- clinical diabetic nephropathy. *Kidney Int* **31**: 673, 1987.
- 3) Heptinstall RH. Diabetes mellitus. Pathology of the Kidney (3rd Ed.) Little Brown, Boston, 1983, p.1397.
- 4) Rao KV, Crosson JT. Idiopathic membranous glomerulonephritis in diabetic patients. *Arch Intern Med* **140**: 624, 1980.
- 5) Kasinath BS, Mujais SK, Spargo BH, Katz AI. Non-diabetic renal diseases in patients with diabetes mellitus. *Am J Med* **75**: 613, 1983.
- 6) Amoah E, Grickman JL, Malchoff CD, Sturgill BC, Kaiser DL, Bolton WK. Clinical identification of non diabetic renal diseases in diabetic patients with type I and type II disease presenting with renal dysfunction. *Am J Nephrol* **8**: 204, 1988.
- 7) Carstens SA, Hebert LA, Garancis JC, Piering WF, Lemann J. Rapidly progressive glomerulonephritis superimposed on diabetic glomerulosclerosis. *J Am Med Assoc* **247**: 1453, 1982.
- 8) Chihara J, Takebayashi S, Taguchi T, Yokoyama K, Harada T, Naito S. Glomerulonephritis in diabetic patients and its effect on the prognosis. *Nephron* **43**: 45, 1986.
- 9) Gellman DD, Pirani CL, Soothill JF, Muehrcke RC, Kark RM. Diabetic nephropathy: A clinical and pathologic study based on renal biopsies. *Medicine* **38**: 321, 1959.
- 10) Nakamoto Y, Takazakura E, Hayakawa H, et al. Intrarenal microaneurysms in diabetic nephropathy. *Lab Invest* **42**: 433, 1980.
- 11) Hall GFM. Factors in the aetiology of diabetic glomerulosclerosis. *Q J Med* **21**: 385, 1952.
- 12) Henderson LL, Sprau RG, Wagener HP. Intercapillary glomerulosclerosis. *Am J Med* **3**: 131, 1947.
- 13) Rogers J, Robbins SL, Jeghers H. Intercapillary glomerulosclerosis: A clinical and pathologic study. II. A clinical study of 100 anatomically proven cases. *Am J Med* **12**: 692, 1952.
- 14) Lambie AT, MacFarlane A. A clinico-pathological study of diabetic glomerulosclerosis. *Q J Med* **24**: 125, 1955.
- 15) Mauer SM, Steffes MW, Ellis EN, Sutherland DER, Brown DM, Goetz FC. Structural-functional relationships in diabetic nephropathy. *J Clin Invest* **74**: 1143, 1984.
- 16) Bader R, Bader H, Grund KE, Mackensen-Haen S, Christ H, Bohle A. Structure and function of the kidney in diabetic glomerulosclerosis. Correlations between morphologic and functional parameters. *Path Res Pract* **167**: 204, 1980.
- 17) Gundersen HJG, Østerby R. Glomerular size and structure in diabetes mellitus. II. Late abnormalities. *Diabetologia* **13**: 43, 1977.

---

1. Supplementary

a. Late Complications of Diabetes Mellitus: Risk Factors in Patients on Sulfonylureas for More than 10 Years

Mitsuru HOSHI and Shyunsaku FUJITA

Department of Medicine, Osaka Kosei-Nenkin Hospital, Osaka

From the time sulfonylureas (Su) were introduced into the Japanese market almost 50 yr ago, clinical experience has accumulated. Therefore it seems beneficial to evaluate Su in daily practice.

Subjects and methods

Fifty diabetic patients receiving only Su for more than 10 yr in our out-patient clinic were selected. The fasting blood glucose level on hospital visit was examined and averaged on an annual basis successively for the total observation period. Skewed Restricted Design was applied to divide the patients into three groups: adequate group (AG; average

fasting blood glucose level from 141 to 199 mg/dl throughout the period), failure group (FG; more than 200 mg/dl due to primary or secondary failure), and prefer diet group (PDG; less than 140 mg/dl, retrospectively these were concluded to switch diet alone). Among these three groups no significant differences were noted in any clinico-laboratory data except the fasting blood glucose level and HbA1 level at the time of analysis.

Results and discussion

The Markov process was applied for the estimation of the development of late complications of

diabetes. Retinopathy was graded in 4 stages: non-diabetic retinopathy (NDR), simple diabetic retinopathy (SDR), pre-proliferative diabetic retinopathy (PPDR) and proliferative diabetic retinopathy (PDR). The development of PDR was 7% at 10 yr and 33% at 20 yr in FG, however it was 0% in PDG and 4% in AG at 20 yr.

In the pilot study of macrovascular disease, ECG changes were examined. Three steps were adopted: normal ECG, arrhythmia and left ventricular hypertrophy, myocardial changes and myocardial infarction with atrial fibrillation (MC.MI.AF). MC.MI.AF was developed in 40% and 47% at 10 yr and 50% and 55% at 20 yr in PDG and FG, respectively, compared with 14% at 10 yr and 15% at 20 yr in AG.

Regarding nephropathy, proteinuria was staged: negative proteinuria, intermittent proteinuria, and persistent proteinuria. In contrast to retinopathy, persistent proteinuria developed in 13% and 14% at 10 yr and 28% and 29% at 20 yr in PDG and FG, respectively, compared with 6% at 10 yr and 12% at 20 yr in AG. According to the correlation analysis, proteinuria was correlated with HbA1 and retinopathy ($p < 0.01$) and with HDL-cholesterol, systolic blood pressure, changes in aortic arch and

ECG ($p < 0.05$). In the results of the principal component analysis, the systolic blood pressure was isolated from other factors raised in the correlation study and was strongly suspected to be an independent risk factor for the development of nephropathy. Blood pressure of PDG was not significantly different from that of AG and FG patients. Therefore PDG was examined in each patient irregardless of whether the blood pressure was elevated to 160/90. Five out of 11 were subgrouped in a hypertension group (HTG) and analyzed using the Markov process. This analysis revealed that persistent proteinuria developed in 13% at 10 yr and 28% at 20 yr, identical to the rate in total PDG.

Conclusion

Good to fair blood glucose control is necessary to prevent retinopathy. PDG with good control of the blood glucose level is recommended to examine the risk factors for macrovascular complications. For the prevention of nephropathy, the blood pressure should be managed along with the blood glucose level and antisclerotic measures should be taken.

---

1. Supplementary

b. Studies on the Cause and the Treatment of Hyporeninemic Selected Hypoaldosteronism in Diabetic Nephropathy

Soitsu FUKUCHI

The Third Department of Internal Medicine,
Fukushima Medical College, Fukushima

This study was designed to clarify the cause of hyporeninemic selective hypoaldosteronism (HSHA) associated with diabetes mellitus. One hundred and eighteen diabetic patients were divided into 4 groups: (I) 28 patients without neuropathy or nephropathy, (II) 30 patients with neuropathy and without nephropathy, (III) 21 patients without neuropathy and with nephropathy, and (IV) 39 patients with both neuropathy and nephropathy (3 HSHA were

also included). Eight normal subjects and 18 patients with chronic glomerulonephritis served as controls. In these subjects, plasma renin activity (PRA) and aldosterone (PAC) were determined before and after 2-h upright position with administration of 60 mg furosemide. Active and inactive renin contents in plasma (ARC and IRC) were estimated before and after administration of 25 mg captopril in the 4 groups of diabetic patients. The statistical correla-