

THE EFFECTS OF A CYCLOHEXENON DERIVATIVE (MM-101) ON THE VESICAL FUNCTION OF RATS WITH EXPERIMENTAL CHRONIC DIABETES

Hypothesis / aims of study

Cyclohexenon derivative (MM-101) is known to act on the central nervous system and to induce extension of the dendrites. Their action mechanism is now gradually being elucidated through various investigations. Their effects on the peripheral nerves are also under experimental explorations.

The bladders of rats with experimental diabetes become functionally hypoactive around four weeks after the disease onset. In our previous paper we reported that the impaired vesical function due to diabetes tended to improve with the administration of cyclohexenon derivative (MM-101). In the present experiment, we maintained rats in the diabetic condition for a longer period of time and evaluated their vesical function and observed the functional changes in their bladders brought about by the administration of MM-101.

Study design, materials and methods

Seven-week-old female Wistar rats were raised in two groups: one that consisted of diabetic animals (Non-MM group) and the other that received MM-101 (MM group). The Non-MM group was intraperitoneally given, after 24 hours' fasting, 60mg/kg of streptozotocin (STZ) dissolved in 0.05M citrate buffer in one dose. The MM group was treated with STZ in the same manner as in the Non-MM group and, after the determination of serum glucose levels 24 hours later, only the rats showing glucose levels at 250mg/dl or higher were chosen and intraperitoneally injected with 8mg/kg of MM-101 every day for two weeks, beginning at six and ten weeks after the STZ injection.

For the purpose of cystometry, the animals were anesthetized with 30mg/kg of pentobarbital, and a polyethylene indwelling catheter (PE-50) was introduced from the animal's back into its bladder. The end of the catheter was subcutaneously embedded under the dorsal skin. Seventy-two hours later, with the animal anesthetized with diethyl ether, the end of the ether was pulled out to conduct cystometry. The animals were kept in cages of our own contrivance, each one of which is provided with a scale (GX-200, A & D CO., LTD.) beneath it to determine the single urine output simultaneously. For both Non-MM and MM groups, the measurements were repeated at 8th and 12th weeks after the STZ administration. The values examined on the occasion included: body weight; serum glucose level; single urine output; basic vesical pressure; liminal urination pressure; maximum contraction pressure at urination; residual urine amount; vesical capacity. The results were statistically evaluated by means of Mann-Whitney's U test. The level of significance was set at $p < 0.05$.

Results

It was found that, both at 8th and 12th weeks after the STZ administration, the MM group showed, as compared with the Non-MM group, a decrease in the single urine output, residual urine amount, and vesical capacity, and an increase in the basic vesical pressure, liminal urination pressure, and maximum contraction pressure at urination.

Interpretation of results

It was thus indicated that the administration of cyclohexenon derivative (MM-101) relieved the disturbance of vesical function resulting from chronic diabetes.

Concluding message

While the vesical function in rats long suffering from diabetes becomes hypoactive, it was suggested that cyclohexenon derivative (MM-101) had therapeutic effects on the impaired vesical function of diabetic origin, as attested by the decreased residual urine amount and the increased maximum contraction pressure at urination following its injection. We intend to continue our investigation so as to elucidate its action mechanism.

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ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by guidelines for animal experiments of the Nihon University School of Medicine