RESPONSE OF A DIABETIC STRAIN OF MOUSE TO ORAL TOLBUTAMIDE

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Search is constantly going on to find an animal with diabetes mellitus like features so that a model akin to human diabetes is available for screening of potential hypoglycemic agents of both plant and synthetic origin. The KK strain of mice was discovered by Nakamura (1). Nakamura (1) has shown by carrying out glucose tolerance tests on 28 KK strain of mice that the majority show a blood sugar curve similar to human diabetics. The insulin content of the pancreas was in excess of that found in normal mice. The response of the blood sugar level in this strain of mice to oral tolbutamide has not yet been investigated and in this study this response has been studied in ten mice of the KK strain. In further ten animals the effect of alloxan on the blood sugar level has been seen.

Oral tolbutamide at a dose of 20 mg/kg orally was administered to ten mice of the KK strain after a level of fasting blood sugar was obtained. Three hours later another sample of blood was collected from

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the tail vein of the mice and the blood sugar estimated. Blood glucose determination was made by the Hagedorn-Jensen method. In another group of ten KK strain of mice, alloxan (40 mg/kg) was administered intraperitoneally and the blood sugar estimated a week later.

The results showed that while the fasting blood sugar varied from 30.5 mg to 50.94 mg there was a hypoglycemic response to 20 tng/kg of oral tolbutamide in every animal. The percentage fall in the blood sugar level was 30.4, 61.4, 36.4, 38.4, 40.3, 18.9, 13.5, 51.8, 36.3 and 12.7 in ten mice. In the ten mice to which alloxan (40 mg/kg i.p.) had been administered a week prior to the test there was a rise in the blood sugar level in every animal. The percentage rise in the blood sugar was 312.8, 17.1, 127.4, 355.3, 218.9, 235.4, 194.2, 218.9, 52.1 and 117.7 in ten KK strain of mice after alloxan.

These results obtained with the KK strain of mice indicate that tolbutamide does cause a fall in the blood sugar level in these mice. These mice could, therefore, be satisfactorily used for the screening of substances which have a mechanism of action similar to tolbutamide. The rise in the blood sugar level after administration of alloxan indicates that these animals respond in a similar way as normal mice to alloxan in spite of the fact that the pancreas contains more insulin than present normally in mice pancreas (1).

REFERENCE


PERIPHERAL COMPONENT IN RESERPINE INDUCED MIOSIS

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Reserpine, on systemic administration (1) as well as after intracerebroventricular injection (2), exerts parasympathomimetic effects such as miosis, salivation, and diarrhoea. These effects have been attributed to increased central parasympathetic activity since reserpine increases the acetylcholine contents of the hypothalamus (3). A direct parasympathomimetic action of reserpine has been excluded by Beckman (4). However these observations do not exclude the possiblility of a peripheral component of action in the reserpine induced miosis. Therefore, it was planned to study the effect of topical application of reserpine on the pupillary size in rabbits. Four adult albino rabbits of either sex weighing from 1.0 to 1.4 kg were employed in the present study. The drug was applied topically as 0.1% ointment in one eye while in the other eye (control eye) only vaseline was applied. The ointment was applied daily for seven days and the pupillary size was measured each day before the application of the drug. Pupillary size was measured according to the method of Chen and Way (5) suitably modified by providing gradually increasing sized apertures instead of the black dots. The pupil was continuously observed for one minute through the appropriate aperture of the pupillometer kept at a constant distance from the rabbit eye and the diameter noted.

| Table 1. Effect of topical application of reserpine on pupillary diameter. |
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| Number of rabbits | Average diameter of rabbit pupil ± S.E. in mm |
| | Control eye | Treated eye |
| 4 | 7.38 ± 0.21 | 5.90 ± 0.12 |

S.E. : Standard error