# Diet Therapy With Diacylglycerol Oil Delays the Progression of Renal Failure in Type 2 Diabetic Patients With Nephropathy

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Diet therapy for diabetic nephropathy is important in preventing the progression of renal failure by controlling hyperglycemia, hypertension, hyperlipidemia, and obesity (1,2). Edible oil containing mainly diacylglycerol (DAG) oil, compared with conventional triacylglycerol oil, has been reported to possess unique nutritional properties with respect to serum lipids and body fat metabolism (3–6). We previously reported that a 3-month intake of DAG oil significantly reduced fasting serum triglycerides in subjects of type 2 diabetes with hypertriglyceridemia (7).

In the present study, we conducted a further clinical study for 6 months with an additional 3-year follow-up period to investigate the long-term effects of DAG oil in dietary therapy in subjects with type 2 diabetes with nephropathy.

## RESEARCH DESIGN AND METHODS

— The subjects were 15 outpatients (aged 47–77 years) at the Itami City Hospital who were diagnosed with type 2 diabetes in stage IIIb (macroalbuminuric stage with renal dysfunction; $n = 2$) and stage IV (renal failure stage; $n = 13$) according to the classification of diabetic nephropathy (Ministry of Health and Welfare, Japan) (8) who were receiving nutritional counseling for 13 months on average. The duration of diabetes was 18.2 ± 7.8 (range 5–28) years. Subjects were fully informed of the study and provided signed consent forms to the investigator. The study was conducted in a single-center, open-labeled, parallel design. After a 1-month lead-in period, the subjects were divided into either a DAG group ($n = 8$) or a control group ($n = 7$). The subjects in the DAG group were requested to replace the usual cooking oil used at home with the DAG oil prepared as previously described (7), whereas subjects in the control group were asked to use their usual cooking oil containing mainly triacylglycerol for 6 months. The target intake for both types of cooking oils was 10 g per day. Dietary instructions were provided to the participants each month. The target energy and protein intake were 30 kcal/kg and 0.8 g/kg of their ideal body weight ($22 \times H^2$, where H is the height in meters), respectively. Blood samples were collected after fasting for ~12 h and measured by standard laboratory procedures.

After the 6-month treatment period, DAG oil was recommended for all subjects and the same measurements were continued for 3 years in a follow-up study.

All data are expressed as means ± SD. A paired *t* test was used to assess changes from the baseline. Differences between the groups in percent changes from the baseline at 6 months were assessed by the Student's *t* test. A value of $P < 0.05$ was considered statistically significant. Analyses were performed using SPSS (version 11.0; SPSS, Chicago, IL).

## RESULTS

— No significant differences in the duration of diabetes, the stages of nephropathy, or other measurements at baseline were found between the groups. The type and dose of the medications were not changed during the study period.

The results of measurements during the 6-month study are shown in Table 1. In the DAG group, body weight, BMI, and serum triglyceride levels were significantly decreased from the baseline to 6 months, and the percent changes were significantly different between the groups. The DAG group maintained their serum creatinine levels during the study period, whereas the control group was significantly increased from the baseline. There were no significant changes in the other measurements.

In a 3-year follow-up period after the 6-month treatment, eight subjects in the DAG group continued to use DAG oil. Two subjects in the control group switched their cooking oil to DAG oil, and the remaining five subjects continued to use their usual cooking oil. Three of five subjects who continued to use their usual cooking oil started hemodialysis (1.5, 2.2, and 2.5 years after the treatment period) and the other two subjects died of heart failure (1.8 and 2.5 years). In the subjects who used DAG oil in the follow-up period, 2 of 10 started hemodialysis (at 2.5 and 2.8 years). The remaining eight subjects maintained their renal function at a level requiring no dialysis.

## CONCLUSIONS

— Consistent with the previous study (7), DAG oil consumption significantly reduced fasting serum triglyceride levels in subjects with type 2 diabetes with nephropathy. The delayed

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**Abbreviations:** DAG, diacylglycerol.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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**Table 1—*Clinical characteristics and laboratory data for subjects during the treatment period***

| | Control group | | | DAG group | | |
|---|---|---|---|---|---|---|
| | Baseline | 6 months | Change (%) | Baseline | 6 months | Change (%) |
| Age (years) | 66.0 ± 9.2 | | | 60.3 ± 7.0 | | |
| Sex (male/female) | 6/1 | | | 7/1 | | |
| Duration of diabetes (years) | 19.9 ± 7.4 | | | 16.8 ± 8.4 | | |
| Stage of nephropathy* | 1/6 (IIIb/ IV) | | | 1/7 (IIIb/ IV) | | |
| Weight (kg) | 66.9 ± 8.1 | 68.1 ± 8.1 | 1.9 ± 3.8 | 67.6 ± 10.9 | 64.0 ± 10.4‡ | −5.1 ± 3.7‖ |
| BMI (kg/m$^2$) | 24.6 ± 2.5 | 25.1 ± 3.0 | 1.9 ± 3.8 | 25.1 ± 4.0 | 23.8 ± 4.0‡ | −5.1 ± 3.7‖ |
| Systolic blood pressure (mmHg) | 147 ± 26 | 145 ± 21 | 1.8 ± 24.7 | 141 ± 18 | 148 ± 21 | 5.5 ± 11.1 |
| Diastolic blood pressure (mmHg) | 75 ± 18 | 78 ± 14 | 9.6 ± 35.7 | 84 ± 12 | 82 ± 15 | −3.1 ± 7.7 |
| Triglyceride (mmol/l) | 2.05 ± 0.63 | 2.08 ± 0.75 | 6.8 ± 37.0 | 2.56 ± 1.21 | 1.72 ± 0.46† | −26.5 ± 20.5§ |
| Glucose (mmol/l) | 8.3 ± 2.9 | 8.3 ± 2.3 | 2.3 ± 16.0 | 7.8 ± 3.0 | 6.7 ± 1.2 | −6.2 ± 27.0 |
| $HbA_{1c}$ (%) | 7.4 ± 2.0 | 7.3 ± 1.5 | 1.5 ± 12.4 | 7.3 ± 1.8 | 6.3 ± 1.0 | −10.4 ± 16.3 |
| Blood urea nitrogen (mmol/l) | 9.2 ± 2.6 | 9.7 ± 2.9 | 6.6 ± 19.9 | 11.1 ± 5.3 | 10.3 ± 3.0 | −1.1 ± 25.5 |
| Creatinine (μmol/l) | 164.2 ± 63.3 | 207.1 ± 89.8† | 24.4 ± 15.2 | 198.9 ± 99.2 | 189.0 ± 90.4 | −3.7 ± 18.4‖ |

Data are means ± SD. *Stages of nephropathy: IIIb, macroalbuminuric stage with renal dysfunction; IV, renal failure stage. Significantly different from the baseline to 6 months: †$P < 0.05$, ‡$P < 0.01$. Significantly different in percent changes from the baseline to 6 months between the groups: §$P < 0.05$, ‖$P < 0.01$.

progression of renal failure by DAG consumption may have resulted from the improvement in hypertriglyceridemia, a predictor of progressive renal dysfunction (9–12).

Hirano et al. (13) reported that the prevalence of dyslipidemia in diabetic nephropathy is associated with the postprandial triglyceride response. DAG oil intake has been reported to reduce the postprandial elevation in serum lipid levels compared with triacylglycerol intake (3,4). These effects were more evident in subjects with insulin resistance and type 2 diabetes (14,15). Therefore, a reduced postprandial response following DAG oil intake may contribute to an improvement in fasting serum triglyceride levels, resulting in the delayed progression of diabetic nephropathy.

It has been reported that DAG oil consumption significantly reduces body weight and body fat mass, particularly abdominal fat mass in long-term studies with mildly overweight Japanese (5) and obese Americans (6). In the present study, a significant weight loss was also observed in the DAG group. It is known that weight loss caused by an insufficient energy intake may lead to a further impairment in renal function (16,17). However, weight loss in the DAG group presumably resulted from body fat loss because subjects in the present study complied well with dietary guidance and took adequate energy, as recommended. Further investigations will be needed to clarify the relation between weight loss and the prevention of renal failure by DAG oil intake.

In conclusion, the long-term intake of DAG oil prevented the progression of renal function in the subjects of type 2 diabetes with nephropathy, delaying the onset of dialysis.

**References**


1. Strippoli GF, Di Paolo S, Cincione R, Di Palma AM, Teutonico A, Grandaliano G, Schena FP, Gesualdo L: Clinical and therapeutic aspects of diabetic nephropathy. *J Nephrol* 16:487–499, 2003
2. Wolf G, Ritz E: Diabetic nephropathy in type 2 diabetes prevention and patient management. *J Am Soc Nephrol* 14:1396–1405, 2003
3. Taguchi H, Watanabe H, Onizawa K, Nagao T, Gotoh N, Yasukawa T, Tsushima R, Shimasaki H, Itakura H: Double-blind controlled study on the effects of dietary diacylglycerol on postprandial serum and chylomicron triacylglycerol responses in healthy humans. *J Am Coll Nutr* 19:789–796, 2000
4. Tada N, Watanabe H, Matsuo N, Tokimitsu I, Okazaki M: Dynamics of postprandial remnant-like lipoprotein particles in serum after loading of diacylglycerols. *Clin Chim Acta* 311:109–117, 2001
5. Nagao T, Watanabe H, Goto N, Onizawa K, Taguchi H, Matsuo N, Yasukawa T, Tsushima R, Shimasaki H, Itakura H: Dietary diacylglycerol suppresses accumulation of body fat compared with triacylglycerol in men in a double-blind controlled trial. *J Nutr* 130:792–797, 2000
6. Maki KC, Davidson MH, Tsushima R, Matsuo N, Tokimitsu I, Umporowicz DM, Dicklin MR, Foster GS, Ingram KA, Anderson BD, Frost SD, Bell M: Consumption of diacylglycerol oil as part of a reduced-energy diet enhances loss of body weight and fat in comparison with consumption of a triacylglycerol control oil. *Am J Clin Nutr* 76:1230–1236, 2002
7. Yamamoto K, Asakawa H, Tokunaga K, Watanabe H, Matsuo N, Tokimitsu I, Yagi N: Long-term ingestion of dietary diacylglycerol lowers serum triacylglycerol in type II diabetic patients with hypertriglyceridemia. *J Nutr* 131:3204–3207, 2001
8. Shigeta Y: Classification of type 2 diabetic nephropathy. In *Report of the National Diabetes Research Group*. Tokyo, Japan, Ministry of Health and Welfare, 1992, p. 317–320 [in Japanese]
9. Smulders YM, van Eeden AE, Stehouwer CD, Weijers RN, Slaats EH, Silberbusch J: Can reduction in hypertriglyceridaemia slow progression of microalbuminuria in patients with non-insulin-dependent diabetes mellitus? *Eur J Clin Invest* 27:997–1002, 1997
10. Elisaf M, Mikhailidis DP: Statins and renal function. *Angiology* 53:493–502, 2002
11. Kim DM, Ahn CW, Park JS, Cha BS, Lim SK, Kim KR, Lee HC, Huh KB: An implication of hypertriglyceridemia in the progression of diabetic nephropathy in metabolically obese, normal weight patients with type 2 diabetes mellitus in Korea. *Diabetes Res Clin Pract* 66 (Suppl. 1): S169–S172, 2004
12. Colhoun HM, Lee ET, Bennett PH, Lu M, Keen H, Wang SL, Stevens LK, Fuller JH: Risk factors for renal failure: the WHO Mulinational Study of Vascular Disease in Diabetes. *Diabetologia* 44 (Suppl. 2):S46–S53, 2001
13. Hirano T, Oi K, Sakai S, Kashiwazaki K, Adachi M, Yoshino G: High prevalence of small dense LDL in diabetic nephropathy is not directly associated with kidney damage: a possible role of postprandial lipemia. *Atherosclerosis* 141: 77–85, 1998
14. Takase H, Shoji K, Hase T, Tokimitsu I:


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Effect of diacylglycerol on postprandial lipid metabolism in non-diabetic subjects with and without insulin resistance. *Atherosclerosis* 180:197–204, 2005
15. Tada N, Shoji K, Takeshita M, Watanabe H, Yoshida H, Hase T, Matsuo N, Tokimitsu I: Effects of diacylglycerol ingestion on postprandial hyperlipidemia in diabetes. *Clin Chim Acta* 353:87–94, 2005
16. Bailey JL, Mitch WE: Mechanisms of protein degradation: what do the rat studies tell us. *J Nephr*ol 13:89–95, 2000
17. Guarnieri G, Antonione R, Biolo G: Mechanisms of malnutrition in uremia. *J Ren Nutr* 13:153–157, 2003

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