Pentoxifylline

Pentoxifylline (PTX) is a methylxanthine derivative clinically proven to improve perfusion in the peripheral microcirculation and has been shown to have neuroprotective effects in brain trauma and global cerebral ischemia in experimental animal models.

Data demonstrate that PTX administration up to 6h after ischemia can reduce brain edema in a model of transient focal cerebral ischemia. The beneficial effects of PTX may be mediated, at least in part, through a decline in TNFα production and BBB breakdown [1)].

An experimental SAH model was induced in male Wistar rats by autologous blood injection into the prechiasmatic cistern, and PTX was injected intraperitoneally immediately after SAH. The effects of PTX were evaluated 24 h after SAH via assessing the cerebral ultrastructure via transmission electron microscopy (TEM). Brain edema, blood-brain barrier (BBB) permeability, red blood cell deformability, tumor necrosis factor-alpha (TNF-alpha), nitrite-nitrate levels and apoptotic neuron death were also determined 24 h after SAH. The BBB permeability was measured by Evans blue (EB) extravasation, erythrocyte deformability was determined by filtration technique, and TNF-alpha and reactive nitrogen metobolites were analyzed in brain tissue by ELISA and spectral analysis, respectively. Apoptotic neurons were determined in brain sections by cleaved caspase-3 immunohistochemical analysis, and expression intensity was quantified using image J software.

Cerebral ultrastructure in SAH group animals revealed intense perivascular edema and distortion in the astrocyte foot processes. PTX treatment attenuated structural deterioration due to SAH. Brain water content, BBB permeability, TNF-alpha, nitrite-nitrate levels and apoptotic neuronal death were significantly increased 24 h after SAH and were significantly alleviated by PTX treatment. There was no significant change in red cell deformability after SAH.

The results show that PTX reduces brain edema, BBB permeability, TNFα expression, reactive nitrogen metobolites and apoptosis in experimental SAH. Based on our findings we suggest that PTX exerts neuroprotection against SAH-induced EBI, which might be associated with the inhibition of inflammation and apoptotic neuronal cell death [2)].

Kelten et al divided 16 adult Wistar albino rats into 2 equal groups: treatment and control. Both groups underwent L1 vertebral total laminectomy to expose the dura. The intramuscular treatment group received pentoxifylline. Four weeks later, epidural fibrosis was studied in both groups using electron microscopy, light microscopy, histology, biochemistry, and macroscopy.

The evaluation of epidural fibrosis in the 2 groups according to macroscopic ($p<0.01$) assessment and light microscopy revealed that epidural scar tissue formation was lower in the treatment group compared to the control group ($p<0.001$) and the number of fibroblasts was also decreased significantly in the pentoxifylline-treated group ($p<0.05$). More immature fibers were demonstrated in the treatment group by electron microscopy in comparison with the control group. In biochemical analysis, a statistically significant decrease was detected in hydroxyproline, which indicates fibrosis and myeloperoxidase activity, and shows an inflammatory response ($P<0.001$).

Systemic pentoxifylline application prevents postoperative epidural fibrosis and adhesions with various mechanisms. The study is the first to present evidence of experimental epidural fibrosis prevention with pentoxifylline [3)].

Case series

Thirty-six patients, aged from 18 to 45 years, with lumbosacral radiculopathy associated with connective tissue dysplasia were examined. Detailed neurological examination, X-ray visualization and MRI of lumbosacral spine section, electromyographic assessment were performed. A five-point scale of neuro-vertebrological symptoms, the Numerical Rating Scale (NRS) and the Roland-Morris Low Back Pain and Disability Questionnaire were used.

The results contained own data on the pathogenesis, clinical manifestations and treatment of dorsopathies in connective tissue dysplasias. Inclusion of long-acting pentoxifylline (vasonite) in the combined therapy in patients with dorsopathy associated with connective tissue dysplasia had a positive effect on disease course, decreased pain intensity and improved life activities [4].

1)
Vakili A, Mojarrad S, Akhavan MM, Rashidy-Pour A. Pentoxifylline attenuates TNF-α protein levels and brain edema following temporary focal cerebral ischemia in rats. Brain Res. 2011 Mar 4;1377:119-25. doi: 10.1016/j.brainres.2011.01.001. Epub 2011 Jan 8. PubMed PMID: 21219888.
2)
Goksu E, Dogan O, Ulker P, Tanrıover G, Konuk E, Dilmac S, Kirac E, Demır N, Aslan M. Pentoxifylline Alleviates Early Brain Injury in a Rat Model of Subarachnoid Hemorrhage. Acta Neurochir (Wien). 2016 Sep;158(9):1721-30. doi: 10.1007/s00701-016-2866-5. Epub 2016 Jun 16. PubMed PMID: 27311763.
3)
Kelten B, Erdogan H, Antar V, Sanel S, Tuncdemir M, Kutnu M, Karaoglan A, Orki T. Pentoxifylline Inhibits Epidural Fibrosis in Post-Laminectomy Rats. Med Sci Monit. 2016 Mar 14;22:840-847. PubMed PMID: 26974057.
4)
Chukhlovina ML, Chukhlovin AA. [Diagnosis and treatment of dorsopathy in patients with connective tissue dysplasia]. Zh Nevrol Psikhiatr Im S S Korsakova. 2017;117(7):43-46. doi: 10.17116/jnevro20171177143-46. Russian. PubMed PMID: 28805759.