Research Article

Improved Blood Glucose Level Associated With Polypeptide-K (Diabegard®), A Polypeptide Isolated from the Seeds of *Momordica charantia* Supplementation: Evaluation of 6 Cases

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ABSTRACT

To describe six cases of glucose management in diabetic and pre-diabetic patients with Diabegard® supplementation. We report the clinical courses of six individuals taking Diabegard® supplementation at 60 and 120 mg/day for 8 weeks. Patients had a maximum of 50% reduction in fasting blood glucose with 42% reduction in glycated haemoglobin (HbA1c). Patients also had improved kidney functions (expressed by normal level of blood urea nitrogen, creatinine and urine microalbumin). In some patients, these three parameters were elevated prior to supplementation. These results suggest that supplementation of Diabegard® will improve patients' glucose management and with reduction of elevated blood glucose level, kidney functions will also improve. However, patients taking this supplementation are advised to seek medical consultation in monitoring their blood sugar levels.

Keywords: Diabetes Mellitus, Diabegard®, *Momordica charantia*,

INTRODUCTION

Diabetes Mellitus (DM) is a major health problem in most developing and developed countries today. Hundreds of millions of people worldwide have diabetes, ranging from 35 to 70 years old[1]. According to Hu[2], the prevalence of diabetes in the world is 171 million while in 2030 it is predicted to exceed 366 million. On the other hand, the prevalence of diabetes in Malaysia is 1.6 million in 2009 and it is estimated to reach 3.5 million in 2030[3].

Approximately 60–80% of the World's population relies on herbal plant-based medicine as their health care system[4]. *Momordica charantia* Linn (MC) or bitter gourd is been commonly used as a traditional in many parts of Asia, Africa, Europe, and South America[5]. MC is a popular plant that has been extensively used for its blood sugar lowering effects. The MC fruit is considered as to have many other benefits such as stimulant, emetic and laxative[4]. The hypoglycemic activity of MC has been reported from its pulps, seeds and leaves[6]. Kanna et al.,[7] isolated polypeptide-p, a peptide from seeds of MC, which decreased blood glucose in an animal model of diabetes. However, Polypeptide-k (Ppk), another peptide which was later isolated from seeds of MC, also possesses blood glucose level-reducing activity which is more potent than that of polypeptide-p and helps in the prevention of diabetes[8].

Indeed, recently we reported Ppk supplemented soft roll caused enhanced reduction in blood glucose level as compared to control soft roll in healthy adults[4]. *In vitro* analysis suggested that this activity was due to the inhibition of α-amylase and α-glucosidase activity (35.58% and 79.18% respectively)[9]. Ppk with high homology to human insulin contains 18 amino acids in a single molecule and may help in reducing blood glucose[10]. It has been distributed in Malaysia under the brand name Diabegard®. We describe six individuals diagnose with diabetes or pre-diabetes taking the dietary supplementation Diabegard®.

METHODS AND RESULTS

Case Reports

Patient 1 was a 45 year old Malay woman, who had been diagnosed with type-2 DM in 2012. Blood analysis revealed that all blood parameters were within normal range (Table 1) except fasting blood glucose and glycated haemoglobin (HbA1c). The major blood electrolytes were within normal range (Table 1). Urinalysis revealed elevated urine microalbumin (Table 1) whereas other urine parameters were normal (Data not shown). She was advised to take 30 mg Ppk QID sublingually (8 tablets/day) and practice healthy life-style. After 8 weeks, fasting blood analysis revealed blood glucose had reduced to approximately 50% from the pre-supplementation of Ppk and HbA1c was reduced by 34%. The urine microalbumin also back within normal values of 7.4 mg/L (Table 2).

Patient 2, a 66 years old Chinese man, also diagnosed in early 2012 with type 2 DM. Blood check revealed blood creatinine and urea nitrogen (BUN) were elevated as with blood glucose and HbA1c (Table 1). The major blood electrolytes were within normal range. He was also advised as patient 1 and after 8 weeks, his blood glucose reduced by approximately 44% and HbA1c reduced by 42% (Table 2). Interestingly, his blood creatinine also reduced by 25.5% and BUN by 37.5% at the end of eighth weeks.

Table 1: Selected biochemical parameters of patients prior to Diabegard® supplementation.

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Reference Range*
Sodium (mmol/L)	148.0	145.0	134.0	144.0	143.0	144.0	132-150
Potassium (mmol/L)	4.30	4.0	5.6	4.2	4.1	4.2	3.5-5.5
Chloride (mmol/L)	103.0	100.0	98.0	105.0	99.0	103.0	95-110
Urine Microalbumin (mg/L)	21.4	ND	ND	ND	176.8	35.2	<20
Urine Creatinine (mmol/L)	10.9	ND	ND	ND	5.1	16.8	0.9-26.5
Blood Urea Nitrogen (mmol/L)	4.4	37.6	18.2	2.8	27.3	4.3	2.3-7.8
Blood Creatinine (µmol/L)	71.0	467.0	279.0	67.0	321.0	72.0	M:<124, F:<106
Glucose (mmol/L)	12.6	10.7	8.9	7.4	6.4	11.0	Fasting: 3.0-6.1
Glycated Hb (%)	9.9	7.2	7.7	7.5	6.3	8.7	Normal:3.5-6.0 Good Ctrl:5.3-7.0 Fair: 7.1-8.0 Poor: >8.0

*Source [19] ND: Not determined

Table 2: Selected biochemical parameters of patients 12 weeks after Diabegard® supplementation.

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Reference Range*
Sodium (mmol/L)	144.0	134.0	133.0	148.0	147.0	136.0	132-150
Potassium(mmol/L)	4.2	5.2	5.6	5.2	4.1	4.2	3.5-5.5
Chloride (mmol/L)	103.0	103.0	101.0	96.0	105.0	103.0	95-110
Urine Microalbumin (mg/L)	7.4	ND	ND	ND	257.5	25.2	<20
Urine Creatinine (mmol/L)	11.6	ND	ND	ND	6.4	16.0	0.9-26.5
Blood Urea Nitrogen (mmol/L)	4.6	23.5	15.6	2.4	20.3	4.2	2.3-7.8
Blood Creatinine (µmol/L)	72.0	348.0	262.0	72.0	293.0	74.0	M:<124, F:<106
Glucose (mmol/L)	6.2 (50.79)	6.0 (43.92)	7.8 (12.36)	4.5 (39.19)	5.4 (15.63)	10.6 (3.6)	Fasting: 3.0-6.1
Glycated Hb (%)	6.5 (34.34)	4.2 (41.67)	6.6 (14.29)	5.5 (26.67)	5.0 (20.63)	7.4 (14.94)	Normal:3.5-6.0 Good Ctrl:5.3-7.0 Fair: 7.1-8.0 Poor: >8.0

*Source [19] ND: Not determined

Patient 3 was a 71 year old Malay woman was presented with lethargy and her blood analysis is presented in Table 1. She had slightly elevated BUN and blood creatinine with 8.9 mmol/L fasting blood glucose and 7.7% HbA1c. She was advised to take 4 tablets daily of Diabegard® (60 mg/day Ppk; two tablets BID sublingually). After 8 weeks, her blood glucose and HbA1c reduced by 12% and 14% respectively. However, the creatinine and BUN were slightly reduced (Table 2). She reported that she felt healthier the last month with higher energy level.

Patient 4 was a 72 year old Indian woman presented for her biannual medical check-up. All of her blood and urine parameters were normal except marginally elevated blood glucose of 7.4 mmol/L and HbA1c of 7.5% (Table 1). She was advised to take 4 tablets daily of Diabegard® (60 mg/day Ppk; two tablets BID sublingually). After 8 weeks, her blood glucose and HbA1c reduced 39 and 27% respectively. Her glucose level was back to normal of 4.4 mmol/L with normal control of glucose level (HbA1c of 5.0%).

Patient 5, 68 year old Chinese woman complaint of lethargy. Blood works revealed elevated BUN, creatinine and slight increase of glucose. She was also advised to take 4 tablets daily of Diabegard® (60 mg/day Ppk; two tablets BID sublingually). After 8 weeks, her blood glucose and HbA1c were back within normal readings with lower levels of BUN and Creatinine (Table 2).

Patient 6 was a 49 year old Indian man diagnose with type 2 DM. Blood analysis showed that all blood parameters were within normal range (Table 1) except fasting blood glucose and glycated haemoglobin (HbA1c). The blood electrolytes were within normal range (table 1). Urinalysis revealed elevated urine microalbumin (Table 1) whereas other urine parameters were normal (Data not shown). He was given Diabegard® as for patient 1. However, after 8 weeks there was no improvement in his glucose parameters but lower urine microalbumin level.

DISCUSSION

Synthetic drugs are more commonly induce adverse drug reactions[11] when compared to herbal preparations. Therefore, numerous reports have been published describing the biomedical properties of various herbs[12,13]. In Malaysia, the use of dietary supplementation and herbal preparations continues to increase yearly[3] as also in other countries[14]. Medical practitioners always encountered with new herbal products. Possible side effects are a big risk for these new supplementations and even more dangerous drug interactions. However, after 12 years Diabegard® usage by general public, to our knowledge there is no adverse reactions reported. Diabegard® (Livvon Marketing, Kuala Lumpur, Malaysia) is an over-the-counter dietary supplement used for blood sugar management and overall health. The exact constituents have been reported recently[9].

Many herbal extracts have been reported to reduce elevated glucose[15,16] but Diabegard® is a single polypeptide which is effective in diabetic and pre-diabetic patients. We present six cases of patients who are diabetic and pre-diabetic. Not all patients have the classical symptoms of diabetes, but with Diabegard® supplementation of 8 weeks, almost all had reported positive effects with these clearly demonstrated by reduction of fasting blood glucose and reduction of HbA1c. The largest reduction of blood glucose was 50% and HbA1c by 42% in just 8 weeks and several patients had normal blood glucose level with normal control of glucose level as expressed by HbA1c level of 3.5 to 6.0%[17]. However, patient 6 did not respond to the Diabegard® supplementation. His sugar and HbA1c just reduced by 3.6% and 15% respectively. Further investigation revealed, he had problem with dosing compliance as he did not strictly follow the physician's advice.

Figure 1 show the exact reduction of blood glucose and reduction of HbA1c. As reported previously, Ppk potently reduce elevated blood glucose[4] and the present case study report further strengthens the efficacy of Ppk in reduction of elevated blood glucose level. Interestingly, patient 4 and patient 5 both recorded normal fasting blood glucose after Diabegard® supplementation. Both patients also recorded normal HbA1c of below 6% which expressed as normal blood glucose management of these patients during 8 weeks of supplementation.

Patient 1 and 6 had elevated urine microalbumin which normalise after supplementation. A microalbumin test is used to detect early signs of kidney damage in people who have a risk of kidney disease[18]. Patients with DM or hypertension have a higher risk of developing kidney damage. A reduction of 65% in this parameter suggests better blood glucose management will reduce the risk of kidney damage. However patient 5 readings did not reduce as the level was severely elevated plus elevated BUN and blood creatinine indicating marked kidney damage prior to the supplementation.

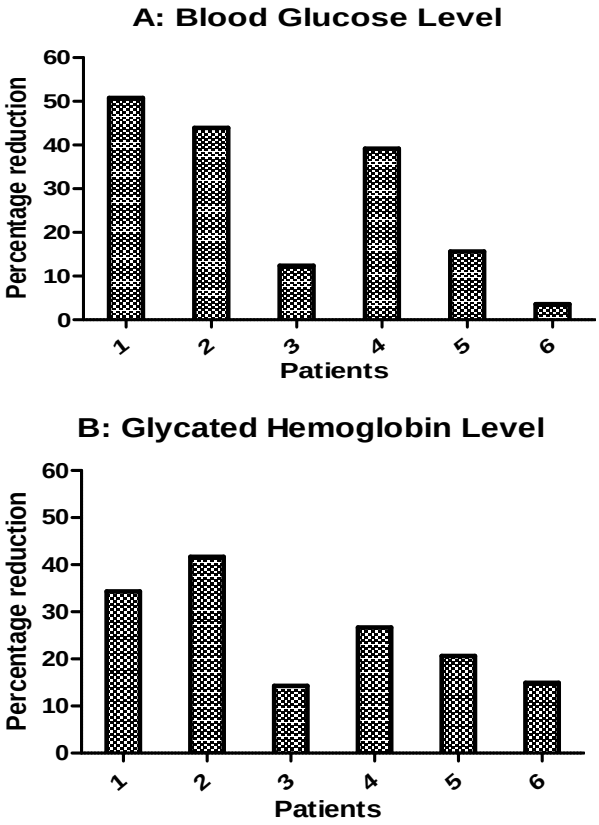

Figure 1: Percentage reduction of Fasting blood glucose and glycated haemoglobin after 8 weeks Diabegard® supplementation

This product labels properly several warnings including consult a physician if having the diagnosis of diabetes before the use of this supplement. These people should consult physicians and monitor their blood glucose level before and after its use. It is exciting to see that glucose management of these six patients improved by the supplementation of Diabegard®. Further studies are needed to clarify the role of each amino acid in this polypeptide with regards to its hypoglycaemic effects.

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