

Effect of weight reduction on renal function through plant based versus animal based diet on type 2 diabetes mellitus with micro- albuminuria

Abstract

Background: Obesity with type 2 diabetes and albuminuria is associated with glomerular dysfunction and rapid deterioration of glomerular filtration rate (GFR).

Objective: To determine the effect of weight reduction in obese type 2 diabetics with microalbuminuria on renal functions using two different modalities of diet according to the source of protein whether animal or plant source.

Design: One year prospective Randomized controlled dietary intervention study comparing two controlled diet regimen using animal-based protein or plant-based protein diet in order to weight loss through caloric restriction.

Subjects: 72 obese patients with type 2 diabetes and microalbuminuria were enrolled in this study and then they were randomly divided into 2 groups according to the types of diet regimen; Group 1 with Plant Based protein regimen and Group 2 with Animal Based protein regimen. Both groups were followed and evaluated at baseline, one month and 12 months after enrollment in this study.

Results: At the end of the study, weight reduction through plant-based protein diet is associated with statistically significant improvement of eGFR and level of Albuminuria more than weight reduction-using animal based protein regimen ($p<0.001$). There was statistically significant improvement in diabetes control and lipid profiles in both patients groups ($p<0.001$).

Conclusion: Change in the source of protein in weight-loss diet in obese diabetic patient with chronic kidney disease (CKD) leads to better improvement in renal function and delays progression to end stage renal disease without adverse outcomes.

Keywords: obesity; glomerular filtration rate; plant-based protein

Abbreviations: GFR, glomerular filtration rate; CKD, chronic kidney disease; eGFR, estimated GFR; ACE, angiotensin converting enzyme; PP, plant-based protein; AP, animal-based protein; MDRD, modification of diet in renal disease

Introduction

Obesity has been linked to deterioration of kidney disease as assessed by decline of glomerular filtration rate (GFR).¹ Microalbuminuria has been considered an early sign of chronic kidney disease (CKD) and a predictor of deterioration to end stage renal failure.² In addition, CKD manifesting with microalbuminuria is a risk factor for mortality and morbidity from coronary vascular diseases, hypertension and diabetes.³ The degree of obesity is associated with the magnitude of microalbuminuria.⁴ Microalbuminuria is one of the risk factor in type 2 diabetes for progression to diabetic nephropathy.⁵ Surgical weight reduction can normalize glomerular hyper filtration and the albumin excretion rate in morbid obesity,⁶ also weight reduction trials through using different diet regimen demonstrated benefits in controlling albuminuria and improvement of the estimated GFR (eGFR) in patients with pre-existing CKD, and preventing further decrease in kidney function.⁷ Some treatments can delay the increase of micro albuminuria including use of Angiotensin converting Enzyme (ACE) inhibitors and/or angiotensin II receptor blockers.⁸ Also, blood glucose control has great benefits in controlling progression of microalbuminuria in diabetic patients.⁹ The effect of decreasing the amount of dietary protein intake to at least 0.8–1.0 g/

kg body wt/day is more questionable and difficult for application.¹⁰ Studies performed in normoalbuminuric individuals with diabetes have suggested that changing the composition of the diet by altering the source of protein from animal to plant up to 4 weeks might produce beneficial renal protection.¹¹

However, in another study, individuals with type 1 or type 2 diabetes and microalbuminuria showed no significant change in renal function when given plant-based protein (PP) versus animal-based protein (AP).¹² In addition to having a possible renal benefit, plant-based diets reduce total and LDL cholesterol.¹³ High-protein low-carbohydrate diets are adversely affecting kidney function, especially among patients with diabetes. Another study showed that a high-protein low-carbohydrate weight loss diet was not associated with harmful effects on GFR and albuminuria compared with a low-fat diet. In our study we hypothesized that loss of weight through normal protein diet from plant-based protein will have more beneficial renal effect than loss of weight through animal-based protein in obese patients with type 2 diabetes and microalbuminuria.

Subjects and methods

Subjects

80 type 2 diabetic overweight and obese patients (BMI 25–30 kg/m² and >30 kg/m² respectively) were selected for this study. Inclusion criteria were the presence of micro albuminuria and eGFR more than 30 mL/min/1.73 m².⁸ patients were excluded due to non-compliance

to plant-based protein diet so the total numbers of patients who completed our study was 72 patients. They were enrolled from either diabetes and nephrology clinics at Zagazig university hospitals or who were admitted to internal medicine department during the period between May 2015 and April 2016. Exclusion criteria: We excluded patients with advanced CKD (eGFR below 30 ml/ min/1.73m²), hypertension, liver dysfunction, advanced cancer and other different causes of microalbuminuria.

After Enrollment, patients were randomly divided into 2 groups according to the types of diet regimen; Group 1 with Plant Based protein regimen and Group 2 with Animal Based protein regimen. Both groups were followed and evaluated at baseline, one month and 12 months after enrolment in this study see Figure 1. All patients underwent general examination including history, physical examination and blood tests; the medical history was performed to discover previous disorder primarily or metabolic diseases, the physical examination included inspection of general condition, blood pressure measurement and heart, lung and abdominal examination.

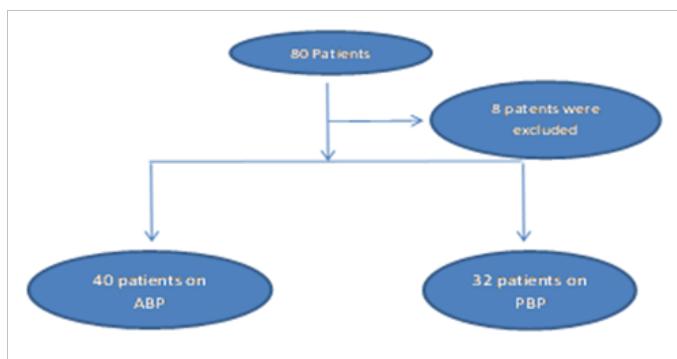


Figure 1 Patient's selections and groups.

Laboratory investigations

Blood biomarkers were analyzed in Zagazig university lab. Blood samples were drawn at 8AM after twelve hour fast at the beginning of the study and after twelve months. Albumin (ALBT2, Tinaquant, Roche, Germany) Serum glucose levels, HbA1C, total, HDL-, and LDL-cholesterol, triglycerides were measured with enzymatic assays using the automated Roche/Hitachi Cobas System (Roche, Germany). Body weight was measured to the nearest 0.1 kg without shoes. Height was measured to the nearest millimeter with the use of a wall-mounted stadiometer at baseline for BMI determination. Serum creatinine (Cr) levels were assayed by kinetic colorimetric Jaffe method. The sensitivity of the assay was 0.2 mg/dL [0.2 to 1.5 mg/dL]. The estimated GFR calculated in mL/min/1.73m² using the revised "175" Modification of Diet in Renal Disease (MDRD) study equation was; 175 (standardized serum creatinine (Scr) in mg/dL)^{-1.154} x (Age)^{-0.203} x 0.742 with creatinine values entered in mg/dL into the equation.¹⁴ Urine albumin was measured by an immunoturbidimetric method (Dako A/S, Glostrup, Denmark).

Diet

According to the source of protein in diet we divided our patients to two groups; the first group has 32 patients (plant-based protein diet) and the second has 40 patients (animal-based protein). Diet was designed to provide low caloric diet 25% fat, 20% protein with average protein intake 1.5 gm/kg/day.

Statistical analysis

Quantitative variables are presented as the means \pm standard deviation, and the qualitative variables are presented as proportions. Statistical analysis was conducted using SPSS version 17. Comparison of continuous data was performed utilizing student t test, while categorical data were done using Chi-square test. P value less than 0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the institutional review board of the faculty of Medicine, Zagazig University, Egypt. All patients gave written informed consent to participate in the study and for performing all relevant interventions.

Results

In both groups of patients, Group 1 (plant-based protein diet) and Group 2 (Animal-based protein diet), they were subdivided into 2 subgroups according to eGFR. The first subgroup is eGFR between 30-59 ml/ min/1.73 m² and the second subgroup is eGFR >60 ml/ min/1.73m². Table 1 shows basal characteristic of all groups. During follow up, there was highly significant gradual loss of weight reached an average of 8.9 ± 8.2 kg for the plant-based protein diet group and 7.8 ± 6.5 kg for the animal-based protein diet group ($p = 0.001$). Serum glucose and HbA1C significantly improved in both groups and accordingly, most of glucose lowering medications was readjusted. Also, there was highly significant improvement in lipid parameters in both groups ($p = 0.001$) See Tables 2 & 3.

GFR changes after 12 months follow up period: see Table 2 & Table 3

In patients with preexisting CKD stage 2 (eGFR >60 min/1.73m²), there was significant improvement of eGFR after weight-loss from 77 ± 13.2 to 92 ± 11.2 ml/ min/1.73 m² ($p < 0.001$) in plant-based protein group, also there was significant improvement in eGFR from 75 ± 18.2 to 81 ± 8.2 ($p < 0.05$) in animal-based protein group. In patients with preexisting CKD stage 3 (eGFR (30-59 ml/ min/1.73 m²), there was significant improvement of eGFR from 51 ± 8.2 to 66 ± 9.2 ($p < 0.001$) in plant-based protein group. However, no significant changes were found in eGFR in animal-based protein group ($p = 0.21$).

Microalbuminuria after 12 months follow up periods

There was significant decrease of microalbuminuria in plant-based protein diet group in CKD stage 2 from 20.1 ± 30 to 15 ± 21.2 mg/d ($p < 0.001$). While there was no significant difference in patients with CKD stage 3 ($p = 0.5$). There were also no significant differences in animal-based protein diet group both in 2 and 3 stages of CKD ($p = 0.09$) and ($p = 0.61$) respectively see Tables 2 & 3.

Diabetic control

In both diet groups, there was significant improvement of HbA1C ($p < 0.001$). This is due to loss of weight not related to the source of protein in diet see Tables 2 & 3.

Lipid profile

There was significant improvement in total cholesterol, HDL, LDL and TG in both groups ($p < 0.001$) and it is mostly not related to the diet type, but to the weight loss see Tables 2 & 3.

Table 1 Baseline characteristics of the studied groups

Group 1 (PBP) n=32		Group 2 (ABP) n=40		
Parameter	eGFR (30-59mL/min/1.73 m ²)	eGFR ≥60 mL/min/1.73 m ²	eGFR (30-59mL/min/1.73 m ²)	eGFR ≥60 mL/min/1.73 m ²
eGFR mL/min/1.73 m ²	51±8.2	77±13.2	49±9.1	75±18.2
Age Year	50±6	49±5	52±9	44±13
Gender F/M	11-Apr	12-May	6-Apr	18-Dec
BMI (kg/m ²)	29±2.5	30±3.1	28±3.8	31±2.1
LDL mmol/L	114±31.2	119±25.6	116±30.9	120±35.2
HDL mmol/L	35.9±7.1	34.1±8.2	35.2±11.2	33.1±5.6
TG mmol/L	179±78.1	181±90.9	178±91.7	190±62.7
Urine Albumin mg/d	25.9±61.2	37.8±70.5	20.1±30	41±71.2

Table 2 Comparison between basal and after 12 months parameters according to eGFR in plant-based protein diet group

	eGFR (30-59 mL/min/1.73 m ²) (n=15)			eGFR ≥60 mL/min/1.73 m ² (n=17)		
	Basal	After 12 Months	P value	Basal	After 12 Months	P value
eGFR	51±82	66±9.2	<0.001	77±13.2	92±11.2	<0.001
BMI	29±2.5	22±2.1	<0.001	30±31	23±2.5	<0.001
Urine Albumin	25.9±61.2	22.1±49.2	0.5	20.1±30	15±21.2	<0.001
LD	114±31.2	99±22.8	<0.001	119±25.6	100±11.8	<0.001
HDL	35.9±7.1	39.1±8.2	<0.001	35.2±11.2	40.1±12.1	<0.001
TG	179±78.1	120±81.2	<0.001	181±70.5	125±61.3	<0.001
HbA1C	9.2±2.5	6.1±1.5	<0.001	9.4±1.5	6.2±1	<0.001

Table 3 Comparison between basal and after 12 months parameters according to eGFR in animal-based protein diet group

	eGFR (30-59 mL/min/1.73 m ²) (n=10)			eGFR ≥60 mL/min/1.73 m ² (n=30)		
	Basal	After 12 Months	P value	Basal	After 12 Months	P value
eGFR	49±9.1	52±8.2	0.21	75±18.2	81±18.2	<0.005
BMI	28±3.8	22±2.5	0.001	31±2.1	23±1.8	<0.001
Urine Albumin	20.1±30	18.2±40	0.61	41±71.2	36±61.1	0.09
LDL	116±30.9	101±21.2	<0.001	120±35.2	98.9±31.1	<0.001
HDL	35.2±11.2	41.1±8.1	<0.001	33.1±5.6	40.2±5.1	<0.001
TG	178±91.7	120±71.2	<0.001	190±62.7	110±70.1	<0.001
HbA1C	9.5±1.8	7±1.2	<0.001	9.1±2.1	6.5±1.1	<0.001

Discussion

In this study we described the effect of weight loss through animal-based versus plant-based protein diet on renal function in patients with type 2 diabetes and microalbuminuria. We found that loss of weight through both diet regimens showed improvement in eGFR but the greatest improvement occurred in plant-based protein diet regimen and it was more prominent in patients with mild renal impairment (eGFR ≥60 mL/min/1.73m²) than in patients with moderate renal impairment (eGFR (30-59 mL/min/1.73m²). Though over one year period weight loss through normal amount of protein is not harmful

and beneficial, however longer follow up is needed to confirm these effects. Decrease caloric intake improves renal function regardless of the amount of dietary protein in unilaterally nephrectomized hypertensive rats.¹⁵

The effect of energy restriction on changes in albuminuria in overweight and obese patients has been studied and showed decrease in protein excretion between 30% and 80% in comparison with the baseline after weight loss in non-diabetics.¹⁶ Also there was a decrease in protein excretion related to weight loss found in 22 obese diabetic nephropathy patients.¹⁷ Thus we would expect that if weight loss is

maintained, the future risk of obesity on more sever renal disease should be reduced. A previous study lasting for a week in type1 diabetes patients found that eGFR and urinary albumin excretion were lower with plant protein compared with animal protein diet.

Another study on advanced diabetic nephropathy (serum creatinine between 1 and 2.5 mg/d and with macroalbuminuria) during seven weeks of 65% vegetarian diet in comparison with 70% animal-based diet showed reduced urinary albumin excretion.¹⁸ Another study showed improved kidney function while their patients were or mainly protein based diet.¹⁹ Our results are compatible with their findings, and we found more dramatic improvement in urinary protein excretion in weight-loss plant-based protein diet after one year and this may be due to the pure plant protein diet used in our study. Taking together, plant-based protein diet maybe beneficial for the control of albuminuria in type 2 diabetic patients with chronic kidney disease. The mechanism of beneficial effect of plant-based protein over animal-based protein maybe due to the distribution of amino acids between diets or due to improved phosphorus homeostasis in plant-based protein diet.²⁰

We found that HbA1C and dyslipidemia improved dramatically with each diet. The improvement in both groups maybe due to decrease in total caloric intake leading to weight loss rather than the source of protein in diet. Dietary recommendations for chronic kidney disease are confusing, we can simplify the approach by asking patients to eat more plant-based food and less prepared food and less meat, which can lead to increase dietary compliance and improve or delay progression of CKD.²¹ This study has some benefits as it is accurately designed and the patients groups were well selected and randomised into 2 groups with follow up periods up to one year. However, its main limitation is the small number of patients enrolled in this study.

Conclusion

Weight reduction through plant-based protein diet improves eGFR and albuminuria in patients with type 2 diabetes with microalbuminuria, especially in mild chronic kidney disease. However because of the limited sample size of our study, the effect of weight reduction on kidney function should be further examined in a prospective design with a larger number of subjects.

Acknowledgments

None.

Conflicts of interest

The author declares there is conflict of interest.

References

1. Wahba IM, Mak RH. Obesity and obesity-initiated metabolic syndrome: mechanistic links to chronic kidney disease. *Clin J Am Soc Nephrol*. 2007;2(3):550–562.
2. Keane WF, Eknayan G. Proteinuria, albuminuria, Risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. *Am J Kidney Dis*. 1999;33(5):1004–1010.
3. Asselbergs FW, Dierckx GF, Hillege HL, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. *Circulation*. 2004;110:2809–2816.
4. Praga M, Morales E. Obesity, proteinuria and progression of renal failure. *Curr Opin Nephrol Hypertens*. 2006;15(5):481–486.
5. Gerstein HC, Mann JFE, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and non diabetic individuals. *JAMA*. 2001;286(4):421–426.
6. Navaneethan SD, Yehnert H. Bariatric surgery and progression of chronic kidney disease. *Surg Obes Relat Dis*. 2009;5(6):662–665.
7. Navaneethan SD, Yehnert H, Moustarah F, et al. Weight loss interventions in chronic kidney disease: a systematic review and meta-analysis. *Clin J Am Soc Nephrol*. 2009;4(10):1565–1574.
8. Parving HH, Lehnert H, Brochner-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med*. 2001;345(12):870–878.
9. The Diabetes Control and Complications Trial Research Group. Effect of intensive therapy on the development and progression of diabetic nephropathy in the Diabetes Control and Complications Trial. *Kidney Int*. 1995;47(6):1703–1720.
10. Franz MJ, Bantle JP, Beebe CA. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications (Technical Report). *Diabetes Care*. 2002;25:148–198.
11. Kontessis PA, Bossinakou I, Sarika L, et al. Renal, metabolic, and hormonal responses to proteins of different origin in normotensive, nonproteinuric type I diabetic patients. *Diabetes Care*. 1995;18(9):1233–1240.
12. Nakamura H, Takasawa M, Kasahara S, et al. Effects of acute protein loads of different sources on renal function of patients with diabetic nephropathy. *Tohoku J Exp Med*. 1989;159(2):153–162.
13. Hermansen K, Sondergaard M, Hoie L, et al. Beneficial effects of a soy-based dietary supplement on lipid levels and cardiovascular risk markers in type 2 diabetic subjects. *Diabetes Care*. 2001;24(2):228–233.
14. Mathew TH, Johnson DW, Jones GR. Australasian Creatinine Consensus Working Group (2007) Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: revised recommendations. *Med J Aust*. 1999;187(8):459–463.
15. Reisin E, Harris KY, Azar S, et al. A low-calorie unrestricted protein diet attenuates kidney damage in uni- nephrectomized spontaneously hypertensive rats. *Am J Nephrol*. 1999;19(3):433–440.
16. Morales E, Valero MA, Leon M, et al. Beneficial effects of weight loss in overweight patients with chronic proteinuric nephropathies. *Am J Kidney Dis*. 2003;41(2):319–327.
17. Saiki A, Nagayama D, Ohhira M, et al. Effect of weight loss using formula diet on renal function in obese patients with diabetic nephropathy. *Int J Obes (Lond)*. 2005;29(9):1115–1120.
18. Azadbakht L, Esmaillzadeh A. Soy-protein consumption and kidney-related biomarkers among type 2 diabetics: A crossover randomized clinical trial. *J Ren Nutr*. 2009;19(6):479–486.
19. Jibani MM, Bloodworth LL, Foden E, et al. Predominantly vegetarian diet in patients with incipient and early clinical diabetic nephropathy: effects on albumin excretion rate and nutritional status. *Diabet Med*. 1991;8(10):949–953.
20. Moe SM, Zidehsarai MP, Chambers MA, et al. Vegetarian Compared with Meat Dietary Protein Source and Phosphorus Homeostasis in Chronic Kidney Disease. *Clin J Am Soc Nephrol*. 2011;6(2):257–264.
21. Sherman RA, Mehta O. Dietary phosphorus restriction in dialysis patients: Potential impact of processed meat, poultry, and fish products as protein sources. *Am J Kidney Dis*. 2009;54(1):18–23.