2007). Mesenchymal stem cells: from biology to clinical use. *Blood Transfusion*, 5(3), 120-129. doi:10.2450/2007.0029-07
40. Kuratake M, Yoshioka K, Shigetani Y, et al. (2008). Immunohistochemical analysis of nestin, osteopontin, and proliferating cells in the reparative process of exposed dental pulp capped with mineral trioxide aggregate. *Journal of Endodontics*, 34(8), 970-974. doi:10.1016/j.joen.2008.03.021
41. Lei L, Chen Y, Zhou R, et al. (2015). Histologic and Immunohistochemical Findings of a Human Immature Permanent Tooth with Apical Periodontitis after Regenerative Endodontic Treatment. *Journal of Endodontics*, 41(7), 1172-1179. doi:10.1016/j.joen.2015.03.012
42. Mao JJ, Kim SG, Zhou J, et al. (2012). Regenerative endodontics: barriers and strategies for clinical translation. *Dental Clinics of North America*, 56(3), 639-649. doi:10.1016/j.cden.2012.05.005
43. Martin DE, De Almeida JF, Henry MA, et al. (2014). Concentration-dependent effect of sodium hypochlorite on stem cells of apical papilla survival and differentiation. *Journal of Endodontics*, 40(1), 51-55. doi:10.1016/j.joen.2013.07.026
44. Miller EK, Lee JY, Tawil PZ, et al. (2012). Emerging therapies for the management of traumatized immature permanent incisors. *Pediatric Dentistry*, 34(1), 66-69.
45. Mohammadi Z. (2008). Sodium hypochlorite in endodontics: an update review. *International Dental Journal*, 58(6), 329-341.
46. Mohammadi Z, Shalavi S, & Jafarzadeh H. (2013). Ethylenediaminetetraacetic acid in endodontics. *European Journal of Dentistry*, 7(Suppl 1), S135-142. doi:10.4103/1305-7456.119091
47. Montero-Miralles P, Martin-Gonzalez J, Alonso-Espeleta O, et al. (2018). Effectiveness and clinical implications of the use of topical antibiotics in regenerative endodontic procedures: a review. *International Endodontic Journal*, 51(9), 981-988. doi:10.1111/iej.12913
48. Moore KA, & Lemischka IR. (2006). Stem cells and their niches. *Science*, 311(5769), 1880-1885. doi:10.1126/science.1110542
49. Morotomi T, Washio A, & Kitamura C. (2019). Current and future options for dental pulp therapy. *Japanese Dental Science Review*, 55(1), 5-11. doi:10.1016/j.jdsr.2018.09.001
50. Nazzal H, & Duggal MS. (2017). Regenerative endodontics: a true paradigm shift or a bandwagon about to be derailed? *European Archives of Paediatric Dentistry*, 18(1), 3-15. doi:10.1007/s40368-016-0265-5
51. Nosrat A, Kolahdouzan,A, Hosseini F, et al. (2015). Histologic Outcomes of Uninfected Human Immature Teeth Treated with Regenerative Endodontics: 2 Case Reports. *Journal of Endodontics*, 41(10), 1725-1729. doi:10.1016/j.joen.2015.05.004
52. Nosrat A, Seifi A, & Asgary S. (2011). Regenerative endodontic treatment (revascularization) for necrotic immature permanent molars: a review and report of two cases with a new biomaterial. *Journal of Endodontics*, 37(4), 562-567. doi:10.1016/j.joen.2011.01.011
53. Park JY, Yang C, Jung IH, et al. (2015). Regeneration of rabbit calvarial defects using cells-implanted nano-hydroxyapatite coated silk scaffolds. *Biomaterials Research*, 19, 7. doi:10.1186/s40824-015-0027-1

54. Prescott RS, Alsanea R, Fayad MI, et al. (2008). In vivo generation of dental pulp-like tissue by using dental pulp stem cells, a collagen scaffold, and dentin matrix protein 1 after subcutaneous transplantation in mice. *Journal of Endodontics*, 34(4), 421-426. doi:10.1016/j.joen.2008.02.005
55. Rajasekharan S, Martens LC, Cauwels R, et al. (2018). Correction to: Biobentine material characteristics and clinical applications: a 3 year literature review and update. *European Archives of Paediatric Dentistry*, 19(2), 129. doi:10.1007/s40368-018-0335-y
56. Reyes-Carmona JF, Felippe MS, & Felippe WT. (2009). Biominerization ability and interaction of mineral trioxide aggregate and white portland cement with dentin in a phosphate-containing fluid. *Journal of Endodontics*, 35(5), 731-736. doi:10.1016/j.joen.2009.02.011
57. Reynolds K, Johnson JD, & Cohenca N. (2009). Pulp revascularization of necrotic bilateral bicuspids using a modified novel technique to eliminate potential coronal discolouration: a case report. *International Endodontic Journal*, 42(1), 84-92. doi:10.1111/j.1365-2591.2008.01467.x
58. Ruparel NB, Teixeira FB, Ferraz CC, et al. (2012). Direct effect of intracanal medicaments on survival of stem cells of the apical papilla. *Journal of Endodontics*, 38(10), 1372-1375. doi:10.1016/j.joen.2012.06.018
59. Sato I, Ando-Kurihara N, Kota K, et al. (1996). Sterilization of infected root-canal dentine by topical application of a mixture of ciprofloxacin, metronidazole and minocycline in situ. *International Endodontic Journal*, 29(2), 118-124.
60. Sharma S, Srivastava D, Grover S, et al. (2014). Biomaterials in tooth tissue engineering: a review. *Journal of Clinical and Diagnostic Research*, 8(1), 309-315. doi:10.7860/JCDR/2014/7609.3937
61. Shivashankar VY, Johns DA, Vidyanath S, et al. (2012). Platelet Rich Fibrin in the revitalization of tooth with necrotic pulp and open apex. *Journal of Conservative Dentistry*, 15(4), 395-398. doi:10.4103/0972-0707.101926
62. Sobhani A, Khanlarkhani N, Baazm M, et al. (2017). Multipotent Stem Cell and Current Application. *Acta Medica Iranica*, 55(1), 6-23.
63. Sonoyama W, Liu Y, Fang D, et al. (2006). Mesenchymal stem cell-mediated functional tooth regeneration in swine. *PLoS One*, 1, e79. doi:10.1371/journal.pone.0000079
64. Staffoli S, Plotino G, Nunez Torrijos BG, et al. (2019). Regenerative Endodontic Procedures Using Contemporary Endodontic Materials. *Materials (Basel)*, 12(6). doi:10.3390/ma12060908
65. Takushige T, Cruz EV, Asgor Moral A, et al. (2004). Endodontic treatment of primary teeth using a combination of antibacterial drugs. *International Endodontic Journal*, 37(2), 132-138.
66. Thibodeau B, & Trope M. (2007). Pulp revascularization of a necrotic infected immature permanent tooth: case report and review of the literature. *Pediatric Dentistry*, 29(1), 47-50.
67. Topcuoglu G, & Topcuoglu HS. (2016). Regenerative Endodontic Therapy in a Single Visit Using Platelet-rich Plasma and Biodentine in Necrotic and Asymptomatic Immature Molar Teeth: A Report of 3 Cases. *Journal of Endodontics*, 42(9), 1344-1346. doi:10.1016/j.joen.2016.06.005
68. Torabinejad M, Anderson P, Bader J, et al. (2007). Outcomes of root canal treatment and restoration, implant-supported single crowns, fixed partial dentures, and extraction without replacement: a systematic review. *Journal of Prosthetic Dentistry*, 98(4), 285-311. doi:10.1016/S0022-3913(07)60102-4
69. Torabinejad M, & Faras H. (2012). A clinical and histological report of a tooth with an open apex treated with regenerative endodontics using platelet-rich plasma. *Journal of Endodontics*, 38(6), 864-868. doi:10.1016/j.joen.2012.03.006
70. Torabinejad M, Nosrat A, Verma P, et al. (2017). Regenerative Endodontic Treatment or Mineral Trioxide Aggregate Apical Plug in Teeth with Necrotic Pulps and Open Apices: A Systematic Review and Meta-analysis. *Journal of Endodontics*, 43(11), 1806-1820. doi:10.1016/j.joen.2017.06.029
71. Torabinejad M, Parirokh M, & Dummer PMH. (2018). Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview - part II: other clinical applications and complications. *International Endodontic Journal*, 51(3), 284-317. doi:10.1111/iej.12843

72. Torabinejad M, & Turman M. (2011). Revitalization of tooth with necrotic pulp and open apex by using platelet-rich plasma: a case report. *Journal of Endodontics*, 37(2), 265-268. doi:10.1016/j.joen.2010.11.004
73. Trevino EG, Patwardhan AN, Henry MA, et al. (2011). Effect of irrigants on the survival of human stem cells of the apical papilla in a platelet-rich plasma scaffold in human root tips. *Journal of Endodontics*, 37(8), 1109-1115. doi:10.1016/j.joen.2011.05.013
74. Trope M. (2010). Treatment of the immature tooth with a non-vital pulp and apical periodontitis. *Dental Clinics of North America*, 54(2), 313-324. doi:10.1016/j.cden.2009.12.006
75. Vaissiere G, Chevallay B, Herbage D, et al. (2000). Comparative analysis of different collagen-based biomaterials as scaffolds for long-term culture of human fibroblasts. *Medical & Biological Engineering & Computing*, 38(2), 205-210.
76. Wakao S, Kitada M, Kuroda Y, et al. (2011). Multilineage-differentiating stress-enduring (Muse) cells are a primary source of induced pluripotent stem cells in human fibroblasts. *Proceedings of the National Academy of Sciences*, 108(24), 9875-9880. doi:10.1073/pnas.1100816108
77. Wang X, Thibodeau B, Trope M, et al. (2010). Histologic characterization of regenerated tissues in canal space after the revitalization/revascularization procedure of immature dog teeth with apical periodontitis. *Journal of Endodontics*, 36(1), 56-63. doi:10.1016/j.joen.2009.09.039
78. Windle W, 3rd Teixeira F, Levin L, et al. (2005). Disinfection of immature teeth with a triple antibiotic paste. *Journal of Endodontics*, 31(6), 439-443.
79. Yang JW, Zhang YF, Sun ZY, et al. (2015). Dental pulp tissue engineering with bFGF-incorporated silk fibroin scaffolds. *Journal of Biomaterials Applications*, 30(2), 221-229. doi:10.1177/0885328215577296
80. Yuan Z, Nie H, Wang S, et al. (2011). Biomaterial selection for tooth regeneration. *Tissue Engineering Part B: Reviews*, 17(5), 373-388. doi:10.1089/ten.TEB.2011.0041
81. Zehnder M. (2006). Root canal irrigants. *Journal of Endodontics*, 32(5), 389-398. doi:10.1016/j.joen.2005.09.014
82. Zhai Q, Dong Z, Wang W, et al. (2019). Dental stem cell and dental tissue regeneration. *Frontiers of Medicine*, 13(2), 152-159. doi:10.1007/s11684-018-0628-x
83. Zhou C, Yang G, Chen M, et al. (2015). Lhx8 mediated Wnt and TGFbeta pathways in tooth development and regeneration. *Biomaterials*, 63, 35-46. doi:10.1016/j.biomaterials.2015.06.004
84. Zhu X, Zhang C, Huang GT, et al. (2012). Transplantation of dental pulp stem cells and platelet-rich plasma for pulp regeneration. *Journal of Endodontics*, 38(12), 1604-1609. doi:10.1016/j.joen.2012.09.001