

Short Communication

Does the Exposure to 2,5-Hexanedione Hasten the Onset of Peripheral Neuropathy in Streptozotocin-Induced Diabetic Rats?

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Diabetic neuropathy and n-hexane neuropathy represent metabolic and toxic neuropathy, respectively. In today's industrial workplace, it is expected that industrial workers with diabetes mellitus could also often be exposed to n-hexane, but there have been no reports about any possible potentiating effects of exposure to n-hexane on diabetic neuropathy. The purpose of this study was to evaluate the influence of exposure to 2,5-hexanedione (2,5-HD) (which is commonly believed to be the causative agent in the development of n-hexane neuropathy) on nerve conduction velocity in experimental diabetic rats¹.

Materials and Methods

Animals and treatment

A total of 24 eight-week-old male Wistar rats (Seiwa Experimental Animal Institute, Japan), weighting 284.2 ± 12.2 g (mean \pm SD), were randomly allocated to diabetic and normal (non-diabetic) groups (12 in each group). The rats allocated to the diabetic group were injected intraperitoneally with streptozotocin at a dose of 60 mg/kg to induce diabetes. Two weeks after the injection, 11 rats whose nonfasting serum glucose concentrations were higher than 250 mg/dl were assigned to the diabetic group. Five diabetic rats were subcutaneously injected in the back with 2,5-HD (100 mg/kg/day) dissolved in 0.2 ml of 0.9% NaCl solution, five days a week, for 6 weeks (group DM + HD). The remaining 6 diabetic rats were injected with 0.2 ml of 0.9% NaCl solution alone and allocated as diabetic controls (group DM). The 12 normal non-diabetic rats were also subdivided into two groups, one group of 6 rats were treated with 2,5-HD (100 mg/kg/day) in the same manner as the DM + HD group rats (group HD), and the remaining 6 rats were injected with 0.2 ml of 0.9% NaCl solution alone and allocated to the control group.

The rats were fed CE-2 rat chow (Clea Company Japan) and water *ad libitum*.

Electrophysiological examinations

The measurements of motor nerve conduction velocity (MCV) were carried out every two weeks during the

experiment under general anesthesia by intraperitoneal injection of sodium amobarbital. The electrophysiological technique used has been described in detail in previous reports^{2,3}. The tail of the rat was kept in a 37°C liquid paraffin bath controlled by a thermostat to keep the subcutaneous temperature of the rat tail constant.

The experiments were performed in accordance with the Guidelines for Animal Experimentation of Oita Medical University.

Chemicals

Chemicals used in this study were purchased from Wako Pure Chemical Industries Ltd., Japan.

Statistics

Data were analysed by one-way analysis of variance (ANOVA), followed by Duncan's multiple range test with SPSS software (SPSS Inc. 1990), and $P < 0.05$ was considered significant. In addition, when the distribution of data was not Gaussian, the Mann-Whitney U test was used.

Results

As shown in Table 1, the diabetic groups showed signs of severe hyperglycemia and significant decrease in body weight as compared with the non-diabetic groups ($P < 0.05$).

The MCV values for the treated groups and controls are summarized in Table 2. A significant decrease in MCV in the DM + HD group was seen 4 weeks after 2,5-HD treatment as compared with that of the DM group, and after 6 weeks of 2,5-HD treatment, the MCV in the DM + HD group decreased significantly not only as compared with that of the DM group, but also with those of the control group and the HD group ($P < 0.05$). No other significant difference was found in this experiment between the DM, HD and control groups.

Discussion

Diabetic neuropathy and n-hexane neuropathy are representative of metabolic and toxic neuropathy, respectively, and therefore the pathogenesis of these neuropathies have been carefully examined⁴⁻⁶. But to our knowledge, there have been no reports that paid attention to the interaction between the aetiologic factors in diabetic neuropathy and n-hexane neuropathy.

Streptozotocin destroys the β cells in the islets of Langerhans of rats and induces diabetes mellitus. It has been reported that in streptozotocin-induced diabetic rats, a slowing of MCV developed about a few weeks after the onset of diabetes⁷⁻⁹. On the other hand, several studies have demonstrated early and progressive reduction in the conduction velocities of tail nerves in rats receiving n-hexane or its metabolites¹⁰⁻¹².

In this study, we demonstrated the possibility that 2,5-HD (which was commonly believed to be the metabolite responsible for n-hexane neuropathy) could hasten the onset of peripheral neuropathy in streptozotocin-induced diabetic rats. As shown in Table 2, after 4 weeks of 2,5-HD treatment, the MCV in the DM + HD group began to decrease, and after

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