

Primary prevention of nephropathy in obese type 2 diabetic patient

Case Report

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Abstract: We report a case of a 36-year-old obese man who presented with newly onset diabetes mellitus type 2 and hypertension. The estimated value of glomerular filtration rate – 203.7 ml/min was associated with the patient being at high risk of developing progressive renal disease. In this case, in order to prevent nephropathy, the preferred therapy was a gradual bodyweight reduction. A low-calorie diet providing an 800 kcal/day deficit was recommended to the patient, as well as an increase in physical activity. After a total weight reduction of 50 kg (33% of initial bodyweight), the patient's glomerular filtration, body mass index, and blood pressure normalized without any drug therapy. Glucose, blood pressure and lipid target levels can only be simultaneously achieved through body-weight reduction. In the presented case, we show the beneficial effects of bodyweight reduction, and dietary and physical activity changes on high glomerular filtration rate. Bodyweight reduction stops the cascade of events that are caused by glomerular hyperfiltration and the progression toward irreversible renal damage.

Keywords: Diabetes mellitus type 2 • Glomerular hyperfiltration • Diabetic nephropathy • Primary prevention

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1. Introduction

Diabetic and vessel nephropathy are major factors for the development of end-stage renal failure in the world [1]. We obtain significant results from managing the stage of clinically diagnosed diabetic, hypertensive or obesity-associated nephropathy. However, the improved nephropathy treatment practically leads to an increase in the number of patients, which is reaching epidemic proportions. This case report describes the optimal strategy for the primary prevention of nephropathy in a obese, type 2 diabetic patient with hypertension.

2. Case Report

A 36-year-old man presented to the emergency department in February 2006 with newly onset hyperglycemia and diabetic ketosis. He described a 3-month history of asthenia and polyuria. His prior

medical history included progressive weight gain since puberty, and also obesity since the age of 20. The patient had obese parents and a type 2 diabetic grandmother. Physical examination showed that he was obese (height 200 cm, weight 152 kg, body mass index (BMI) 38 kg/m²) (Figure 1A). No blood pressure (BP) was taken before hospitalization. His BP was 150/100 mm Hg. Initial laboratory test results at admission (Table 1, column 2) showed abnormal laboratory values of glucose 28.8 mmol/L, uric acid 425 µmol/L, total cholesterol 5.9 mmol/L, triglycerides 4.4 mmol/L and HbA_{1c} - 11.1 %. Urinalysis was positive for ketones and glucose. He tested negative for GAD-65 and IA-2 antibodies. The initial treatment included insulin therapy and metformin, angiotensin-converting enzyme inhibitor and fenofibrate intake (Table 1, column 2).

Diabetes mellitus (DM) type 2 accompanied with hyperinsulinemia [2], obesity [3], hyperlipidemia [4] and hypertension [5] leads to hyperfiltration as the first stage of nephropathy. Thus, the patient's glomerular filtration

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Table 1. Anthropometric parameters, blood pressure, laboratory data, renal function parameters and drug therapy changes observed at admission, 6 and 18 months later.

Parameter	At admission	After 6 months	After 18 months
Weight (kg)	152	129	102
BMI [‡] (kg/m ²)	38	32,25	25,5
Waist circumference (cm)	126	118	108
SBP [†] (mm Hg)	150	130	120
DBP ^{††} (mm Hg)	100	80	80
Total cholesterol (mmol/l)	5,9	5,2	5,1
LDL* cholesterol (mmol/l)	3,9	3,1	2,6
HDL** cholesterol (mmol/l)	0,97	1,24	1,75
Triglycerides (mmol/l)	4,4	1,6	0,96
Fasting plasma glucose (mmol/l)	16,8	6,2	5,2
Postprandial plasma glucose (mmol/l)	28,9	6,5	6,7
HbA1C (%)	11,1	6,2	5,3
Creatinine (μmol/l)	75,3	88,2	87,9
Creatinine clearance (ml/min)	203,7	160,4	136,6
Uric acid (μmol/l)	425	318	287
Albumin/creatinine ratio (g/mol)	2,59	2,66	2,17
Antidiabetic treatment	Insulin premix 70/30 – 36 U/day + Metformin 850 mg three times a day	Metformin 850 mg three times a day + Glimeperide 1 mg	Not medicated
Antihypertensive treatment	Lizinopril 10 mg twice daily	Lizinopril 10 mg once daily	Not medicated
Antilipemic treatment	Fenofibrat 200 mg once daily	Fenofibrat 200 mg once daily	Not medicated

[‡]BMI - body mass index; [†]SBP - systolic blood pressure; ^{††}DBP - diastolic blood pressure; *LDL - low-density lipoprotein;

**HDL - high-density lipoprotein.

rate (GFR) was estimated using creatinine clearance - measured by 24-h urine sample. The use of creatinine clearance makes it possible to avoid any mistakes and corrections associated with the application of GFR evaluation formulas of obese patients. The estimated high GFR – 203.7 mL/min showed that the patient was at high risk of developing progressive renal disease. In order to prevent nephropathy in this case, the preferred therapy was a gradual bodyweight reduction. A low-calorie diet providing an 800 kcal/day deficit was recommended to the patient, as well as an increase in physical activity - starting with 20-minute walks for 5 days a week. After 6 months the diet and the exercise led to a weight loss of 23 kg, drug therapy reduction and reduction of GFR to 160.4 ml/min (Table 1, column 3). All parameters normalized after 18 months. After a total weight reduction of 50 kg (33% of initial bodyweight) the patient's glomerular filtration, BMI, and BP reached normal levels without any drug therapy (Table 1, column 3). Currently, the patient (Figure 1B) is at no risk of nephropathy. Also, his quality of life is better than before.

Figure 1. A. The patient at admission. B. The same healthy man now.

3. Discussion

Prevention and treatment of diabetic nephropathy has become a major treatment goal for diabetic patients. In order to adequately prevent overweight patients with diabetes mellitus type 2 from developing nephropathy, the beginning (functional) stage when the patient is more overweight than ill, should be managed. Through

this method we will avoid irreversible nephropathy, which can only be slowed down not cured. This is achievable if the risk factors initiating the process can be first identified and treated.

Experimental and clinical data show that obesity produces glomerular hyperfiltration [3] and hyperinsulinemia [2]. Moreover, fat tissue may contribute to the increase of angiotensin II, which enhances tubular sodium reabsorption and activates tubuloglomerular feedback [6]. These mechanisms lead to vasodilatation of the afferent arterioles with a consequent increase in renal blood flow, intraglomerular pressure, and GFR [3,7]. Therefore, obesity may lead to obesity-associated renal damage, even in the absence of diabetes. However, the glomerular hyperfiltration rate is significantly higher in patients with diabetes mellitus with hyperglycemia and hyperinsulinemia [2]. Glomerular hyperfiltration is especially pronounced in patients with newly diagnosed diabetes mellitus and during intervals of poor metabolic control [8].

The BP and lipid target levels in obese patients with new onset type 2 diabetes mellitus can be simultaneously achieved through body-weight reduction.

In the presented case, we also show the optimal effect of bodyweight reduction on high GFR through dietary and physical activity changes. This stops the cascade of events that are caused by glomerular hyperfiltration and the evolution toward irreversible renal damage. Glomerular hyperfiltration is the earliest marker of nephropathy in obese type 2 diabetics and its reduction can be viewed as a method for primary prevention of nephropathy. Early measurements of GFR (using estimated GFR calculator in clinical practice) to identify patients at risk of subsequently developing nephropathy is necessary to achieve this goal. Our case highlights that educated patients' awareness of the effects of adequate diet and exercise on their condition gives a better result than all other means in preventing the development and progression of nephropathy in obese type 2 diabetics. All patients with severe obesity should be advised about these measures. Thus, although the individual risk for developing obesity-associated nephropathy is low [9], the cumulative impact of obesity on the public health is large because of its wide prevalence.

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