



EFFECTS OF AGGRESSIVE APPROACH TO THE MULTIPLE RISK FACTORS FOR DIABETIC NEPHROPATHY ON PROTEINURIA REDUCTION IN DIABETES TYPE 2 PATIENTS

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ABSTRACT

Dietary interventions with protein and salt restriction, good glucose control, smoking cessation, aggressive blood pressure control, good control of cholesterol and triglycerides, use of ACE inhibitors and ARBs can delay the progression of diabetic nephropathy.

The aim of this study was to present the effects of aggressive treatment of the multiple risk factors for diabetic nephropathy on proteinuria in patients with type 2 diabetes. In this study we included 15 patients with diabetes type 2 and insufficient regulation of glycaemia. The patients were followed for three months period. Glycated haemoglobin (HbA_{1c}), fasting plasma glucose (FPG), postprandial plasma glucose (PPG), blood pressure, cholesterol and triglycerides and proteinuria were followed prior and after the study. Prior the study patients were treated with premix insulin divided in two daily doses + metformin after the lunch and they had insufficient regulation of glycaemia. During the study patients were treated with one daily dose of basal insulin, three doses of metformin (2550 mg), one daily dose of atorvastatin (20 mg) and one daily dose of ramipril (5 to 10 mg). Doses of insulin were titrated separately for each patients (0,7-1,0 IU/kg). Patients were advised to start with lifestyle modification, increased physical activity and dietary interventions with protein and salt restriction, energy restricted diet and smoking cessation. A total of 20 patients (male 12 and female 8) with diabetes type 2 were studied. The mean age of the subjects was 53±5,25 years. The mean diabetes duration was 4,05±1,96 years. The mean body mass index decreased from 28,1±1,67 kg/m² to 25,9 ±1,22 kg/m² after the study. Mean HbA_{1c} decreased from 8,82 ± 0,53 % to 7,15 ± 0,23 % (p<0,05). Mean fasting glycemia decreased from 8,79±0,58 mmol/dm³ to 7,03±0,18 mmol/dm³ (p < 0,05). Mean postmeal glycemia decreased from 9,93 ± 0,77 mmol/dm³ to 7,62 ± 0,42 mmol/dm³ (p<0,05). The mean cholesterol level decreased from 7,99 ±0,64 mmol/dm³ to 5,93 ±

0,65 mmol/dm³ (p<0,05). The mean triglycerides level decreased from 4,05 ± 0,97 mmol/dm³ to 1,96 ± 0,24 mmol/dm³ (p<0,05). The significant decrease of proteinuria was recorded, prior the study the mean albuminuria was 1,05 ± 0,31 g/dm³ and after the study was 0,07 ± 0,145 g/dm³ (p<0,05). Mean blood pressure prior the study was 153±8,69/91,5 ± 3,78 mm Hg (p<0,05), after the study was 125 ± 6,32/ 79,25±3,26 mmHg.

Effective control of glycaemia, blood pressure, cholesterol and triglycerides, use of ACE inhibitors, dietary interventions with protein and salt restriction, smoking cessation, can delay the progression of nephropathy in type 2 diabetes.

KEY WORDS: diabetes type 2, diabetic nephropathy, proteinuria reduction

INTRODUCTION

Diabetes mellitus is leading cause for diabetic nephropathy and it is strong risk factor for end stage of renal disease. The prognosis of diabetic patients with nephropathy is very bad due to cardiovascular disease which is leading course for mortality in this population. Diabetic nephropathy is manifested by proteinuria. Prevalence of proteinuria is the same in both types of diabetes. Improved glycemic control, aggressive control of hypertension and dyslipidemia can reduce the incidence of end stage renal disease in both types of diabetes (1). 35% - 57% of type 1 and 25% - 46% of type 2 patients with long lasting diabetes, develop nephropathy, indicated by proteinuria (2). The results of recent prospective studies present that good glycemic control can reduce microalbuminuria in patients in the early stage of diabetes. ACE inhibitors and angiotensin II receptor blockers in clinical trials reduced microalbuminuria in diabetic patients in the absence of hypertension (3). Long term clinical studies which included patients with type 1 and 2 diabetes have documented the beneficial effects of glucose control, blood pressure and serum cholesterol control in improving of urinary protein level (4). The United Kingdom Diabetes Study showed that the treatment for establishing good glycemic control was less important then the achieving good control, with HbA_{1c} less than 7% and preprandial glucose in the range of 6,1 mmol/dm³ to 7,2 mmol/ dm³. Tight glycemic control can reduced the incidence for diabetic nephropathy for 50% (5). Hypertension and microalbuminuria is presented in almost 50% of persons at the time of diagnosis of type 2 diabetes, therefore detection and treatment of proteinuria is very important for prevention of diabetic nephropathy and end stage of renal disease (6).

The aim of this study was to present the effects of aggressive treatment of the multiple risk factors for diabetic nephropathy (dietary interventions with protein and salt restriction, good glycemic control, smoking

cessation, aggressive blood pressure control, good control of cholesterol and triglycerides, use of ACE inhibitors) on proteinuria in patients with type 2 diabetes.

MATERIAL AND METHODS

A total of 20 (male 12 and female 8) patients with diabetes type 2 were studied. The patients were followed for six months period. Glycosilated haemoglobin (HbA_{1c}), body mass index (BMI), fasting plasma glucosae (FPG), postprandial plasma glucose (PPG), blood pressure, cholesterol and triglycerides and proteinuria were followed prior and after the study. The mean age of the subjects was 53±5,25 years. The mean diabetes duration was 4,05±1,96 years. The mean body mass index decreased from 28,1±1,67 kg/m² to 25,9 ±1,22 kg/m² after the study. Prior the study patients were treated with premix insulin divided in two daily doses + metformin after the lunch and they had insufficient regulation of glycaemia. During the study patients were treated with one daily dose of basal insulin, three doses of metformin (2550 mg), one daily dose of atorvastatin (20 mg) and one daily dose of ramipril (5 to 10 mg). Doses of insulin were titrated separately for each patient (0,7- 1,0 IU/kg). Patients were advised to start with lifestyle modification, increased physical activity and dietary interventions with protein and salt restriction, energy restricted diet and smoking cessation. Doses of insulin were titrated separately for each patients (0,7- 1,0 IU/kg).

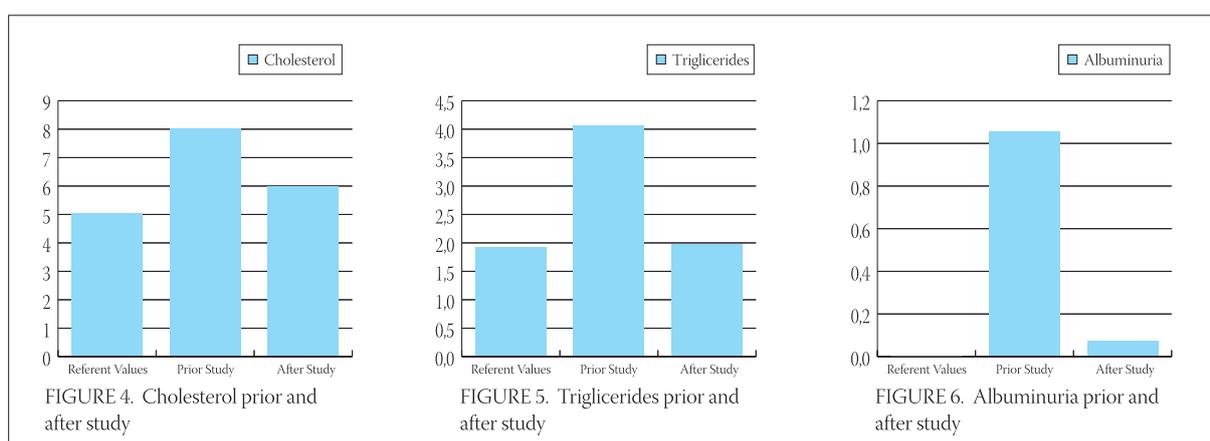
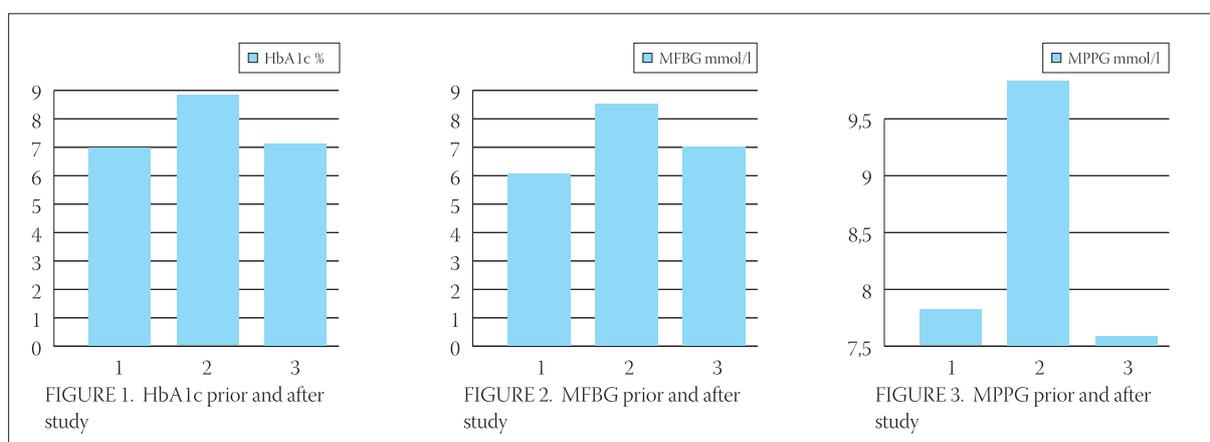
RESULTS

After six months of treatment with one daily dose of basal insulin, three doses of metformin (2550 mg), one daily dose of atorvastatin (20 mg) and one daily dose of ramipril (5 to 10 mg) significant decrease was observed in fasting glucose, postmeal glucose level, glycosilated haemoglobin, blood pressure and proteinuria level. Weight reduction, holesterol, and tryglicerides level were recorded after the study. A total of 20 patients (male 12 and female 8) with diabetes type 2 were studied. The mean age of the sub-

jects was $53 \pm 5,25$ years. The mean diabetes duration was $4,05 \pm 1,96$ years. The mean body mass index decreased from $28,1 \pm 1,67$ kg/m² to $25,9 \pm 1,22$ kg/m² after the study. Mean HbA_{1c} decreased from $8,82 \pm 0,53$ % to $7,15 \pm 0,23$ ($p < 0,05$), Table 1., Figure 1. Mean fasting glycemia decreased from $8,79 \pm 0,58$ mmol/dm³ to $7,03 \pm 0,18$ mmol/dm³ ($p < 0,05$), Table 1., Figure 2. Mean postmeal glycemia decreased from $9,93 \pm 0,77$ mmol/dm³ to $7,62 \pm 0,42$ mmol/dm³ ($p < 0,05$), Table 1., Figure 3. The mean cholesterol level decreased from $7,99 \pm 0,64$ mmol/dm³ to $5,93 \pm 0,65$ mmol/dm³ ($p < 0,05$), Table 2., Figure 4. The mean triglycerides level decreased from $4,05 \pm 0,97$ mmol/dm³ to $1,96 \pm 0,24$ mmol/dm³ ($p < 0,05$), Table 2., Figure 5. The significant decrease of proteinuria was recorded, prior the study the mean albuminuria was $1,05 \pm 0,31$ g/dm³ and after the study was $0,07 \pm 0,145$ g/dm³ ($p < 0,05$), Table 2., Figure 6. Mean blood pressure prior the study was $153 \pm 8,69/91,5 \pm 3,78$ mm Hg ($p < 0,05$), after the study was $125 \pm 6,32/79,25 \pm 3,26$ mmHg, Table 2 Figure 7, 8.

Parameters	Referent Values	Prior Study	After Study
HbA _{1c} %	7	8,82	7,15
MFBG mmol/dm ³	6,1	8,79	7,03
MPPG mmol/dm ³	7,8	9,93	7,62

TABLE 1. Group of patients treated with one daily dose of basal insulin analog + metformin



DISCUSSION

Type 2 diabetes is ever-growing health problem in the world. It is expected that around 330 millions people will be affected by the year 2025. Development of macrovascular and microvascular complications in patients with diabetes mellitus type 2 is proportionally to the level of morbidity and mortality in this population.

Prevention and delay of late complications of diabetes is important for this population. Good treatment of the risk factors such as glycaemia, hypertension and dyslipidemia, with life style modification could prevent micro and macrovascular complications in this population. In the United States there are about 400.000 patients with end stage renal disease. Diabetes mellitus is risk factor for renal disease and 40% of end

Parameters	Referent Values	Prior Study	After Study
Cholesterol	5,0	7,99	5,93
Triglycerides	1,9	4,05	1,96
Systolic Blood Pressure	120	153	125
Diastolic Blood Pressure	80	91,5	79,25
Albuminuria	0	1,05	0,07

TABLE 2. Level of cholesterol, triglycerides, albuminuria, blood pressure prior and after the study

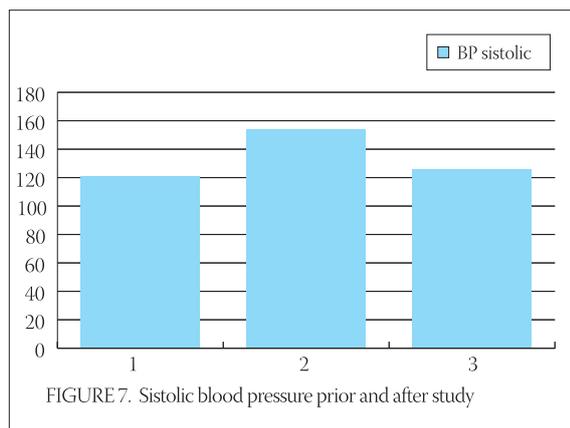


FIGURE 7. Systolic blood pressure prior and after study

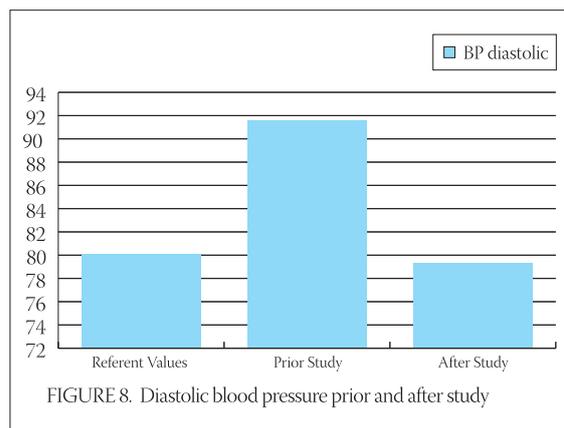


FIGURE 8. Diastolic blood pressure prior and after study

stage renal disease is caused by diabetes mellitus. Diabetic nephropathy is microvascular complication which is common for both types of diabetes. The amount of proteinuria is predictor for diabetes nephropathy progression and for development of cardiovascular diseases. ACE inhibitors and ARBs can reduce the progression of albuminuria in both types of diabetes and they become a gold standard treatment in diabetic patients with hypertension or albuminuria (7, 8). Blood pressure lowering and antiproteinuric effects of the antihypertensive medications (ACE inhibitors) can be supported by salt restriction diet (9). World Health organization recommend for screening for microalbuminuria at least yearly for all pa-

tients with type 1 of more than five years duration and age above 12, and all patients with type 2 at the diagnosis until age 70. If abnormal it should be confirmed by repeat testing and repeated every 6 months. USA National Kidney Foundation recommend at least a yearly screening for microalbuminuria in patients with diabetes mellitus, in first morning urine or random urine sample. Positive result should be confirmed (10). In our study we improved control of glycaemia, hypertension, albuminuria, and dyslipidemia by using of basal insulin analogue and metformin, ACE inhibitors, atorvastatin, dietary interventions with protein and salt restriction, smoking cessation. Long term prospective studies have documented the beneficial effects of targeting these risk factors for prevention of diabetic nephropathy.

CONCLUSION

Effective control of glycaemia, blood pressure, cholesterol and triglycerides, use of ACE inhibitors, dietary interventions with protein and salt restriction, smoking cessation, can delay the progression of nephropathy in type 2 diabetes.

List of Abbreviations

HbA _{1c}	-	glycated haemoglobin
BMI	-	body mass index
MFBG	-	mean fasting blood glycaemia
MPPG	-	mean postprandial blood glycaemia
ARBs	-	angiotensin II receptor blockers
ACE inhibitors	-	angiotensin converting enzyme inhibitors

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