Intrathecal verapamil

Although effective results of nimodipine and nicardipine's intrathecal administration are well-known, intrathecal verapamil has not been considered earlier.

Akkaya et al., used an experimental subarachnoid hemorrhage induced vasospasm model for the evaluation of vasodilator and neuroprotective effects of intrathecal verapamil.

24 Sprague-Dawley rats were randomly divided into 3 groups. Group 1(sham), group 2(subarachnoid hemorrhage), and group 3(verapamil). Double hemorrhage method was used. Group 2 did not receive any treatment. Verapamil (rhEPO;Eporon, Dem Ilac, Turkey) at a dose of 1,000 µg/kg was given intrathecally to group 3 rats. The animals were sacrified on day 7 of the procedure. Arterial wall thicknesses and lumen diameters in the basilar arterial cross-sectional areas, endothelin-1 serum levels, oxidative stress index, and apoptosis were measured in all groups.

In the verapamil group, the wall thickness, endothelin-1 levels, oxidative stress index, and apoptosis were found significantly lower than in the subarachnoid hemorrhage group, but the lumen diameter was found to be greater. Intrathecal verapamil was found to decrease vasospasm parameters and apoptosis and increase the antioxidant and antiapoptotic pathways.

The findings suggest that intrathecal verapamil can prevent vasospasm, oxidative stress, and apoptosis following experimental subarachnoid hemorrhage [1)].

Unclassified

2: Sawada T, Omuro Y, Kobayashi T, Hishima T, Koizumi F, Kanemasa Y, Shimoyama T, Sasaki E, Maeda Y. Long-term complete remission in a patient with intravascular large B-cell lymphoma with central nervous system involvement. Onco Targets Ther. 2014 Nov 18;7:2133-6. doi: 10.2147/OTT.S72596. eCollection 2014. PubMed PMID: 25429230; PubMed Central PMCID: PMC4242899.

3: Matsunami M, Miki T, Nishiura K, Hayashi Y, Okawa Y, Nishikawa H, Sekiguchi F, Kubo L, Ozaki T, Tsujiuchi T, Kawabata A. Involvement of the endogenous hydrogen sulfide/Ca(v) 3.2 T-type Ca2+ channel pathway in cystitis-related bladder pain in mice. Br J Pharmacol. 2012 Oct;167(4):917-28. doi: 10.1111/j.1476-5381.2012.02060.x. PubMed PMID: 22646666; PubMed Central PMCID: PMC3575789.

4: Takasusuki T, Yaksh TL. Regulation of spinal substance p release by intrathecal calcium channel blockade. Anesthesiology. 2011 Jul;115(1):153-64. doi: 10.1097/ALN.0b013e31821950c2. PubMed PMID: 21577088; PubMed Central PMCID: PMC3360553.

5: Sorkin LS, Doom CM, Maruyama KP, Nanigian DB. Secondary hyperalgesia in the rat first degree burn model is independent of spinal cyclooxygenase and nitric oxide synthase. Eur J Pharmacol. 2008 Jun 10;587(1-3):118-23. doi: 10.1016/j.ejphar.2008.03.033. Epub 2008 Apr 1. PubMed PMID: 18440503; PubMed Central PMCID: PMC2703817.

6: Su X, Leon LA, Laping NJ. Role of spinal Cav2.2 and Cav2.1 ion channels in bladder nociception. J Urol. 2008 Jun;179(6):2464-9. doi: 10.1016/j.juro.2008.01.088. Epub 2008 Apr 23. PubMed PMID: 18433788.

7: Scott JA, Wood M, Flood P. The pronociceptive effect of ondansetron in the setting of P-glycoprotein inhibition. Anesth Analg. 2006 Sep;103(3):742-6. PubMed PMID: 16931690.

8: Cheng JK, Chen CC, Yang JR, Chiou LC. The antiallodynic action target of intrathecal gabapentin: Ca2+ channels, KATP channels or N-methyl-d-aspartic acid receptors? Anesth Analg. 2006 Jan;102(1):182-7. PubMed PMID: 16368827.

9: Horvath G, Brodacz B, Holzer-Petsche U. Blood pressure changes after intrathecal co-administration of calcium channel blockers with morphine or clonidine at the spinal level. Naunyn Schmiedebergs Arch Pharmacol. 2002 Sep;366(3):270-5. Epub 2002 Jun 20. PubMed PMID: 12172710.

10: Horváth G, Brodacz B, Holzer-Petsche U. Role of calcium channels in the spinal transmission of nociceptive information from the mesentery. Pain. 2001 Jul;93(1):35-41. PubMed PMID: 11406336.

11: Hara K, Saito Y, Kirihara Y, Sakura S, Kosaka Y. Antinociceptive effects of intrathecal L-type calcium channel blockers on visceral and somatic stimuli in the rat. Anesth Analg. 1998 Aug;87(2):382-7. PubMed PMID: 9706935.

12: Diaz A, Dickenson AH. Blockade of spinal N- and P-type, but not L-type, calcium channels inhibits the excitability of rat dorsal horn neurones produced by subcutaneous formalin inflammation. Pain. 1997 Jan;69(1-2):93-100. PubMed PMID: 9060018.

13: Zhang Z, Li F, Ren M, Liu J. Effects of dynorphin A (1-17) on motor function and spinal intracellular messenger systems in rat. Chin Med Sci J. 1996 Jun;11(2):63-8. PubMed PMID: 9387410.

14: Omote K, Iwasaki H, Kawamata M, Satoh O, Namiki A. Effects of verapamil on spinal anesthesia with local anesthetics. Anesth Analg. 1995 Mar;80(3):444-8. PubMed PMID: 7864405.

15: Chaplan SR, Pogrel JW, Yaksh TL. Role of voltage-dependent calcium channel subtypes in experimental tactile allodynia. J Pharmacol Exp Ther. 1994 Jun;269(3):1117-23. PubMed PMID: 8014856.

16: Omote K, Sonoda H, Kawamata M, Iwasaki H, Namiki A. Potentiation of antinociceptive effects of morphine by calcium-channel blockers at the level of the spinal cord. Anesthesiology. 1993 Oct;79(4):746-52. PubMed PMID: 8214754.

17: Kamei J, Hitosugi H, Kawashima N, Misawa M, Kasuya Y. Antinociceptive effects of intrathecally administered endothelin-1 in mice. Neurosci Lett. 1993 Apr 16;153(1):69-72. PubMed PMID: 8510826.

18: Coderre TJ, Melzack R. The role of NMDA receptor-operated calcium channels in persistent nociception after formalin-induced tissue injury. J Neurosci. 1992 Sep;12(9):3671-5. PubMed PMID: 1326611.

19: Lux F, Welch SP, Brase DA, Dewey WL. Interaction of morphine with intrathecally administered calcium and calcium antagonists: evidence for supraspinal endogenous opioid mediation of intrathecal calcium-induced antinociception in mice. J Pharmacol Exp Ther. 1988 Aug;246(2):500-7. PubMed PMID: 3136242.

1)

Akkaya E, Evran Ş, Çalış F, Çevik S, Hanımoğlu H, Seyithanoğlu MH, Katar S, Karataş E, Koçyiğit A, Sağlam MY, Hatiboğlu MA, Kaynar MY. Effects of intrathecal verapamil on cerebral vasopasm in experimental rat study. World Neurosurg. 2019 Apr 10. pii: S1878-8750(19)31042-3. doi: 10.1016/j.wneu.2019.04.050. [Epub ahead of print] PubMed PMID: 30980985.