10. Bölüm
SPİNAL KORD İSKEMİ REPERFÜZYON

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10.1. Spinal Kord Fizyoloji

Spinal kord, merkezi sinir sistemi (MSS)'nin vertebral kanalında bulunan hayati bir yapıdır. Kaudal olarak uzanır ve vertebral kanalın kemikli yapısı tarafından korunmaktadır. Vertebral kanal foramen magnumdan sakral aralığa kadar uzanır. Spinal kord ise foramen oksipitale magnumda medullanın rostrum sınırından başlar. Fetusta vertebral kanal boyunca uzanırken, yendioğanda üçüncü lomber vertebra, erişkinde birinci lomber vertebrada sonlanır (1,2). Spinal kord, servikal, torasik, lomber ve sakral olmak üzere dört bölüme ayrılabilir. Biri servikal diğer ise lomber bölgede olan iki yerde genişleme gösterir. Lomber bölgedeki genişleme sonrası incelir ve konus medullaris adını alarak sonlanır (1). Spinal kord, dura mater, araknoid ve en içte bulunan pia mater ile kaplıdır. İç tarafta gri cevher dış tarafta ise beyaz cevher bulunmaktadır. Gri cevher motor ve duyusal nöron gövdeleri, internöronlar, nöroglia ve myelinsiz aksonlar tarafından oluşturulmuştur. Beyaz cevher ise myelinli motor ve duyusal aksonlar tarafından oluşturulmuştur. Gri cevherin öne doğru (ön boynuz) ve arkaya doğru (arka boynuz) olan uzantıları vardır. Anterior ve posterior median fissürler, kordu enine anterior ve posterior komissürlerle birbirine bağlanan iki simetrik kısma böler. Sağ ve sol gri cevher arasında spinal kord boyunca uzanan santral kanal içerisinde beyin

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Kaynaklar

1. Taner D, Atasever A, Durgun B. Medulla spinali. In: Fonksiyonel nöroanatomi. Ankara: ODTÜ Geliştirme Vakfı 2014;33-48.
2. A Nógrádi, G Vrbová. Anatomy and physiology of the spinal cord. In: Transplantation of neural tissue into the spinal cord. 2nd ed. USA: Springer 2006;1-23.
3. Harrow-Mortelliti M, Reddy V, Jimsheleishvili G. Physiology, Spinal Cord. 2021 Feb 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 31334987.
4. Stoelting RK, Miller RD, Akkaya ÖT, Ateş Y, Batislam Y. Spinal ve Epidural Anestezi. In: Temel anestezi. 5th ed. Ankara: Güneş Tıp Kitabevleri; 2010;241–71.
5. Sheerin F. Spinal cord injury: anatomy and physiology of the spinal cord. Emerg Nurse. 2004 Dec;12(8):30-6.
6. Tetik Ö, Gürbüz A. Spinal kord korunması. Türk Göğüs Kalp Damar Cerrahisi Dergisi. 2000;8(2):587-92.
7. Elmacı T, Aydogan U, Dindar A, Onursal E. An Unusual Complication After Aortic Coarctation Repair: Spinal Cord Injury. Turk Kardiyol Dern Ars 2000;28(8):516-8.
8. Hasan S, Arain A. Spinal Cord Arteries. In: Neuroanatomy [Internet]. StatPearls Publishing; 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539889/
9. Carrel A. VIII. On the Experimental Surgery of the Thoracic Aorta and Heart. Ann Surg. 1910 Jul;52(1):83-95.
10. Gelman S. The pathophysiology of aortic cross-clamping and unclamping. Anesthesiology 1995;82(4):1026-60.
11. Katz NM, Blackstone EH, Kirklin JW, Karp RB. Incremental risk factors for spinal cord injury following operation for acute traumatic aortic transection. J Thorac Cardiovasc Surg 1981;81(5):669-74.
12. Hollier LH. Protecting the brain and spinal cord. J Vasc Surg 1987;5(3):524-8.
13. Wadouh F, Lindemann EM, Arndt CF, Hetzer R, Borst HG. The arteria radicularis magna anterior as a decisive factor influencing spinal cord damage during aortic occlusion. J Thorac Cardiovasc Surg 1984;88(1):1-10.
14. Reece TB, Okonkwo DO, Ellman PI, Warren PS, Smith RL, Hawkins AS, et al. The evolution of ischemic spinal cord injury in function, cytoarchitecture, and inflammation and the effects of adenosine A2A receptor activation. J Thorac Cardiovasc Surg 2004;128(6):925-32.
15. Gharagozloo F, Neville RF Jr, Cox JL. Spinal cord protection during surgical procedures on the descending thoracic and thoracoabdominal aorta: a critical overview. Semin Thorac Cardiovasc Surg 1998;10(1):73-86.
16. Braughler JM, Hall ED. Central nervous system trauma and stroke. I. Biochemical considerations for oxygen radical formation and lipid peroxidation. Free Radic Biol Med 1989;6(3):289-301.
17. İpek G, Demirsoy E, Arbatlı H, Balkanay M, Olgaç V, Şişmanoğlu M, et al. Spinal Kord İskemisi ve Reperfüzyon Hasarının Önlenmesinde İntraaortik Katalaz Kullanımı: Deneysel Çalışma. GKD Cer Derg 1997;5:83-7.
18. Svensson LG, Von Ritter CM, Groeneveld HT, Rickards ES, Hunter SJ, Robinson MF, et al. Cross-clamping of the thoracic aorta. Influence of aortic shunts, laminectomy, papaverine, calcium channel blocker, allopurinol, and superoxide dismutase on spinal cord blood flow and paraplegia in baboons. Ann Surg 1986;204(1):38-47.
19. Jacobs TP, Kempski O, McKinley D, Dutka AJ, Hallenbeck JM, Feuerstein G. Blood flow and vascular permeability during motor dysfunction in a rabbit model of spinal cord ischemia. Stroke 1992;23(3):367-73.
20. Ullery BW, Cheung AT, Fairman RM, Jackson BM, Woo EY, Bavaria J, et al. Risk factors, outcomes, and clinical manifestations of spinal cord ischemia following thoracic endovascular aortic repair. J Vasc Surg 2011;54(3):677-84.

21. Li Y, Si R, Feng Y, Chen HH, Zou L, Wang E, et al. Myocardial ischemia activates an injurious innate immune signaling via cardiac heat shock protein 60 and Toll-like receptor 4. J Biol Chem 2011;286(36):31308-19.
22. Ormstad H, Aass HC, Lund-Sørensen N, Amthor KF, Sandvik L. Serum levels of cytokines and C-reactive protein in acute ischemic stroke patients, and their relationship to stroke lateralization, type, and infarct volume. J Neurol 2011;258(4):677-85.
23. Smith PD, Bell MT, Puskas F, Meng X, Cleveland JC Jr, Weyant MJ, et al. Preservation of motor function after spinal cord ischemia and reperfusion injury through microglial inhibition. Ann Thorac Surg 2013;95(5):1647-53.
24. Nakata T, Kawachi K, Nagashima M, Yasugi T, Izutani H, Ryugo M, et al. Transient ischemia-induced paresis and complete paraplegia displayed distinct reactions of microglia and macrophages. Brain Res 2011;1420:114-24.
25. Matsumoto S, Matsumoto M, Yamashita A, Ohtake K, Ishida K, Morimoto Y, et al. The temporal profile of the reaction of microglia, astrocytes, and macrophages in the delayed onset paraplegia after transient spinal cord ischemia in rabbits. Anesth Analg 2003;96(6):1777-84.
26. Zhu P, Li JX, Fujino M, Zhuang J, Li XK. Development and treatments of inflammatory cells and cytokines in spinal cord ischemia-reperfusion injury. Mediators Inflamm 2013;2013:701970. doi: 10.1155/2013/701970.
27. Wong TP, Howland JG, Wang YT. NMDA Receptors and Disease+C464. In: Encyclopedia of Neuroscience [Internet]. Elsevier; 2009 [cited 2021 Feb 20]. p. 1177–82.
28. Papakostas JC, Matsagas MI, Toumpoulis IK, Malamou-Mitsi VD, Pappa LS, et al. Evolution of spinal cord injury in a porcine model of prolonged aortic occlusion. J Surg Res 2006;133(2):159-66.
29. Tsuruta S, Matsumoto M, Fukuda S, Yamashita A, Cui YJ, Wakamatsu H, et al. The effects of cyclosporin A and insulin on ischemic spinal cord injury in rabbits. Anesth Analg 2006;102(6):1722-7.
30. Temiz C, Solmaz I, Tehli O, Kaya S, Onguru O, Arslan E, et al. The effects of splenectomy on lipid peroxidation and neuronal loss in experimental spinal cord ischemia/reperfusion injury. Turk Neurosurg 2013;23(1):67-74.
31. Hasturk A, Atalay B, Calisaneller T, Ozdemir O, Oruckaptan H, Altinors N. Analysis of serum pro-inflammatory cytokine levels after rat spinal cord ischemia/reperfusion injury and correlation with tissue damage. Turk Neurosurg 2009;19(4):353-9.
32. Tikka T, Fiebich BL, Goldsteins G, Keinanen R, Koistinaho J. Minocycline, a tetracycline derivative, is neuroprotective against excitotoxicity by inhibiting activation and proliferation of microglia. J Neurosci 2001;21(8):2580-8.
33. Hermann GE, Rogers RC, Bresnahan JC, Beattie MS. Tumor necrosis factor-alpha induces cFOS and strongly potentiates glutamate-mediated cell death in the rat spinal cord. Neurobiol Dis 2001;8(4):590-9.
34. Fan L, Wang K, Shi Z, Die J, Wang C, Dang X. Tetramethylpyrazine protects spinal cord and reduces inflammation in a rat model of spinal cord ischemia-reperfusion injury. J Vasc Surg 2011;54(1):192-200.
35. Smith PD, Puskas F, Meng X, Lee JH, Cleveland JC Jr, Weyant MJ, et al. The evolution of chemokine release supports a bimodal mechanism of spinal cord ischemia and reperfusion injury. Circulation 2012;126(11 Suppl 1):S110-7.
36. Kunihara T, Sasaki S, Shiiya N, Miyatake T, Mafune N, Yasuda K. Proinflammatory cytokines in cerebrospinal fluid in repair of thoracoabdominal aorta. Ann Thorac Surg 2001;71(3):801-6.
37. Plunkett JA, Yu CG, Easton JM, Bethea JR, Yezierski RP. Effects of interleukin-10 (IL-10) on pain behavior and gene expression following excitotoxic spinal cord injury in the rat. Exp Neurol 2001;168(1):144-54.

38. Oruckaptan HH, Ozisik P, Atilla P, Tuncel M, Kilinc K, Geyik PO, et al. Systemic administration of interleukin-10 attenuates early ischemic response following spinal cord ischemia reperfusion injury in rats. J Surg Res 2009;155(2):345-56.
39. Simon F, Oberhuber A. Ischemia and reperfusion injury of the spinal cord: experimental strategies to examine postischemic paraplegia. Neural Regen Res 2016;11(3):414-5.
40. Livesay JJ, Cooley DA, Ventemiglia RA, Montero CG, Warrian RK, Brown DM, et al. Surgical experience in descending thoracic aneurysmectomy with and without adjuncts to avoid ischemia. Ann Thorac Surg 1985;39(1):37-46.
41. Svensson LG, Patel V, Robinson MF, Ueda T, Roehm JO Jr, Crawford ES. Influence of preservation or perfusion of intraoperatively identified spinal cord blood supply on spinal motor evoked potentials and paraplegia after aortic surgery. J Vasc Surg 1991;13(3):355-65.
42. Sun J, Hirsch D, Svensson G. Spinal cord protection by papaverine and intrathecal cooling during aortic crossclamping. J Cardiovasc Surg (Torino) 1998;39(6):839-42.
43. Maughan RE, Mohan C, Nathan IM, Ascer E, Damiani P, Jacobowitz IJ, et al. Intrathecal perfusion of an oxygenated perfluorocarbon prevents paraplegia after aortic occlusion. Ann Thorac Surg 1992;54(5):818-24; discussion 824-5.
44. Cassada DC, Tribble CG, Long SM, Laubach VE, Kaza AK, Linden J, et al. Adenosine A2A analogue ATL-146e reduces systemic tumor necrosing factor-alpha and spinal cord capillary platelet-endothelial cell adhesion molecule-1 expression after spinal cord ischemia. J Vasc Surg 2002;35(5):994-8.
45. Zhu DJ, Xia B, Bi Q, Zhang SJ, Qiu BS, Zhao C. Functional protection of pentoxifylline against spinal cord ischemia/reperfusion injury in rabbits: necrosis and apoptosis effects. Chin Med J (Engl) 2008;121(23):2444-9.
46. Lu K, Cho CL, Liang CL, Chen SD, Liliang PC, Wang SY, et al. Inhibition of the MEK/ERK pathway reduces microglial activation and interleukin-1-beta expression in spinal cord ischemia/reperfusion injury in rats. J Thorac Cardiovasc Surg 2007;133(4):934-41.
47. Lu K, Liang CL, Liliang PC, Yang CH, Cho CL, Weng HC, et al. Inhibition of extracellular signal-regulated kinases 1/2 provides neuroprotection in spinal cord ischemia/reperfusion injury in rats: relationship with the nuclear factor-kappaB-regulated anti-apoptotic mechanisms. J Neurochem 2010;114(1):237-46.
48. Guven C, Borcek AO, Cemil B, Kurt G, Yildirim Z, Ucankus NL, et al. Neuroprotective effects of infliximab in experimental spinal cord ischemic injury. J Clin Neurosci 2010;17(12):1563-7.
49. Akuzawa S, Kazui T, Shi E, Yamashita K, Bashar AH, Terada H. Interleukin-1 receptor antagonist attenuates the severity of spinal cord ischemic injury in rabbits. J Vasc Surg 2008;48(3):694-700.
50. Hirose K, Okajima K, Taoka Y, Uchiba M, Tagami H, Nakano K, et al. Activated protein C reduces the ischemia/reperfusion-induced spinal cord injury in rats by inhibiting neutrophil activation. Ann Surg 2000;232(2):272-80.
51. Nazli Y, Colak N, Alpay MF, Uysal S, Uzunlar AK, Cakir O. Neuroprotective effect of atorvastatin in spinal cord ischemia-reperfusion injury. Clinics (Sao Paulo) 2015;70(1):52-60.
52. Hu JR, Lv GH, Yin BL. Altered microRNA expression in the ischemic-reperfusion spinal cord with atorvastatin therapy. J Pharmacol Sci 2013;121(4):343-6.
53. Ning N, Dang X, Bai C, Zhang C, Wang K. Panax notoginsenoside produces neuroprotective effects in rat model of acute spinal cord ischemia-reperfusion injury. J Ethnopharmacol 2012;139(2):504-12.
54. Gong G, Yuan LB, Hu L, Wu W, Yin L, Hou JL, Liu YH, Zhou LS. Glycyrrhizin attenuates rat ischemic spinal cord injury by suppressing inflammatory cytokines and HMGB1. Acta Pharmacol Sin 2012;33(1):11-8.
55. Huang Y, Xie K, Li J, Xu N, Gong G, Wang G, et al. Beneficial effects of hydrogen gas against spinal cord ischemia-reperfusion injury in rabbits. Brain Res 2011;1378:125-36.

56. Zhang Q, Huang C, Meng B, Tang T, Shi Q, Yang H. Acute effect of Ghrelin on ischemia/reperfusion injury in the rat spinal cord. Int J Mol Sci 2012;13(8):9864-76.
57. Lee CJ, Kim KW, Lee HM, Nahm FS, Lim YJ, Park JH, et al. The effect of thalidomide on spinal cord ischemia/reperfusion injury in a rabbit model. Spinal Cord 2007;45(2):149-57.
58. Hirose K, Okajima K, Uchiba M, Nakano KY, Utoh J, Kitamura N. Antithrombin reduces the ischemia/reperfusion-induced spinal cord injury in rats by attenuating inflammatory responses. Thromb Haemost 2004;91(1):162-70.
59. Kunihara T, Sasaki S, Shiiya N, Ishikura H, Kawarada Y, Matsukawa A, et al. Lazaroid reduces production of IL-8 and IL-1 receptor antagonist in ischemic spinal cord injury. Ann Thorac Surg 2000;69(3):792-8.
60. Laschinger JC, Cunningham JN Jr, Cooper MM, Krieger K, Nathan IM, Spencer FC. Prevention of ischemic spinal cord injury following aortic cross-clamping: use of corticosteroids. Ann Thorac Surg 1984;38(5):500-7.
61. Woloszyn TT, Marini CP, Coons MS, Nathan IM, Basu S, Acinapura AJ, et al. Cerebrospinal fluid drainage and steroids provide better spinal cord protection during aortic cross-clamping than does either treatment alone. Ann Thorac Surg 1990;49(1):78-82; discussion 83.
62. Rokkas CK, Cronin CS, Nitta T, Helfrich LR Jr, Lobner DC, Choi DW, Kouchoukos NT. Profound systemic hypothermia inhibits the release of neurotransmitter amino acids in spinal cord ischemia. J Thorac Cardiovasc Surg 1995;110(1):27-35.
63. Schittek A, Bennink GB, Cooley DA, Langford LA. Spinal cord protection with intravenous nimodipine. A functional and morphologic evaluation. J Thorac Cardiovasc Surg 1992;104(4):1100-5.
64. Fansa I, Altug ME, Melek I, Ucar E, Kontas T, Akcora B, et al. The neuroprotective and anti-inflammatory effects of diltiazem in spinal cord ischaemia-reperfusion injury. J Int Med Res 2009;37(2):520-33.
65. Mauney MC, Blackbourne LH, Langenburg SE, Buchanan SA, Kron IL, Tribble CG. Prevention of spinal cord injury after repair of the thoracic or thoracoabdominal aorta. Ann Thorac Surg 1995;59(1):245-52.
66. Tobinaga S. Spinal cord protection: effect of N-methyl-D-aspartate receptor antagonist MK-801 for spinal cord ischemia in a rabbit model. Kurume Med J 2000;47(1):45-53.
67. Naslund TC, Hollier LH, Money SR, Facundus EC, Skenderis BS 2nd. Protecting the ischemic spinal cord during aortic clamping. The influence of anesthetics and hypothermia. Ann Surg 1992;215(5):409-15; discussion 415-6.
68. Breckwoldt WL, Genco CM, Connolly RJ, Cleveland RJ, Diehl JT. Spinal cord protection during aortic occlusion: efficacy of intrathecal tetracaine. Ann Thorac Surg 1991;51(6):959-63.
69. Zhang N, Fang M, Chen H, Gou F, Ding M. Evaluation of spinal cord injury animal models. Neural Regen Res 2014;9(22):2008-12.
70. Sharif-Alhoseini M, Khormali M, Rezaei M, Safdarian M, Hajighadery A, Khalatbari MM, et al. Animal models of spinal cord injury: a systematic review. Spinal Cord 2017;55(8):714-721.
71. Coston A, Laville M, Baud P, Bussel B, Jalfre M. Aortic occlusion by a balloon catheter: a method to induce hind limb rigidity in rats. Physiol Behav 1983;30(6):967-9.
72. Biersteker PA, Van Harreveld A. The nature of the rigidity caused by spinal cord asphyxiation. J Physiol 1963;166(2):382-94.
73. Watson BD, Prado R, Dietrich WD, Ginsberg MD, Green BA. Photochemically induced spinal cord injury in the rat. Brain Res 1986;367(1-2):296-300.
74. Piao MS, Lee JK, Jang JW, Kim SH, Kim HS. A mouse model of photochemically induced spinal cord injury. J Korean Neurosurg Soc 2009;46(5):479-83.