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Evaluation of a Low Dose Administration of Aspirin, Dipyridamol and Steroid. Therapeutic Effects on Motor Function and Protective Effects on Na^+-K^+-Activated ATPase Activity Against Lipid Peroxidation in an Experimental Model of Spinal Cord Injury*

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Lombardi reported effective treatment of acute spinal cord injury with early administration of a low dose of aspirin (ASA) and dipyridamol (DIP) (1982). We studied the effects of a low dose of ASA, DIP and methylpredonosolone on the motor performance, activity of crude synaptosomal Na^+-K^+-activated ATPase (Na^+-K^+-ATPase), prostaglandin metabolites (6-keto-$PGF_{1\alpha}$ and thromboxane B_2) and lipid peroxide barbituric acid reactive substance: TBA-RS) on the spinal cord of rats. Drugs were administered intravenously via the femoral vein 30 minutes before spinal cord compression was induced with the rats under thiobarturate anaesthesia. To observe the motor performance at 2 weeks, ASA, DIP were administered intraperitoneally 30 min before the spinal cord compression and once a day after operation. The spinal cord lesion was made by compression at the T-2–T-3 level with a Sugita aneurysm clip, following laminectomy. The motor performance was assessed quantitatively by the inclined plane method of Rivlin and Tator (1978). Ouabain sensitive NA^+-K^+-ATPase activity and membrane bound Na^+-K^+-ATPase activity were measured by a modified Allen method by Nakamura and Mori (1958). 6-keto-$PGF_{1\alpha}$, direct metabolite of PGI_2 and thromboxane B_2, direct metabolite of thromboxane A_2, were estimated radioimmunologically. These rats were killed 30 min after spinal cord injury and the biochemical analyses carried out.

Motor performance in the groups treated with ASA (5 mg/kg) + DIP (5 mg/kg) and ASA (50 mg/kg) were significantly improved from the second day after operation in the former group and from the 7th day in the latter group. The activity of Na^+-K^+-ATPase was reduced to about a half (50·3 per cent) of the normal animals. ASA + DIP (each 5 mg/kg) activated this enzyme to supernormal levels (113·6 per cent) in the intact rats and ASA treatment 30 min before

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the injury significantly and dose-dependently prevented the deterioration of this enzyme activity by trauma (ASA 5 mg : 58·8 per cent, 15 mg : 73·0 per cent, 50 mg : 104·0 per cent). Pre-treatment with methylpredonisolone (10 mg/kg : 91·4 per cent and 20 mg/kg : 62·3 per cent) also prevented deterioration of this enzyme by trauma, but was less effective in the group treated with 20 mg/kg than in those given to 10 mg/kg group. The addition of 5 mg/kg of ASA to 10 mg/kg or 20 mg/kg methylpredonosolone did not significantly enhance the preventive effect on the reduction of the enzyme activity.

Prostaglandin metabolites were altered by treatment with ASA, ASA + DIP and steroid. The total content of these metabolites (6-keto-PGF_1 + thromboxane B_2) was dose-dependently decreased in the group treated with ASA or/and steroid, but 10 mg/kg steroid administration increased these metabolites to a greater extent than was seen with no treatment; and the additions of 5 mg/kg ASA to the steroid increased dose-dependently the total content. Ratios of these metabolites (thromboxane B_2/6-keto-PGF_1) were increased dose-dependently in the rats treated with steroid but not dose-dependently in the animals treated with ASA. Changes of TBA-RS content in the animals treated with SAS, DIP and steroid were significantly reduced but there was no significant difference.

We conclude that ASA (5 to 50 mg/kg) was effective for recovery of the motor performance following induced spinal cord injury with deterioration Na^+-K^+-ATPase of the synaptosomes. Activity of this enzyme reciprocally paralleled the contents of PG metabolites in rats treated with ASA. It is suggested that ASA prevents peroxidation of lipid, a moiety of NA^+-K^+-ATPase, and SH group in the enzyme. However the results of steroid administration indicate that steroid may not participate in preventing Na-K-ATPase deterioration through protection against lipid peroxidation. Changes in the ratios of PG metabolites with this treatment indicate that PGI_2 and thromboxane A_2 may not participate in pathogenesis and progression of spinal cord injury. The possibility that these PGs may play a role in platelet aggregation in the microvessels after spinal injury was not excluded.

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