



Effects of Thiamine and Thiamine Pyrophosphate on Oxidative Stress By Methotrexate in The Rat Brain

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SUMMARY. Methotrexate (MTX) is a folic acid antimetabolite and have serious side effects such as neurotoxicity. There is no solution has been developed for MTX toxicity yet. Thiamine pyrophosphate (TPP) is active metabolite of thiamine. In thiamine deficiency nervous system disorders developed. MTX neurotoxicity may be contributed to the inhibition of TPP through thiamine. In this study, the effects of thiamine and TPP on oxidative injury caused by MTX in the rat brain were investigated comparatively on 28 rats divided into four groups. One group received 20 mg/kg thiamine and the other received 20 mg/kg TPP through the intraperitoneal route. The control group received distilled water as solvent. All the animal groups received an injection of 5 mg/kg MTX. Malonyldialdehyde (MDA), myeloperoxidase (MPO), glutathion (GSH), glutathione peroxidase (GPx) and superoxide dismutase (SOD) levels in the cerebrum tissue were measured. The experiment results of MDA, MPO, GSH, GPx and SOD levels in the brain tissue of the methotrexate group were $13.8 \pm 2.9 \mu\text{mol/g protein}$, $18.1 \pm 3.4 \text{ u/g protein}$, $4.1 \pm 1.1 \text{ nmol/g protein}$, $4.8 \pm 1.4 \text{ u/g protein}$ and $6.8 \pm 1.5 \text{ u/g protein}$, respectively, while the values in the thiamin group were $12.6 \pm 2.5 \mu\text{mol/g protein}$, $17.1 \pm 3.5 \text{ u/g protein}$, $4.5 \pm 1.2 \text{ nmol/g protein}$, $5.6 \pm 2.1 \text{ u/g protein}$ and $8.0 \pm 2.4 \text{ u/g protein}$, respectively. The levels in the TPP group for the same parameters were $5.0 \pm 0.5 \mu\text{mol/g protein}$, $6.4 \pm 0.8 \text{ u/g protein}$, $8.1 \pm 0.5 \text{ nmol/g protein}$, $11.2 \pm 0.7 \text{ u/g protein}$ and $15.6 \pm 1.5 \text{ u/g protein}$, respectively. In the control group, they were determined as $4.4 \pm 0.8 \mu\text{mol/g protein}$, $5.8 \pm 1.1 \text{ u/g protein}$, $9.8 \pm 2 \text{ nmol/g protein}$, $12.8 \pm 1.9 \text{ u/g protein}$ and $18.8 \pm 2.5 \text{ u/g protein}$, respectively. TPP was found to have prevented the increase in MDA and MPO levels, and to have prevented the decrease in GSH, GPx and SOD levels by methotrexate, while thiamine did not. These findings suggested that methotrexate may be a thiamine antimetabolite.

KEY WORDS: Methotrexate, Oxidative stress, Rat, Thiamine pyrophosphate

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