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Neuroprotective action of new pyrimidine derivatives on rat spinal cord injury

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Abstract

Effects of the systemic administration of xymedon and its derivatives-L-ascorbate and para-aminobenzoate 1,2-dihydro-4,6-dimethyl-l-(2-hydroxyethyl) pyrimid-2-one (compounds 29D and 34D, respectively) - have been studied on a contusion model (Th8 level) of spinal cord injury in rats. Experiments showed the impact of treatment on recovery of motor function, spinal cord tissue safety, population and phenotypic characteristics of astrocytes in the zones of gray and white matter. Xymedon produced a stimulating effect on recovery of the locomotor function. In this respect, compounds 29D and 34D were more effective than xymedon, although no significant differences between the action of compounds 29D and 34D was observed. Each of the three investigated pyrimidine derivatives significantly reduced the total area of pathologic cavities in spinal cord. In this respect, compounds 29D and 34D were also more effective than xymedon. Compound 29D exhibited a more pronounced effect in the dorsal root entry zone (DREZ), while compound 34D more significantly supported preservation of tissue in the ventral horns (VHs). Within 60 days after administration of compounds of 29D and 34D, the number of GFAP+ astrocytes in gray matter zones decreased as compared to the group treated with xymedon, and the expression of this marker protein of intermediate filaments decreased. In the white matter, the number of GFAP+ cells increased under the influence of compound 29D and decreased under the action of compound 34D. Differences between the effects of compounds 29D and 34D (on the background of their equal influence on recovery of the locomotor function) may be indicative of different cellular and molecular mechanisms of action, in agreement with data on their action on tissue safety.

Keywords

Neuroregeneration, Pyrimidine, Rats, Spinal cord injury, Xymedon