The Therapeutic Potential of Hematopoietic Growth Factors for Treatment of Carbon Monoxide Neurotoxicity

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Hematopoietic growth factors involved granulocyte-colony stimulating factor (G-CSF) and erythropoietin (EPO) are cytokines involved in the regulation of normal hematopoiesis, influence stem cells survival, proliferation, and differentiation commitment [1,2]. These growth factors, significantly, have been considered in the management of many different neurodegenerative disorders with unknown definite treatment such as stroke [3,4], Alzheimer disease [5-7], Parkinson [8,9], Both G-CSF and EPO have a noticeable role in central nervous system. Their special receptors are expressed in many regions of CNS and it is shown that they are upregulated in experimental models of stroke [10,11]. Several mechanisms are considered to describe the neuroprotective effects such as mobilization of hematopoietic stem cells to the injured regions [12,13], differentiation of neuronal stem cells as well as neurogenesis, angiogenesis , anti-inflammatory [12,14,15], anti-excitotoxicity, antioxidant and anti-apoptotic effects [2,10,16].

CO intoxication, a common cause of death especially during winter, induces cerebral hypoxia-ischaemia. It triggers neuropathological events include neutrophil degradation, enhancement and activation of myeloperoxidase, oxidative stress and lipid peroxidation, inflammation, apoptosis, demyelination and necrosis which may result in delayed neurological sequel [17,18]. There is no effective medication for managing neurological deficits following CO poisoning. It seems drugs or compounds which can inhibit any stages of neuropathological cascade, can exert a potential role in prevention and treatment of neurological outcome after CO exposure. G-CSF and EPO are shown to have robust neuroprotective properties. In recent experimental and clinical studies they could effectively promote neurological conditions after stroke. They recovered behavioral and histological impairments successfully [19,20]. In a recent study, CO intoxication proposed as a hypoxia induced neurotoxicity in a rat model. A single dose of G-CSF and EPO could attenuate CO neurotoxicity, alleviated histological changes such as neutrophil infiltration and neural necrosis which was shown by H&E staining. It seems they inhibit neural apoptosis as well, since relative expression of activated caspase 3 decreases following treatments. G-CSF declines apoptotic cells showed by tunnel test. EPO significantly decreased myeloperoxidase (MPO) activity, a key biomarker of inflammation while G-CSF did not influenced MPO activity significantly. Regarding to anti-inflammatory and anti-oxidant effects of these hematopoietic growth factors, they could successfully reduce edema and lipid peroxidation (MDA content) of the brain tissue. Both growth factors enhanced myelin basic protein (MBP) expression and remyelinated brain tissue which was impaired after poisoning. This was revealed after luxol fast blue (LFB) staining of brain tissue slices. After performing FPLC method on poisoned and treated brains it is was obvious that EPO regenerated MBP since the pattern of this protein renormalized. In order to affirm our data, the effect of G-CSF and EPO on serum levels of neurological biomarkers was investigated. Serum concentration of S100-β and GFAP elevated after CO exposure. G-CSF and EPO significantly decreased these two biomarkers as a result of protective effect on astroglial cells [20-23]. According to obtained results it may be possible to deliberate hematopoietic growth factors as potential therapies for sever CO poisoning in clinical trial.

References

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