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Case Report

A Report of Six Clinical Cases of Lowered Blood Cholesterol Profile Associated with Supplementation with Polypeptide K (Diabegard®), a Polypeptide Isolated from the Seeds of *Momordica charantia* Linn

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Abstract

Purpose: *To assess six patients with Diabegard® supplementation with reference to cholesterol profiles.*
Methods: *We report the clinical courses of six individuals taking Diabegard® supplementation at 60 and 120 mg/day for 8 weeks.*
Results: *Patients had a maximum of 52.13 % reduction in low-density lipoprotein (LDL) cholesterol, 47.67 % reduction in triglycerides and 35.78 % reduction in total cholesterol (TC) within 8 weeks of Diabegard® supplementation. Interestingly, high-density lipoprotein (HDL) cholesterol increased by approximately 23.29 %. Patients also had reduced readings for C-reactive protein (CRP) and homocysteine (with maximum reduction of 81.58 % and 57.41 % respectively). In some patients, these parameters were elevated prior to supplementation.*
Conclusion: *These results suggest that supplementation of Diabegard® will improve patients' cholesterol profile by reduction of LDL and TC. Patients also expressed lower CRP and homocysteine indicating reduced inflammation and reduction of cardiovascular diseases (CVD) risk. However, patients taking this supplementation are advised to seek medical consultation in monitoring their cholesterol and other biochemical profile levels.*

Keywords: *Hypocholesterolemia, Diabegard®, Momordica charantia, C-reactive protein, Inflammation, Cardiovascular disease*

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INTRODUCTION

Approximately 20 % of deaths per year in both developing and developed countries are caused by cardiovascular diseases (CVD) which mainly include coronary heart (CHD) disease and stroke [1]. CHD is considered a world epidemic [2]. Elevated blood cholesterol or hypercholesterolemia is one of the major contributing factors for CHD and other CVD. Therefore, it is a major worldwide economic and medical challenge that most countries are facing now [3].

One of the treatments for hypercholesterolemia is using Statins (simvastatin, pravastatin and

atorvastatin) to reduce the body cholesterol biosynthesis that will lead to lower blood levels of cholesterol by inhibiting 3-hydroxy-3-methylglutarylcoenzyme A reductase [4]. Statins are very effective in lowering the low-density lipoprotein (LDL) cholesterol by approximately 21 to 43 % [5]. Unfortunately, statins induce many adverse drug reactions. Moreover, patients are at risk to more serious ADRs from the long-term ingestion of statins which may include mutagenic, teratogenic and carcinogenic effects [6].

Therefore, about 60–80 % of the World's population now are on herbal plant-based medicine as their main health care system [7]. *Momordica charantia* Linn (MC) or bitter gourd is the popular plant used for its biomedical properties [8]. MC has been extensively used for its blood sugar lowering effects [7]. The hypoglycemic activity of MC has been reported from its pulps, seeds and leaves [9]. Polypeptide-k (Ppk), apolypeptide isolated from seeds of MC, possesses blood glucose level-reducing activity and a small clinical study revealed Ppk not only reduces elevated blood glucose but also elevated blood cholesterol [10]. We have recently reported the exact constituents of PpK [11]. Ppk is sold under the trade name Diabegard® (Livvon Marketing, Kuala Lumpur, Malaysia). Diabegard® is an over-the-counter dietary supplement used for blood sugar management and overall health. This report describes the outcome of six individuals taking Diabegard® supplementation with reference to cholesterol profiles.

EXPERIMENTAL

All patients were presented for their annual medical examination and a written consent was taken for this report. Patients were observed by the physicians from February 2012 till September 2012. All procedures are in accordance with The Declaration of Helsinki [12]. Ethical clearance for this study was reviewed and approved by the Faculty of Medicine and Health Sciences Medical Research Ethics Committee, Universiti Putra Malaysia (Approval no. UPM/FPSK/PADS/T7-MJKEtikaPe./F01-158. OKT [03]-72.

Case reports

Patient 1 was a 45-year old Malay woman, who had been diagnosed with type-2 Diabetes Mellitus (DM) in 2012. She was in the clinic for her normal medical check-up. Her blood parameters are presented in Table 1. All parameters were normal except slight increment of lymphocyte counts and marginally elevated γ-glutamyltransferase (GGT). However, her cholesterol profile was elevated TC, LDL-cholesterol and HDL-cholesterol (Table 3). Her CRP level was 7.1 mg/L indicating acute inflammation and elevated homocysteine of 10.7 µmol/L. She was advised to take 30 mg Ppk QID sublingually (8 tablets Diabegard®/day) and practice healthy life-style. After 8 weeks, fasting blood analysis revealed a reduction of 24 % TC and 29 % LDL-cholesterol. Her HDL-cholesterol level was increased by 21 %. The CRP and homocysteine levels reduced by 57 % and 18 %, respectively. Her elevated of lymphocyte counts also reduced to normal levels.

Patient 2, a 66-year old Chinese man, also diagnosed in early 2012 with type 2 DM. His blood picture was normal (Table 1) except a low RBC count. His cholesterol profile was fair with only slight elevation of LDL-cholesterol and low HDL-cholesterol (Table 3). He was also advised as patient 1 for his DM condition and after 8 weeks, his HDL-cholesterol increased by approximately 23 % and LDL-cholesterol reduced by 52 % back to optimal level (Table 4).

Patient 3 was a 71-year old Malay woman presented with lethargy and her blood analysis is shown in Table 1. Her blood picture was normal except a low RBC count. Her cholesterol profile was undesirable as her TC, LDL-cholesterol and triglycerides were very high 7.49, 5.24 and 3.65 mmol/L respectively (Table 3). Her homocysteine also at the high risk level of 27.1 µmol/L. She was advised to take 4 tablets of Diabegard® daily (60 mg/day Ppk; two tablets BID sublingually). After 8 weeks, her TC reduced by 35 %, LDL-cholesterol by 47 % and triglycerides also by 47 %. The homocysteine level reduced to 11.6 µmol/L which is a massive 57.41 % to borderline levels.

Patient 4 was a 72-year old Indian woman presented for her biannual medical check-up.Her blood picture was normal (Table 1) but due to her slight elevation of glucose (data not shown), She was advised to take 4 tablets daily of Diabegard® (60 mg/day Ppk; two tablets BID sublingually). Her cholesterol profile was fair with borderline levels of TC, LDL-cholesterol and HDL-cholesterol (Table 3). After 8 weeks, her cholesterol profile was better with reduction of TC and LDL-cholesterol with 12 % HDL-cholesterol increment.

Patient 5, a 68-year old Chinese woman presented with complaint of lethargy. Her blood picture revealed lowered RBC count, elevated leukocytes with increased GGT (Table 1). Her

TC, LDL-cholesterol and triglycerides were slight elevated. The CRP and homocysteine level were also elevated (Table 3). She was also advised to take 4 tablets of Diabegard® daily (60 mg/day Ppk; two tablets BID sublingually). After 8 weeks, the TC was reduced by 9 %, LDL-cholesterol by 13 % and triglycerides reduced by 35 % (Table 3). Interestingly, her HDL-cholesterol increased by 9 % and CRP dropped by a massive 81%. The homocysteine also reduced by 49 %.

Patient 6 was a 49-year old Indian man diagnosed with type 2 DM. Analysis showed that all blood parameters were within normal range (Table 1) except his liver function enzymes which were mildly elevated (Table 1). His cholesterol profile was also slightly elevated with elevation of TC, LDL-cholesterol and triglycerides. He was given Diabegard® as for patient 1. After 8 weeks of supplementation, his liver function was back to normal (Table2). Table 4 expresses his lowered cholesterol level.

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*
Red blood cell (mil/cmm)	4.7	2.3	3.2	4.0	3.6	5.35	M:4.5-6.5 F:3.8-5.8
White Blood Cell (tho/cmm)	9.7	7.2	7.1	5.4	6.8	11.0	4.0-11.0
Neutrophils (%)	40.0	75.0	64.0	47.0	76.0	60.0	40-75
Lymphocytes (%)	54.0	20.0	26.0	45.0	18.0	34.0	20-45
Monocytes(%)	5.7	4.0	6.0	6.0	4.0	5.0	2-10
Eosinophils(%)	0.3	1.0	4.0	2.0	2.0	1.0	1-6
Basophils(%)	0	0	0	0	0	0	0-1
AST (U/L)	32.0	17.0	29.0	25.0	39.0	45.0	<40.0
ALT (U/L)	31.0	17.0	16.0	14.0	21.0	55.0	<50.0
GGT (U/L)	65.0	18.0	12.0	14.0	255.0	68.0	<50.0
ALP (U/L)	78.0	84.0	44.0	91.0	46.0	67.0	M:<125 F:<115
Total protein (g/L)	82.0	56.0	68.0	68.0	75.0	76.0	62-82
Total bilirubin (µmol/L)	10.3	5.1	10.3	10.2	17.8	16.1	<25.7

**Source: Ref [17]*

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*
Red blood cell (mil/cmm)	4.0	2.0	3.0	4.5	3.5	5.3	M:4.5-6.5 F:3.8-5.8
White blood Cell (tho/cmm)	9.9	6.3	6.9	8.5	6.9	9.7	4.0-11.0
Neutrophils (%)	45.0	74.0	69.0	75.0	75.0	62	40-75
Lymphocytes (%)	42.0	18.0	23.0	20.0	19.0	27	20-45

Monocytes (%)	10.0	4.0	5.0	4.0	4.0	7	2-10
Eosinophils (%)	3.0	4.0	3.0	1.0	2.0	3	1-6
Basophils (%)	0	0	0	0	0	1	0-1
AST (U/L)	17.0	23.0	18.0	27.0	33.0	39.0	<40.0
ALT (U/L)	19.0	15.0	9.0	19.0	16.0	29.0	<50.0
GGT (U/L)	35.0	14.0	9.0	18.0	88.0	47.0	<50.0
ALP (U/L)	49.0	61.0	52.0	58.0	40.0	62.0	M:<125 F:<115
Total protein (g/L)	73.0	54.0	73.0	75.0	77.0	76.0	62-82
Total bilirubin (µmol/L)	5.6	5.6	9.1	12.5	17.9	14.7	<25.7

**Source: Ref [17]*

Table 3: Lipid profile and cardiovascular risk of patients prior to Diabegard supplementation

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Reference range*
Total cholesterol (mmol/L)	6.54	4.49	7.49	5.59	6.60	7.20	Desirable:<5.17 High:>6.20
HDL-cholesterol (mmol/L)	1.64	0.73	1.18	1.41	1.37	1.51	Low:<1.04 High:>1.55
LDL-cholesterol (mmol/L)	4.27	3.76	5.24	3.78	4.32	4.95	Optimal:<2.58 High:4.14
Triglycerides(mmol/L)	1.36	2.12	3.65	0.88	2.50	3.23	Normal:<1.69 High:>2.25
Total/HDL-cholesterol ratio (Index)	4.0	6.2	6.3	4.0	4.8	4.8	Optimal:<3.5 High:>5.0
C-reactive protein (mg/L)	7.1	ND	3.0	ND	11.4	19.4	Risk-Low:<1.0 High:>3.0 Acute Inflam:>5.0
Homocysteine (µmol/L)	10.7	ND	27.1	ND	36.4	ND	Low risk:<10 High:>15

**Source: Ref [17]*

Table 4: Lipid profile and cardiovascular risk of patients 12 weeks after Diabegard supplementation

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Reference range*
Total cholesterol (mmol/L)	4.96 (-24.16)	4.4 (-2.00)	4.81 (-35.78)	4.96 (-11.27)	5.99 (-9.24)	6.74 (-6.39)	Desirable:<5.17 High:>6.20
HDL-cholesterol (mmol/L)	1.99 (+21.34)	0.90 (+23.29)	1.18 (0)	1.58 (+12.06)	1.50 (+9.49)	1.22 (-23.77)	Low:<1.04 High:>1.55
LDL-cholesterol (mmol/L)	3.03 (-29.04)	1.80 (-52.13)	2.75 (-47.52)	2.93 (-22.49)	3.75 (-13.19)	4.74 (-4.24)	Optimal:<2.58 High:4.14

Triglycerides (mmol/L)	2.26 (+66.17)	1.90 (-10.34)	1.91 (-47.67)	0.97 (+10.23)	1.62 (-35.2)	3.63 (+12.39)	Normal:<1.69 High:>2.25
Total/HDL-cholesterol Ratio (Index)	5.0	4.9	4.1	3.1	3.99	5.5	Optimal:<3.5 High:>5.0
C-reactive protein (mg/L)	3.0 (-57.75)	ND	ND	ND	2.1 (-81.58)	ND	Risk-Low:<1.0 High:>3.0 Acute Inflam:>5.0
Homocysteine (µmol/L)	8.7 (-18.69)	ND	11.6 (-57.41)	ND	18.5 (-49.18)	ND	Low risk:<10 High:>15

**Source: Ref [17]*

DISCUSSION

Abnormal levels of blood cholesterol, i.e. high LDL-cholesterol and low HDL-cholesterol are strongly associated with CVD because these conditions favour atheroma development and may lead to myocardial infarction, stroke, and/or peripheral vascular disease [13,14]. This report describes the cholesterol profile changes in 6 patients on Diabegard® supplementation for 8 weeks. The results suggest that Diabegard® supplementation improves the cholesterol profile of an individual without any drug therapy.

All 6 patients showed reduction in TC and LDL-cholesterol from 2 % to as high as 52.13 % (Table 3) in just 8 weeks. Their total/HDL-cholesterol ratio, a predictor for CHD [15] improved from 6.3 prior to supplementation to 3.1 post-supplementation. Indeed, these parameters suggest that generally patients will have healthier cholesterol profile after Diabegard® supplementation. Three of the patients were having elevated CRP and homocysteine levels. CRP level rises when there are inflammatory processes occurring in the body [16]. Hypercholesterolemia will induce intravascular inflammation and susceptibility to artherosclerosis [13]. CRP dropped to the maximum by 81.58 % in Patient 5 suggesting healthier cholesterol profile and reduction of inflammation. These also followed by the reduction of homocysteine, which is a predictor of CVD [17].

Commercial synthetic hypercholesterol drugs such as statins are effective in lowering the blood cholesterol level. However, numerous clinical cases have been published reporting the various ADR induced by statins [18,19]. These ADRs include liver damage, myopathy and rhabdomyolysis, myalgias and polyneuropathy [20]. Synthetic drugs may induce more ADRs [21] when compared to herbal remedies [22]. These events initiated the interest for herbal cholesterol-lowering therapy [23,24].. Results from this short report show the possible benefits of herbal based supplementation in reducing and controlling hypercholesterolemia clinically.

Oxidative stress, in this case, hypercholesterolemia may initiate and further progression of atherosclerosis by stimulating inflammation and promoting cytokine production [25]. Ppk has been proven to be a potent anti-oxidant and this maybe the mechanism of the reduction of CRP and homocysteine observed in the patients [11]. Other than drugs and supplementations, diet also plays an important role in the maintenance of optimal cardiovascular health [26]. Physical activity is also useful in reducing bad cholesterol, improve cholesterol profile and reducing risk of CVD [27].

CONCLUSION

The results from this report strongly suggest that Diabegard® supplementation improve the patient's cholesterol profile. However, all patients were advised to continue the supplementation and regular health check-ups. Indeed, further studies are needed to elucidate the exact mechanism for the cholesterol-lowering properties of Ppk. Ppk is not only a supplement for glucose management [10] but also a potent supplement for cholesterol management.

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