Effect of Bakumondo-inshi on various disaccharides and glucose tolerance in KK-Ay mice

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Abstract

The effect of Bakumondo-inshi (BI ; 麦門冬飲子) on various disaccharides and glucose tolerance were studied in KK-Ay mice. BI (1400 mg/kg body weight) improved hyperglycemia after oral administration of maltose, sucrose and glucose. However, BI (1400 mg/kg) did not suppress the blood glucose as measured by oral glucose tolerance in normal mice. Also, no significant effect on lactose tolerance in KK-Ay mice was shown. These findings indicate that BI effect on the blood glucose is selective for sucrose, maltose and glucose. Therefore, BI may be useful for diabetes mellitus.

Key words Bakumondo-inshi, glucose, maltose, sucrose, lactose, KK-Ay mice.

Introduction

Increased sugar absorption is known to be one of the major pathogenic factors of non-insulin-dependent diabetes mellitus (NIDDM), together with the insulin resistance in peripheral tissues and the impairment of glucose-induced insulin secretion from pancreatic beta cells. Although the therapeutic agents to inhibit alpha-glucosidase (for example, acarbose or voglibose) have been used for NIDDM patients, drugs to decrease glucose absorption are not yet directly available clinically.

Bakumondo-inshi (BI ; 麦門冬飲子) was used for diabetes mellitus.[1] However no evidence about it is shown. In the present study, we examined the effect of Bakumondo-inshi (BI) on various disaccharides and glucose tolerance using KK-Ay mice, one of the animal models of non-insulin dependent diabetes mellitus (NIDDM).

Materials and Methods

Materials : BI (TJ-193) was obtained from Tsumura Co. Ltd., Tokyo, Japan (Lot No. 243193010). The constituents of BI were stated to consist of 10 raw ingredients, Ophiopogonis Tuber (ratio 7.0), Ginseng Radix (ratio 2.0), Trichosanthis Radix (ratio 2.0), Anemarrhenae Rhizoma (3.0), Puerariae Radix (ratio 3.0), Rehmanniae Radix (ratio 4.0), Poria (ratio 6.0), Schizandrae Fructus (ratio 1.0), Glycyrrhizae Radix (ratio 1.0), Lophatheri Herba (ratio 1.0). BI contains spray-dried water extracts of 10 crude drugs as a mixture. The yield was 29.27 %. This agent was dissolved in distilled water for oral administration. Tolbutamide was obtained from Sigma Co. Ltd., Tokyo, Japan and acarbose was obtained from Bayer Co. Ltd., Osaka, Japan.

Animals : Adult male ddY mice weighing 22-25 g were used. Male KK-Ay mice (Clea, Tokyo, Japan), 12 weeks old, were also used. Under non-fasting, those with blood glucose levels above 300 mg/dl were considered to be diabetic and used in this study. These mice were housed in an air-conditioned room at 22±2°C with a 12 hour light and 12 hour dark cycle. The animals were kept in the experimental animal room for 7 days with free access to food and water. For the determination of blood glucose levels, blood samples

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(20 μg) were withdrawn from the cavernous sinus with a capillary. Four to ten animals were used for each group.

Oral glucose or dissacharides tolerance test : After overnight (18 hours) fasting, the mice were given BI orally. After 30 min, sugar (maltose, sucrose, glucose or lactose, 2 g/kg body weight,) solution was administered orally. Blood samples were collected before the administration of sugar (0 min), and 30, 60 and 120 min later.

Determination of blood glucose : Blood glucose levels in mice were determined by glucose oxidase method.[2] All the data were expressed as mean±S.E. and Student's t test was used for the statistical analysis. The values were considered to be significantly different when the p value was less than 0.05.

Results

Effect of BI on glucose tolerance test

The glucose tolerance of KK-Ay mice after oral glucose loading is shown in Fig. 1. BI-treated mice (1400 mg/kg) show a decrease in blood glucose when compared with controls. Tolbutamide (a known antidiabetic agent) (50 mg/kg)-treated mice showed lower blood glucose level. However, BI-treated normal mice did not show a decrease in blood glucose (Control (mg/dl) : 123±9 at 0 min, 321±24 at 30 min, 212±30 at 60 min, 138±10 at 120 min ; BI (mg/dl) : 161±12 at 0 min, 340±30 at 30 min, 267±34 at 60 min, 158±15 at 120 min).

Effect of BI on disaccharide tolerance test

The mean blood glucose levels of KK-Ay mice at various time intervals after oral administration of BI

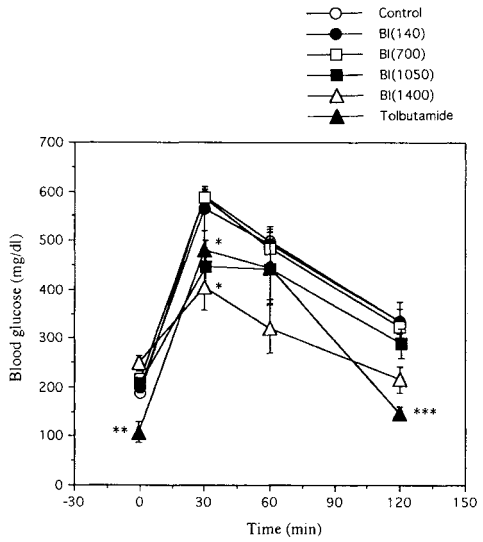

Fig. 1 Oral glucose tolerance test of BI in KK-Ay mice. Each value represents the mean±S.E. from 6-8 mice. Significantly different from control group, $*p<0.05$, $**p<0.01$, $***p<0.001$.

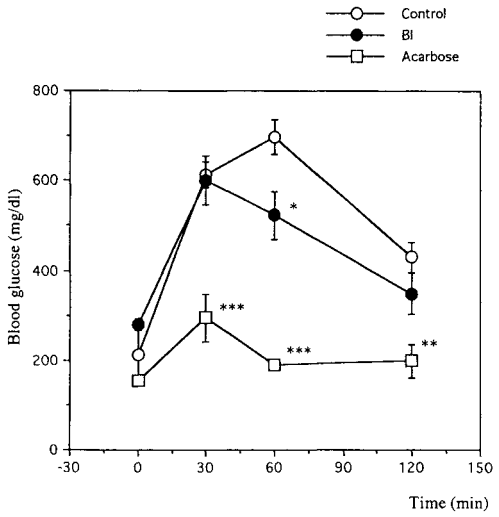

Fig. 2 Oral maltose tolerance test of BI in KK-Ay mice. Each value represents the mean±S.E. from 4-5 mice. Significantly different from control group, $*p<0.05$, $**p<0.01$, $***p<0.001$.

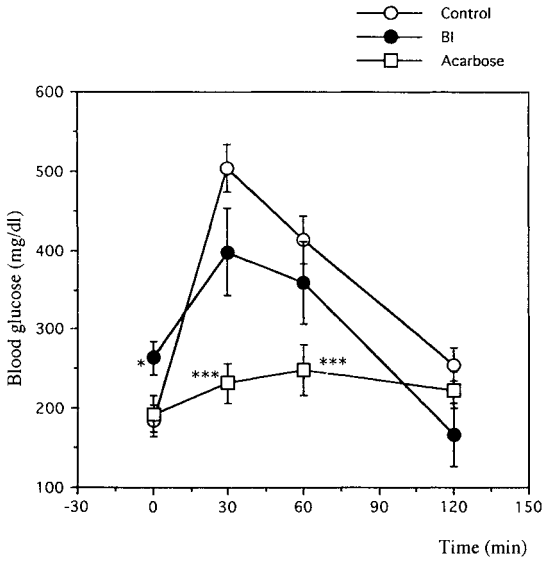

Fig. 3 Oral sucrose tolerance test of BI in KK-Ay mice. Each value represents the mean±S.E. from 6-10 mice, $*p<0.05$, $***p<0.001$.

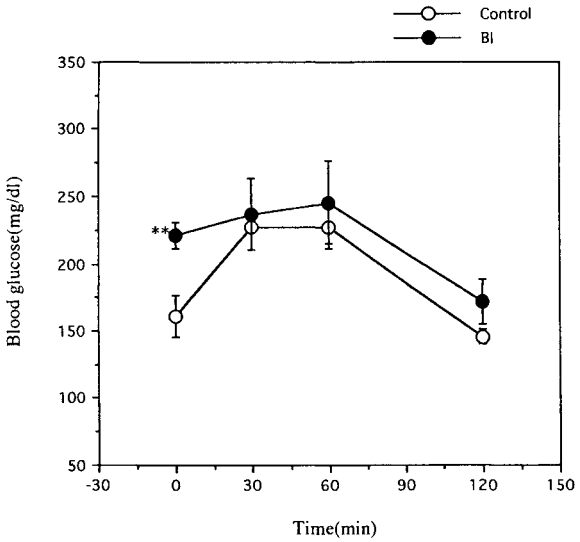

Fig. 4 Oral lactose tolerance test of BI in KK-Ay mice. Each value represents the mean±S.E. from 5-7 mice. $^{**}p<0.01$.

and maltose are shown in Fig. 2. These levels were compared with the values in control mice (maltose alone). BI (1400 mg/kg body weight) lowered blood glucose significantly 30 min after the administration of maltose. Acarbose (alpha-glucosidase inhibitor) (50 mg/kg)-treated mice showed lower blood glucose level 30 min after the administration of maltose.

The mean blood glucose levels of KK-Ay mice at various time intervals after oral administration of BI and sucrose are shown in Fig. 3. These levels were compared with the value in control mice (sucrose alone). BI administration (1400 mg/kg body weight) showed a tendencious decrease in blood glucose 30 and 60 min after the administration of sucrose. Acarbose-treated mice showed lower blood glucose during the period 30 to 60 min after the administration.

The mean blood glucose levels of KK-Ay mice at various time intervals after oral administration of BI and lactose are shown in Fig. 4. No differences in blood glucose were observed, when compared with the values in control mice.

Discussion

The present study clearly showed that BI consistently produced an improvement of tolerance in KK-Ay mice. Before glucose or disaccharides treatment (0 min), hyperglycemia is observed, because of contained sugar (data not shown). After treatment of disaccharide- and glucose-induced hyperglycemic mice, the resulting decrease in blood glucose levels was observed. The efficacy was : glucose>maltose>sucrose. No significant change in blood glucose was observed in the case of lactose induced hyperglycemia. The oligosaccharidases consist of 2 classes : the beta-glucosidases such as lactase (hydrolyses lactose to glucose and galactose) and the alpha-glucosidase such as maltase and sucrase.[3] Moreover, the KK-Ay mice treated with BI were significantly supressed the increased blood glucose levels after glucose-loading. From these findings, it seems likely that BI may inhibit sucrase and maltase in alpha-glucosidases and glucose absorption. In addition, BI-treated normal mice did not show a change in blood glucose level. These findings show that BI may be useful for NIDDM. However, the detail of the mechanism is not clear. Further study would indicate how BI could become a useful drug in the treatment of diabetes.

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和文抄録

麦門冬飲子（BI）の二糖類およびグルコース負荷に対する効果を遺伝的インスリン非依存型糖尿病モデル動物の一つであるKK-Ayマウスで検討した。BI（1400 mg/kg）はマルトース，スクロースおよびグルコースの経口投与後の高血糖を改善した。しかし，正常マウスのグルコース負荷による高血糖を抑制しなかった。また，KK-Ayマウスのラクトース負荷には影響を与えなかった。これらはBIの効果がスクロース，マルトース，グルコースに選択的であることを示している。

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