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Neuroprotection by granulocyte colony-stimulating factor (G-CSF) after focal cerebral ischemia

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While G-CSF is frequently used for the treatment of neutropenia and is considered to be safe and feasible in this subgroup of patients, its potential neuroprotecive effects might implicate beneficial effects after acute brain injury. In this study, we investigated the effects of G-CSF after experimental stroke. First, we investigated the potency of G-CSF on inhibiting excitotoxic injury by microdialysis. Second, we investigated the effects of G-CSF administrated in different time windows after stroke onset. Finally, we compared the effectiveness of erythropoetin and G-CSF during acute cerebral ischemia in terms of infarct reduction. We used the filament model for temporary middle cerebral artery occlusion in rats. In vivo glutamate concentration was analyzed by microdialysis. This method showed that application of G-CSF 30 minutes after MCAO significantly attenuated glutamate release comparing to saline treatment. We administered G-CSF or saline at different time points subsequently after MCAO: G-CSF only at 30 minutes after MCAO, G-CSF 30 minutes after MCAO followed by daily injections, G-CSF administrated daily but starting 24 hours after stroke onset. Evaluation endpoints were 24 hours and 7 days after MCAO. Infarct volume, leukocyte infiltration and apoptosis were evaluated by anti-$MAP_{2,}$ anti-MPO immunohistochemistric and TUNEL staining, respectively. Each animal was tested by a neuroscore and body weight which were measured daily. We found that single application of G-CSF in superacute phase significant reduced infarct size, attenuated leukocytes infiltration and inhibited apoptosis 24 hours after MCAO compared to the control group. Either daily combination of a dosage in supercute phase or daily but

delayed injection of G-CSF significantly reduced infarct size, inhibited apoptosis 7 days after MCAO when comparing to saline treatment group. Body weight regained best in group of continuous daily application of G-CSF. Neuroscores were better in G-CSF treatment groups, but showed no statistic difference comparing to saline treatment group. For comparing difference between G-CSF and EPO, we measured infarct volume, leukocytes infiltration and apoptosis in both groups 24 hours after MCAO, respectively. There was no significant difference between them.

In conclusion, G-CSF intensively attenuated release of glutamate in vivo, inhibited apoptosis and leukocytes infiltration. Even when administrated one day later but repeated injection for several days after MCAO, G-CSF still showed neuroprotective effects. As a neuroprotective agent, G-CSF possessed the same ability as EPO at least in reduce infarct size , attenuation of apoptosis and leukocytes infiltration.