THE EFFECT OF REPEATED INSTILLATION OF INSULIN INTO THE CONJUNCTIVAL SAC ON THE COURSE OF ALLOXAN DIABETES

I. M. Sokoloverova, A. A. Bochkareva, E. P. Volodina, G. A. Voinov, S. Oleks, and E. Tsinberg

Department of Pathological Physiology (Head, Docent I. M. Sokoloverova) and Department of Diseases of the Eye (Head, Docent A. A. Bochkareva), Orenburg Medical Institute (Director, Docent S. S. Mikhailov)
(Presented by Active Member AMN SSSR V. V. Parin)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 53, No. 4, pp. 64-66, April, 1962
Original article submitted December 31, 1960

In a previous communication [1] it was shown that a single instillation of insulin into the conjunctival sac of rabbits with alloxan diabetes leads to a fall in the blood sugar by 40-79% in the majority of animals. The maximal fall is observed between 2 and 3 hours after the beginning of insulin administration. These results served as the basis for investigation of the effect of the repeated instillation of insulin (3 times a day) on the course of alloxan diabetes.

EXPERIMENTAL METHOD

Experiments were conducted on 51 rabbits, in which diabetes was produced by intravenous injection of alloxan in a dose of 150 mg/kg body weight. The insulin solution was prepared as required from crystalline insulin in strengths of from 60 to 500 units/ml. The blood sugar was estimated before administration of insulin and 30 minutes, 1 hour, 1 hour 30 minutes, and 2, 3, 4, and 5 hours after administration.

Rabbits with a well established, chronic form of diabetes were used in the experiments. Insulin was instilled one drop at a time into the conjunctival sac 3 times a day at intervals of 4-5 hours. After 7, 10, and 15 days of insulin administration, intervals of 7-14 days were allowed. After administration of insulin, in 32 rabbits we studied the clinical features and reaction of the eye, and also the intraocular tension; in 25 rabbits we studied the phathohistological changes in the conjunctiva and cornea.

EXPERIMENTAL RESULTS

The results of the first series of experiments showed that for most animals with alloxan diabetes the optimal dose of insulin, causing a significant fall in the blood sugar level, was a concentration of 240 units/ml (pH 3.6). Insulin was given in this concentration in all subsequent experiments.

As an illustration of the action of this concentration of insulin when administered once only, we give below the results of experiments on rabbits Nos. 19 and 41. In rabbit No. 19 the blood sugar after injection of alloxan was 496 mg %. After instillation of insulin the blood sugar fell in 4 hours to 58 mg % (by 88%). In rabbit No. 41, on the 24th day of diabetes the blood sugar rose to 324 mg %. After instillation of insulin it fell in 30 minutes to 190 mg %, in 1 hour to 130 mg %, in 2 hours to 104 mg %, and in 3 hours to 75 mg % (by 77%).

As a result of the repeated instillation of insulin into the conjunctival sac for cycles of 7, 10, and 15 days, the course of the alloxan diabetes was modified.

We give below the results of an experiment on rabbit No. 23. The investigations lasted 84 days. On the 17th day after injection of alloxan, the blood sugar was 506 mg %. Instillation of insulin was started at this time, and given 3 times a day for 2 weeks. The blood sugar fell to 304 mg %, and the diuresis fell from 280 to 80 ml. The sugar concentration in the urine fell from 5.6 to 2%; the rabbit gained 400 g in weight.

After the first course of instillation of insulin, lasting 3 weeks, the blood sugar rose to 510 mg % and the diuresis to 150 ml, while the sugar concentration in the urine rose to 4.9%. The rabbit then received a second

course of instillation of insulin lasting 2 weeks, in the course of which the blood sugar fell gradually to 236, 120, and 78 mg %. The diuresis fell to 20 ml and sugar was absent from the urine.

In some animals the blood sugar remained for some time at the normal level after the insulin administration had ceased. In rabbit No. 20, for instance, after completion of the second course of insulin the tests for sugar in the urine were negative for 11 days and the blood sugar fell to 62 mg %.

Clinical and pathomorphological investigations of the conjunctiva, the cornea, and the deep media of the eye of rabbits with alloxan diabetes showed that no changes took place in these tissues during prolonged instillation of insulin into the conjunctival sac. On the other hand a diminution of the dystrophic processes usually associated with alloxan diabetes was observed. The daily administration of insulin (50 units/ml) to healthy rabbits for 3 months also gave rise to no side effects.

The intraocular tension fell by 2-4 mm Hg during the administration of insulin by this method, which was observed 2 hours after instillation.

In view of these findings there is a case for the clinical trial of this method of administration of insulin to patients with diabetes mellitus.

SUMMARY

In experiments on 51 rabbits the instillation of insulin (240 units/ml) into the conjunctival sac of animals with alloxan diabetes leads to a considerable drop of the sugar level of the blood and urine, and a reduction of diuresis. In individual cases there is a normalization of the blood sugar indices with an absence of sugar in the urine for several days after the interruption of instillation. A marked action of insulin is observed from 30 minutes to 1 hour after the administration. Clinical and pathologico-histological investigations of the conjunctiva, cornea and deep media of the eyes showed no changes connected with this method of insulin administration.

LITERATURE CITED

1. S. Oleks and E. Tsinberg, Probl. Endokrin. i Gormonoter. (1960), No. 3, p. 77.

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
