Postprandial anti-hyperglycemic effect of vitamin B6 (pyridoxine) administration in healthy individuals

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Abstract Postprandial blood glucose lowering effect of vitamin B₆ (pyridoxine) was evaluated in healthy individuals with normal blood glucose levels. Blood glucose levels were measured every 30 min for 2 h after oral sugar administration with or without 50 mg of pyridoxine. Pyridoxine significantly lowered the postprandial blood glucose levels at 30 min (from 165.95 ± 17.19 to 138.36 ± 20.43, $p < 0.01$) and 60 min (from 131.40 ± 17.20 to 118.50 ± 15.95) after administration. In addition, the area under the concentration–time curve (AUC_t) was reduced by about 8.3% (from 257.08 ± 22.38 to 235.71 ± 12.33, $p < 0.05$) and the maximum concentration of blood glucose (C_{max}) was reduced by about 13.8% (from 165.95 ± 17.19 to 143.07 ± 11.34, $p < 0.01$) when compared with those of the control group. Our findings suggest that pyridoxine supplementation may be beneficial for controlling postprandial hyperglycemia.

Keywords Pyridoxine · Pyridoxine hydrochloride · Vitamin B₆ · Anti-hyperglycemic effects · Healthy individuals · Postprandial hyperglycemia

Introduction

Type 2 diabetes mellitus is a metabolic disorder linked to chronic high blood glucose due to lack of insulin, inadequate insulin secretion, and insulin resistance. Chronic hyperglycemia caused by diabetes is associated with long-term side-effects on various organs (American Diabetes Association, 2012). Center for Disease Control and Prevention (CDC, Atlanta, GA, USA, 2015) has been reported that more than 29 million people are assessed to have diagnosed or undiagnosed diabetes and as many as one in three US adults could have diabetes by 2050 (Boyle et al., 2010; Centers for Disease Control and Prevention, 2015).

Regulation of postprandial blood glucose levels is a strategy used for the treatment of diabetes patients. Dietary carbohydrates such as sucrose, maltose, and starch are broken down into monosaccharides such as glucose, fructose, and galactose in the small intestine by α -glucosidases before absorption. α -Glucosidase inhibitors such as acarbose are widely used in the treatment of patients with type 2 diabetes or impaired glucose tolerance (Van de Laar, 2008; Van de Laar et al., 2005). Compared with other oral anti-hyperglycemic agents, α -glucosidase inhibitors are considered to have good efficacy. α -Glucosidase inhibitors retard the digestion or absorption of carbohydrates in the small intestine and thus have a lowering effect on postprandial blood glucose (Van de Laar et al., 2005).

Vitamin B₆ is in a class of water-soluble vitamins and an essential nutrient for health and growth. The term “Vitamin B₆” includes six vitamers: pyridoxine, pyridoxal, pyridoxamine, and its 5'-phosphates (Fig. 1). Of these, pyridoxal 5'-phosphate (PLP) is the metabolically active form and all other vitamers are converted in the body to the PLP (Bender, 2009). Vitamin B₆ functions as an essential

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Fig. 1 Structure of pyridoxine and its derivatives (pyridoxal and pyridoxamine), and commercial α -glucosidase inhibitors (Acarbose[®] and Voglibose[®])

cofactor in the metabolism of carbohydrates, lipids, and amino acids (Odum and Wakwe, 2012; Roth-Maier et al., 2002) and is distributed in various foods. Pyridoxine is the main form found in plant foods, whereas pyridoxal exists as the main form in animal products, and pyridoxamine is found in both food groups (Roth-Maier et al., 2002). Furthermore, it has been reported that Vitamin B₆ can prevent the generation of oxygen radical and lipid peroxidation caused by hydrogen peroxide and had a protective effect under homocysteine-induced oxidative stress (Hsu et al., 2015; Kannan and Jain, 2004). Moreover, many studies have reported that reduced plasma concentration of Vitamin B₆ can affect some diseases such as colorectal cancer, cardiovascular disease, and hyperglycemia (Hou et al., 2011; Morris et al., 2008; Wei et al., 2005). Also, it has been reported that pyridoxine, pyridoxal, and pyridoxamine inhibit various digestive enzymes such as α -glucosidases, sucrase, maltase, and glucoamylase (Kim et al., 2018). Inhibition of these enzymes involved in the absorption of disaccharide can improve post-prandial hyperglycemia due to carbohydrate-based diet (Kim et al., 2018). Many papers have reported on the association between diabetes or blood glucose levels and vitamin B₆ status.

Therefore, the purpose of this study is to determine the effects of pyridoxine supplementation on postprandial blood glucose levels in healthy individuals. We expect that pyridoxine administration with sucrose can lead to reduced postprandial blood glucose levels and retard absorption of glucose in the small intestine by inhibiting carbohydrate-hydrolyzing enzymes.

Materials and methods

Preparation of pyridoxine and sucrose

Pyridoxine was prepared as a dietary supplement from The Vitamin House Inc. (Seoul, Korea) which contained 50 mg of pyridoxine hydrochloride in the form of 200 mg tablets. Sucrose was provided 75 g dissolved in 200 ml of water per person.

Assessment of postprandial blood glucose regulation

This study was a randomized crossover trial performed at Hannam University, Korea, from November to December 2014. The Hannam University Institutional Review Board (IRB) approved the trial (HNU 2014-01 K), and written informed consent was obtained from all participants.

For this clinical trial, 9 healthy volunteers were recruited after explaining about the experimental methods. At first day, control experiment was conducted without oral take of pyridoxine. The two trials periods were separated by a wash-out interval of 1 week. At second day, same procedure was repeated as comparative experiment (pyridoxine experiment) with oral take of 200 mg of pyridoxine supplement tablet (50 mg of pyridoxine hydrochloride) 20 min before sugar administration. Sugar administration was applied with 75 g of sucrose in 200 mL of water.

Mean age, mean weight, and mean height of volunteers were 28.3 ± 7.7 years, 65.9 ± 14.4 kg, and 167.4 ± 6.6 cm, respectively. At first, we measured fasting blood glucose levels after fasting overnight (0 h) and all participants consumed only sucrose solution (75 g/200 mL), and then postprandial blood glucose levels were

determined every 30 min after ingestion for 2 h (0.5, 1, 1.5, and 2 h). The blood glucose monitoring kit (Caresens II, ICENS Co., Ltd., Wonjoo, Korea) was used for blood glucose measurement throughout the test. A few days later, after measuring the fasting glucose levels of participants in the same method, all participants consumed 200 mg of pyridoxine supplement which contained 50 mg of pyridoxine hydrochloride with sucrose solution. And then, postprandial blood glucose levels were determined in the same way. After the tests were completed, we calculated the parameters associated with blood glucose levels using PKSolver®, a freely available menu-driven add-in program for Microsoft Excel written in Visual Basic for Applications, and then the two group were compared to each other. On the basis of our observed data, the maximum concentration of blood glucose (C_{max}), the time to reach peak concentration (T_{max}), and the area under the concentration–time curve (AUC_t) were estimated. AUC_t was calculated by the linear trapezoidal rule.

Statistical analysis

All results are presented as mean $\pm$ S.D. Statistical analyses were carried out using IBM SPSS Statistics 22 (IBM Corp., Armonk, NY, USA) program and significance between the control group and treated group was verified by Student's t test. A p -value < 0.05 was considered statistically significant.

Results and discussion

Effects of pyridoxine on postprandial blood glucose levels

We evaluated the effects of pyridoxine supplementation on postprandial blood glucose levels in healthy individuals with normal blood glucose levels. The blood glucose levels were estimated as described in the Materials and Methods

Fig. 2 Changes in postprandial blood glucose levels in control and pyridoxine treated groups. Each bar represents mean $\pm$ SD ($n = 9$). Control vs. pyridoxine treatment; * $p < 0.05$, ** $p < 0.01$

section. The results showed that pyridoxine significantly lowered postprandial blood glucose levels at 30 min after ingestion (Table 1 and Fig. 2). More specifically, the mean

Fig. 3 The extent of blood glucose increase in control and pyridoxine treated groups. Each bar represents mean $\pm$ SD ($n = 9$). Control vs. pyridoxine treatment; * $p < 0.05$, ** $p < 0.01$

Table 1 Postprandial blood glucose levels (BGL; mg/dL) and blood glucose increase (BGI; mg/dL) in control or after administration of pyridoxine

Group	0 h	0.5 h	1 h	1.5 h	2 h
BGL (mg/dL)					
Sucrose	94.86 $\pm$ 9.67	165.95 $\pm$ 17.19	131.40 $\pm$ 17.20	117.90 $\pm$ 11.26	102.95 $\pm$ 14.78
Pyridoxine	102.50 $\pm$ 9.00	138.36 $\pm$ 20.43**	118.50 $\pm$ 15.95	111.07 $\pm$ 10.88	104.50 $\pm$ 15.17
BGI (mg/dL)					
Sucrose	NA	71.09 $\pm$ 17.79	36.54 $\pm$ 17.30	23.04 $\pm$ 16.65	9.19 $\pm$ 12.84
Pyridoxine	NA	35.86 $\pm$ 20.79**	17.57 $\pm$ 17.08*	10.14 $\pm$ 13.66	5.00 $\pm$ 7.85

Each bar represents mean $\pm$ SD ($n = 9$). Control vs. pyridoxine treatment; * $p < 0.05$, ** $p < 0.01$

Table 2 Pharmacodynamics (PD) parameters in control or after administration of pyridoxine

	Group	PD parameters		
		<i>C_{max}</i>	<i>T_{max}</i>	AUC _t
BGL (mg/dL)	Sucrose	165.95 ± 17.19	0.50 ± 0.00	257.08 ± 22.38
	Pyridoxine	143.07 ± 11.34**	0.64 ± 0.24	235.71 ± 12.33*
BGI (mg/dL)	Sucrose	71.09 ± 17.79	0.50 ± 0.00	67.63 ± 24.54
	Pyridoxine	40.57 ± 14.49**	0.64 ± 0.24	33.04 ± 16.21**

Each bar represents mean ± SD (n = 9). Control vs. pyridoxine treatment; **p* < 0.05, ***p* < 0.01

of postprandial blood glucose levels was reduced from 165.95 ± 17.19 to 138.36 ± 20.43 ($p < 0.01$) at 30 min. Moreover, we observed that pyridoxine significantly lowered *C_{max}* (from 165.95 ± 17.19 to 143.07 ± 11.34 , $p < 0.01$) and AUC_t (from 257.08 ± 22.38 to 235.71 ± 12.33 , $p < 0.05$), but *T_{max}* value had not differed between the two groups (Table 2). In summary, hypoglycemic effect of pyridoxine was the most intense at 30 min, compared to the control group. The blood glucose concentration, *C_{max}*, and AUC_t were reduced by 16.63%, 13.79%, and 8.31%, respectively.

When these results were presented in terms of increase in blood glucose concentrations, we verified similar trends (Tables 1, 2, and Fig. 3), but the decrease rate was much higher when compared to control. The value of blood glucose increase was reduced from 71.09 ± 17.79 to 35.86 ± 20.79 ($p < 0.01$) at 30 min, and from 36.54 ± 17.30 to 17.57 ± 17.08 ($p < 0.05$) at 1 h (Table 1). When compared to control group, the value of blood glucose increase was reduced by 49.56% at 30 min, and 51.91% at 1 h. Also, its *C_{max}* and AUC_t were reduced by 42.93%, and 51.15%, respectively. That is, we confirmed that the increase in postprandial blood glucose levels was significantly blocked by pyridoxine. This method of data analysis provides a better understanding of the effect by adjusting the initial blood glucose levels equally for all groups. Furthermore, in our previous studies using in vitro assay to investigate effects of pyridoxine on carbohydrate-hydrolyzing enzymes such as α -glucosidase and α -amylase, we observed that pyridoxine considerably inhibits the activity of α -glucosidase. Therefore, pyridoxine probably reduces the postprandial blood glucose levels by inhibiting α -glucosidase activity in the small intestine.

The main purpose of this study is to determine the effects of pyridoxine supplementation on postprandial blood glucose levels in healthy individuals. The results showed that pyridoxine significantly lowered postprandial blood glucose levels and increase in blood glucose levels after a meal. Moreover, the parameters associated with blood glucose levels, such as *C_{max}* and AUC_t were significantly reduced, but *T_{max}* was not affected when compared to control group. These results may be due to the

carbohydrate-hydrolyzing enzyme inhibition or retardation of glucose absorption in the small intestine. In conclusion, these results suggest that pyridoxine supplementation might have the potential to be used for the supply of essential nutrients as well as a management of postprandial hyperglycemia.

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Compliance with ethical standards

Conflicts of interest The authors declare no conflict of interest.

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