Changes in Glycosylated Hemoglobin in Short- and Semi Long-Term Streptozotocin-Diabetic Mice and Rats

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It is well known that glycosylated hemoglobin (HbA₁) increases in the blood of diabetic patients. However, only few studies have been reported on the changes in the values of HbA₁ in mice and rats. The degree of increase in HbA₁ levels was not correlated with the severity of hyperglycemia, duration of diabetes, age of the mouse, or body weight in C57BL/KsJ mice (1). In our previous paper, we reported that the HbA₁ value increased in parallel with serum glucose level

after streptozotocin (STZ), and the treatment with nicotinamide before STZ-injection abolished the increase of HbA₁ in both STZ-treated intact and thyroidectomized rats (2). The present study deals with the short- and semi long-term effects of experimental diabetes on the HbA₁ and species differences between mice and rats with regard to these effects. Male ddY mice and Wistar-Imamichi rats were housed in an air-conditioned room (temperature $22 \pm 2^\circ\text{C}$, humidity $55 \pm 5\%$) with

Fig. 1. Changes in body weight with increasing age and duration of experimental diabetes in mice (A) and rats (B). Numbers of animals are shown in parentheses. Values shown are the mean $\pm$ S.E. Controls: citrate buffer treated group, STZ: streptozotocin (170 mg/kg, i.p. in mice, 60 mg/kg, i.v. in rats), $\uparrow$: Collection of blood samples. P values were calculated by Student's *t*-test. ** $P < 0.01$: each citrate buffer group vs. STZ treated group.

a controlled light-dark cycle (light on 06:00–20:00) for one week before treatment. Food and water were available ad libitum. STZ (Sigma Chemical Co., U.S.A.), freshly dissolved in 0.1 M citrate buffer (pH 4.6), was injected intraperitoneally in mice (170 mg/kg, body wt.) and was injected into a saphenous vein of the hind-limb in rats (60 mg/kg, body wt.). Control animals received a similar volume of citrate buffer. Body weights were determined once a week in this experimental period. Criteria for diabetes were the decrease in growth rate, glucosuria (determined by DIASTIX, Miles-Sankyo Co., Tokyo, Japan), and hyperglycemia. Blood samples were obtained from the neck of the animals immediately following the decapitation. The analyses of HbA₁ and blood glucose were made 2, 4, 6, 8, and 9 weeks following the injection of STZ. HbA₁ was determined by the Quik-Sep method (Seikagaku Kogyo Co., Tokyo, Japan) at 22–24°C. Blood glucose was measured by the conventional method using the o-toluidine-boric acid reagent. The results were compared with those obtained in a control group. Data were

analyzed by Student's *t*-test; $P < 0.05$ was considered to be significant.

As shown in Fig. 1, the increase in body weight was much reduced after STZ injection in mice (A) and rats (B) throughout the experimental period. The mean plasma glucose concentrations were 500 and 650 mg/dl in diabetic rats and mice, respectively, which were quite high compared to the levels in control animals (Fig. 2A, B). HbA₁ values were also significantly increased in diabetic mice and rats throughout the experimental period; control animals averaged 1.6–3.0% of total Hb, while mean values in diabetic animals were in the range of 3.2–4.3% until 8 weeks following the injection of STZ. However, the HbA₁ value in mice ($8.234 \pm 0.43\%$) was significantly higher than that found in rats ($3.597 \pm 0.089\%$) after 9 weeks of STZ, and it was more than two-fold higher than that found in 8 weeks of STZ-diabetic mice.

It has recently been reported that HbA₁ values of alloxan or STZ-diabetic rats are about 4% at 8 and 12 months following the induction of diabetes (3). This value is very

Fig. 2. Changes in glycosylated hemoglobin A₁ (HbA₁) and blood glucose (mean $\pm$ S.E.) in intact, buffer and streptozotocin treated diabetic mice (A) and rats (B). Numbers of animals in each group are indicated at the base of each column. I: intact group, B: citrate buffer treated group, S: streptozotocin treated group. AGE 6W: non-treated group, 8W: the group with two weeks after streptozotocin, 10W: the group with four weeks after streptozotocin, 12W: the group with six weeks after streptozotocin, 14W: the group with eight weeks after streptozotocin, 15W: the group with nine weeks after streptozotocin. P values were calculated by Student's *t*-test. ** $P < 0.01$: buffer group vs. streptozotocin group in mice and rats.

close to our data obtained from STZ-treated rats at 8 or 9 weeks of diabetes. Therefore, the unexpectedly high value of HbA_{1c} observed in STZ-diabetic mice at 9 weeks is noteworthy. However, it is not clear from our experimental conditions whether such a phenomenon is continuous or transient. The present results together with our previous paper (2) provides fundamental data for changes in HbA_{1c} which have not been so intensively studied in the laboratory animals. On the other hand, they suggest that further long-term experiments are required for judging the species difference between mice and rats in the diabetic state.

References

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