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Csaba Tóth, Zsófia Clemens

SUMMARY

Metabolic syndrome is made up of a cluster of conditions including obesity, impaired insulin sensitivity, hypertension and altered lipid profile. These conditions are also considered as risk factors for type 2 diabetes and cardiovascular disease. Occurrence of these conditions is on the rise worldwide despite of the increasing number of drugs used. There is evidence from the literature indicating that intervention with low carbohydrate diets, including the paleolithic diet, may be beneficial in the metabolic syndrome. Except for one study with the paleolithic diet these investigations are short in duration. Another limitation is that they do not give clues how to deal with medications patients are treated with. Third, in these studies the paleolithic diet did not produce ketosis which may limit the clinical effectiveness. Here we present a case of a patient with metabolic syndrome and excessively medicated. The patient shifted toward the paleolithic ketogenic diet and was able to discontinue medication, lost weight and her glucose parameters markedly improved. Her hypertension normalized. Currently she is on the diet for 22 months and show good adherence as also confirmed by laboratory tests. She is free of symptoms and no side-effects emerged. Previously we reported cases with epilepsy and type 1 diabetes successfully treated with the same diet. We suggest that a dietary intervention with the paleolithic ketogenic diet may be a simple, feasible and cost-effective method in some forms of chronic disorders in highly motivated patients.

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ABSTRACT

Introduction: Metabolic syndrome is a major public health problem affecting at least 20% of the world's adult population. Components of the metabolic syndrome include obesity, impaired glucose metabolism, hypertension and altered lipid profile. Currently, medical treatment relies on drugs. A major problem is that patients with long-standing disease are excessively medicated because of an increase in the number of symptoms over time. A few clinical studies indicate that low-carbohydrate diets, including the paleolithic as well as the ketogenic diet, may be beneficial in the treatment of conditions associated with the metabolic syndrome. Case Report: Herein, we present a case of patient with metabolic syndrome successfully treated with the paleolithic ketogenic diet. While on the diet the patient was able to discontinue eight medicines, lost weight, showed a continuous improvement in glucose parameters and her blood pressure normalized. Currently, the patient is on the paleolithic ketogenic diet for 22 months, free of symptoms and side effects. Conclusion: We conclude that the paleolithic ketogenic diet was safe, feasible and effective in the treatment of this patient with metabolic syndrome.

Keywords: Diabetes, Hypertension, Metabolic syndrome, Obesity, Paleolithic diet, Paleolithic ketogenic diet

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INTRODUCTION

Obesity, type 2 diabetes and hypertension represent a major health problem. These conditions are components of the metabolic syndrome affecting every fifth adult worldwide [1]. Although it is now acknowledged that type 2 diabetes and hypertension mostly result from lifestyle factors but medical treatment continues to rely on drugs [2]. Symptoms of the metabolic syndrome typically show up in mid-life but the number of co-morbidities are increasing through later years. Typically, symptoms are controlled with an increasing number of drugs. In parallel side effects are also increasing and are usually controlled with additional medications. It is a vicious circle. Currently, a major proportion of elderly in the western world is overmedicated [3]. In sharp contrast with this diseases of civilization are virtually absent in contemporary hunter-gatherer societies [4]. It is suggested that chronic diseases of civilization result from an evolutionary mismatch between our ancient and current diet [5]. It was also suggested that a return to an evolutionary adapted diet may be beneficial for

health [5]. The paleolithic diet has previously been shown to confer metabolic benefits in healthy as well as in patients with metabolic syndrome [6–10]. Voegtlin, first proponent of the human evolutionary diet, suggested an animal fat-meat based diet as being evolutionary adapted [11]. Recently, we reported successful treatment of patients with epilepsy [12] and type 1 diabetes [13] with the paleolithic ketogenic diet. The diet we refer to as the paleolithic ketogenic diet is close to the meat-fat based diet originally proposed by Voegtlin [11]. Herein, we report on a patient with obesity, type 2 diabetes and hypertension whose excessive medication could be discontinued and clinical parameters associated with the metabolic syndrome markedly improved.

CASE REPORT

Previous medical history

The patient's previous medical history included gallbladder surgery in 1987 due to choledocholithiasis and chronic cholecystitis. Hyperglycemia and impaired glucose tolerance was first demonstrated on 24 February 2004. Due to bloody stool Weber test was performed on 25 August 2006 which showed positivity. Therefore, colonoscopy was performed on 19 September 2006 which indicated a 2-cm polyp in the sigmoid colon. Irrigoscopy performed on 25 September 2006 confirmed the above mentioned polyp and also indicated dilation of the colon as well as sigmoid diverticulosis. The polyp was removed on 6 November 2006. Histopathology from this specimen showed tubulovillous adenocarcinoma in polyp (Grade 1). Resection margins were negative. Gastroscopy performed on 21 September 2006 indicated reflux esophagitis and erosive gastritis. Gastroscopy follow-up, three years later, on 26 January 2009 indicated reflux esophagitis but no evidence of gastritis. A next gastroscopy follow-up on 26 January 2011, showed reflux esophagitis and a 5-mm gastric polyp which was removed. Histopathology from this sample showed no abnormalities. A subsequent gastroscopy performed on 14 March 2013 showed reflux esophagitis. Colonoscopy follow-up on 26 January 2007 demonstrated dilation of colon. Subsequent colonoscopy examinations on 27 August 2007, 25 August 2008, 31 August 2009 and 15 April 2013 were able to examine the colon until the transversus lienalis and showed no alterations. A computed tomography (CT) colonography on 27 April 2011 was negative too.

On 10 December 2009, she experienced pressing pain behind the sternum. Echocardiography on 14 December 2009 showed impaired left ventricular diastolic function as well as aortic and mitral insufficiency.

A routine ophthalmological examination on 01 June 2006 showed crossing phenomenon and hyperemic macula, ocular signs of hypertonia and diabetes. Follow-up ophthalmology examination on 20 May 2009 and on 21 May 2010 showed angiopathy while follow-up examinations on 18 May 2012 and 30 July 2013 indicated angiopathy as well as retinopathy.

Medications

Due to elevated blood glucose parameters and high blood pressure from 01 March 2005 onwards the patient was treated with acarbose, ramipril and hydrochlorothiazide. On 02 November 2006 pantoprazole was added because of reflux esophagitis revealed by gastroscopy. Due to increases in blood glucose from 23 August 2007, the patient was also taking metformin. On 14 December 2009 bisoprolol was added because of high blood pressure. Following the cardiological event acetylsalicylic acid was prescribed on 15 April 2010. From 28 October 2010, the patient was prescribed amlodipine due to high blood pressure. The number and the names (active substance) of the medications taken through the course of the disease and the associated 90-min glucose are indicated in Figure 1.

Paleolithic ketogenic diet

We first met the 65-year-old female on 30 January 2013. She was overweight (BMI 37.1, height 160 cm, weight 95 kg), had high blood sugar and frequent high blood pressure spikes despite antidiabetic and antihypertensive medication. At this time her systolic blood pressure was between 130 and 160 mmHg and diastolic blood pressure between 70 and 85 mmHg. Her fasting glucose level was between 144 and 162 mg/dL. Altogether she was taking eight medicines. The patient was motivated in weight loss and in the reduction of her medication. She was advised to start the paleolithic ketogenic diet. She was suggested a diet consisting of at least 70% animal-based food with a fat : protein ratio of at least 2:1. Fat and red meats were preferred over lean meats. Offals meat were encouraged to ensure adequate intake of vitamins. No more than 30% of the diet was suggested as plant-derived food including root vegetables and small amounts of fruit. Dairy, cereals, grains, legumes, solanaceous vegetables, plant oils (including coconut oil), artificial sweeteners and foods with additives were not allowed. In addition to the paleolithic ketogenic diet, she was taking 2000 IU of vitamin D3 for four months then it was stopped. No other vitamin or mineral supplements were used. Typical foods the patient was eating include broth, stew, fried bacon, beef steak, stewed calf liver, braised pork marrow, greaves. Vegetables consumed as garnish were limited and typically included root vegetables, onion and cabbage.

Upon diet commencement (on the third day of the diet) all medications were stopped promptly except for bisoprolol which was discontinued within two weeks. The patient was controlled tightly during the first weeks of the diet. In case of high blood pressure, she was advised to take captopril, a short-acting antihypertensive. Laboratory workup was performed regularly (eight times during 22 months on the diet) in order to control adherence to the diet and to give feedback to the patient (Table 1). All urinary analyses were positive for ketones. While on the paleolithic ketogenic diet blood glucose

Table 1: Laboratory parameters between 2004 and 2014. The red line indicates onset of the paleolithic ketogenic diet. Note that in spite of the withdrawal of eight medications her blood glucose parameters and triglyceride decreased. Dashes indicate that a given parameter was not measured.

		Glucose (mg/dL)	90-min glucose (mg/dL)	HgA1c (%)	Triglyceride (mmol/L)	Cholesterol (mmol/L)	HDL (mmol/L)	LDL (mmol/L)	Uric acid (mmol/L)	ESR (mm/h)	Urinary ketone	Number of medications
2004	24 Feb	133	165	–	–	–	–	–	–	–	–	0
	16 Jun	114	–	5.7	–	4.07	–	–	–	–	negative	0
	30 Sep	126	–	–	1.16	6.47	–	–	209	12	–	0
2005	1 Mar	137	154	6	1.48	5.63	–	3.88	159	19	negative	0
	28 Jul	126	126	6.2	1.25	4.08	1.2	2.31	268	37	negative	3
2006	11 Jul	139	143	6.3	0.77	5.22	1.3	3.5	179	17	positive	3
	02 Nov	149	92	6.2	1.72	5.42	1.08	3.56	241	17	negative	3
2007	13 Feb	130	117	6.12	1.4	6.38	1.62	4.12	277		negative	4
	17 May	126	–	5.6	1.18	5.56	0.95	4.07	324	23	negative	4
	23 Aug	150	125	–	1.48	6.02	1.15	4.2	258	32	negative	4
	29 Nov	116	81	5.03	1.64	5.61	1.03	–	–	–	–	5
2008	11 Mar	129	120	5.6	2.38	5.95	1.23	–	284	21	negative	5
	24 Jun	128	102	6.2	2.37	6.9	1.73	4.09	268	25	negative	5
	09 Oct	106	–	6	2.06	6.1	1.55	3.61	222	34	–	5
2009	15 Jan	141	121	6.3	3.6	6.1	–	3.06	293	35	negative	5
	09 Apr	105	110	–	1.56	5.1	1.1	3.29	348	30	negative	5
	09 Jul	105	90	6	1.97	5.6	–	3.51	–	24	negative	5
	13 Oct	106	99	5.5	1.76	5.2	1.51	2.89	–	29	negative	5
2010	14 Jan	115	103	6.3	1.78	5.2	1.23	3.16	–	19	negative	6
	15 Apr	110	97	6.3	1.48	5	–	3.15	249	15	negative	6
	27 Jul	112	97	6.76	1.34	5.6	–	3.54	207	24	negative	7
	28 Oct	119	115	6	1.62	6.1	1.16	4.2	–	–	–	7
2011	01 Feb	133	146	6.6	2.31	6.4	1.26	4.09	378	20	negative	8
	05 May	114	117	6.2	2.53	5.1	1.14	2.81	–	–	–	8
	16 Aug	132	146	6.7	2.01	5.8	1.26	3.63	305	26	negative	8
	17 Nov	124	119	6.9	1.99	5.9	1.29	3.71	–	–	negative	8
2012	21 Feb	151	173	7.2	2.12	5.3	1.03	–	419	45	negative	8
	12 Mar	123	–	–	–	–	–	–	–	25	–	8
	22 May	124	164	7	1.76	5.6	1.19	3.61	300	23	negative	8
	06 Sep	150	173	7.1	2.88	6.7	1.28	4.11	–	–	–	8
	18 Dec	159	137	–	1.49	6	1.2	4.12	217	21	negative	8
2013	26 Mar	128	114	6.4	1.14	5.3	1.29	3.49	–	–	–	0
	13 Jun	139	123	6.8	0.77	4.5	1.22	2.93	282	8	positive	0
	10 Sep	139	123	6.9	1.09	4.8	1.32	2.98	238	18	positive	0
	09 Oct	110	–	–	–	–	–	–	–	–	–	0
	19 Dec	108	114	7	1	4.51	1.52	2.54	274	20	positive	0
2014	05 Mar	118	–	–	0.69	5.12	–	–	297	–	positive	0
	10 Jun	121	108	6.8	0.96	4.8	1.23	3.13	248	15	positive	0
	04 Dec	108	99	6.5	1.6	5.7	1.19	3.78	274	9	positive	0

Abbreviations: HgA1c glycated hemoglobin, HDL high density lipoprotein, LDL low density lipoprotein, ESR erythrocyte sedimentation rate

level, 90-min glucose on the glucose tolerance test, HgA1c and total cholesterol levels decreased as compared to previous measurements. Triglyceride levels also dropped markedly as well as inflammatory markers including erythrocyte sedimentation rate. A statistical analysis (t-test) comparing laboratory measures during the two years of the paleolithic ketogenic diet and during the previous nine years on a normal diet revealed a significant decrease for HgA1c (p=0.02), cholesterol (p=0.01) and triglyceride (p=0.003). Typically, the patient had two meals a day. She tracked glucose levels daily both preprandially and postprandially before and after the first meal of the day. The patient reported to strictly adhere to the diet insofar not consuming non-paleolithic food at all. At the same time she admitted having some difficulties with fruit restriction and reported that her spikes in blood sugar (Figure 2) and blood pressure to be associated with these events of excess fruit intake. Nevertheless home monitoring of glucose showed a clear decreasing trend both preprandially and postprandially between February 2013 and June 2014 (Figure 2). Then due to the normalization of blood glucose she measured blood glucose levels only occasionally. While on the diet she also reported a decreasing tendency in the frequency of high blood pressure spikes. At the time of writing this case report, she had no high blood pressure spike for six months. Despite no vitamin D supplementation, her winter time vitamin D level (on 05 March 2014) was in the normal range (85 nmol/L). The patient did not perform exercise while on the paleolithic diet.

Currently, she is on the diet for 22 months. While on the diet her weight changed from 95 kg to 81 kg and she is still losing weight. Her BMI changed from 37.1 to 31.6. She reported increased physical fitness and to be free of symptoms. The patient gave written informed consent for publication of her case.

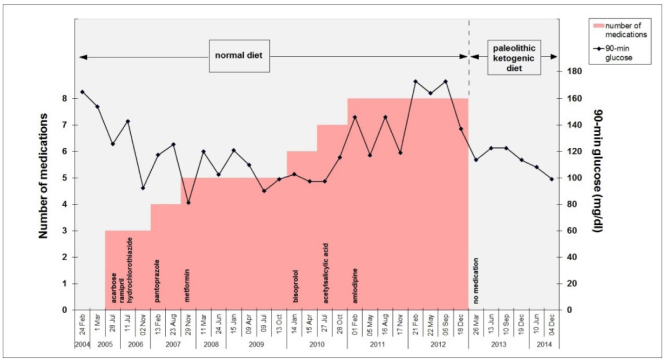

Figure 1: Time course of 90-min glucose level in the glucose tolerance test and the number as well as the names of the medications (active substance) between 2004 and 2014. Note that 90-min glucose levels first tended to decrease with the use of oral antidiabetics. Then from 2011 90-min glucose levels increased again. We attribute decreased glucose tolerance to the use of bisoprolol and amlodipine drugs known for their diabetogenic effect. From January 2013 the patient shifted toward the paleolithic ketogenic diet and was able to discontinue all eight medications. In parallel 90-min glucose levels returned to normal.

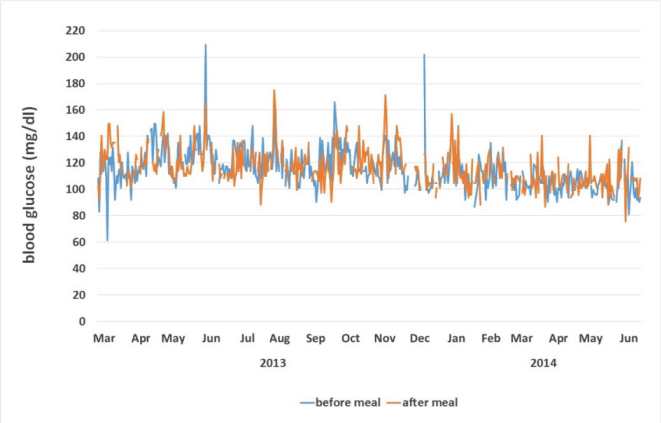

Figure 2: Glucose levels preprandially and postprandially while on the paleolithic ketogenic diet between February 2013 and June 2014. Due to normalized blood glucose levels later on the patient measured blood glucose only occasionally.

DISCUSSION

Recent clinical studies show that low-carbohydrate diets including the paleolithic diet are beneficial in conditions associated with the metabolic syndrome [6–10]. In the current medical practice, patients with metabolic syndrome are generally treated with numerous drugs. Yet studies available on the paleolithic diet does not give clues how to deal with preexisting medications when shifting towards the paleolithic diet. Our experience indicate that upon the shift towards the paleolithic ketogenic diet most drugs become unnecessary and should be discontinued [14].

Herein, we analyzed past medical history of a patient with metabolic syndrome to reveal how her medication might have contributed to the worsening of her disease and how disease was influenced by the paleolithic ketogenic diet.

This case represents a typical disease career of a patient with metabolic syndrome. Her medical history included elevated glucose parameters and hypertension initially controlled with oral antidiabetics and antihypertensives in 2005. Then with the emergence of new diagnostic findings pantoprazole was added. Two years later metformin was added to support glucose metabolism. Nevertheless glucose control deteriorated again in 2011 following the addition of three new drugs. These included bisoprolol, acetylsalicylic acid and amlodipine. Bisoprolol and amlodipine, which belong to beta-blocker and calcium channel blocker type antihypertensives, respectively, are known for their effect to adversely affect glucose metabolism [15, 16]. Glucose parameters further deteriorated in 2012.

Current guidelines first advise lifestyle changes and exercise to treat the metabolic syndrome and to induce

weight loss [1]. Yet these dietary advices usually remain without effect [17]. Also, overweight people are unable to exert considerable physical activity. Therefore, patients are prescribed medications. A main problem is that in current medical practice each component of the metabolic syndrome is treated separately even though targeting one symptom by a drug may worsen another symptom also associated with the metabolic syndrome. Therefore, the number of drugs as well as side effects are increasing.

Our patient was overweight and was taking eight medicines. When shifting towards the paleolithic ketogenic diet she was able to discontinue all medications. Her weight begin to decrease along with improving glucose parameters and lowered blood pressure. Our experience with patients on the paleolithic ketogenic diet indicate that the use of antihypertensive drugs hinder the normalization of glucose levels and weight loss [14]. Also, antihypertensive drugs become unnecessary since the paleolithic ketogenic diet efficiently lowers high blood pressure. In this case, antihypertensive drugs could be discontinued because the patient had no atherosclerosis. In those cases, with atherosclerosis antihypertensives may be discontinued only within a longer time period. The blood pressure lowering effect of the paleolithic ketogenic diet is due to the fact that the paleolithic ketogenic diet limits those food components which result in elevated blood pressure. These components mainly include fruits and foods with added fructose. Drop in blood pressure was also reported in previous studies with the paleolithic diet [6, 8]. Our experience with patients with hypertension indicate that as compared to the paleolithic diet which does not limit fruits and vegetables, the paleolithic ketogenic diet more efficiently normalize blood pressure. Given that in the paleolithic ketogenic diet carbohydrate intake is strongly limited less insulin is required for normoglycemia and therefore oral antidiabetics become unnecessary.

While on the paleolithic ketogenic diet home monitoring of glucose in our patient showed a decreasing tendency both preprandially and postprandially. Laboratory measurements also showed a decreasing tendency in glucose parameters and triglyceride normalized too. Total cholesterol and LDL cholesterol tended to decrease while HDL cholesterol remained relatively unchanged. Uric acid remained in the normal range while on the paleolithic ketogenic diet. These laboratory parameters are similar to those in our two previous cases on the paleolithic ketogenic diet [12, 13]. All six urinary tests were positive for ketones indicating a good adherence to the diet. The patient admitted to occasionally exceed the advised limit for fruit. She also linked excessed fruit intake to high blood pressure spikes which is in accordance with literature data showing high blood pressure to be associated with fructose [18]. Nevertheless our patient reported a decreasing tendency of blood pressure across the 22 months.

Those patients who underwent gallbladder surgery are advised against eating fatty foods and the ketogenic diet too. Our patient, however, reported no gastrointestinal side effects while on the paleolithic ketogenic diet. Of note, her winter-time vitamin D level was normal in spite of no vitamin D supplementation indicating that a regular intake of offal, animal fat and meat may ensure normal vitamin D status. Also, no signs of vitamin or mineral deficiency emerged despite of the lack of supplementation.

Currently, the patient is on the paleolithic ketogenic diet for 22 months. No side effects emerged and she is free of symptoms. She is resoluted to continue the diet.

CONCLUSION

The paleolithic ketogenic diet proved to be a safe, feasible and effective therapy in this patient with metabolic syndrome. Medications could be discontinued and components of the metabolic syndrome improved continuously. We used the paleolithic ketogenic diet in a patient without a gallbladder indicating that, contrary to the widely held notion, this organ is not a prerequisite for maintaining a diet rich in animal fat. Neither vitamin nor other supplements was used indicating the effectiveness of the paleolithic ketogenic diet as a sole therapy.

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Author Contributions

Csaba Tóth – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Zsófia Clemens – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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