COMPARATIVE STUDY OF MONOCOMPONENT INSULINS AND CONVENTIONAL INSULINS ON THE COURSE OF DIABETIC NEPHROPATHY
A Follow-up Study

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SUMMARY

Two matched groups of insulin requiring non-insulin dependent diabetic (NIDDM) patients with mild proteinuria (200 to 999 mg/day), one on mono component (MC) insulin therapy and the other on conventional insulins were studied for a 3 year period to evaluate the course of nephropathy in these two groups.

Twenty-seven and 35 patients were followed-up in the MC insulin and conventional insulin groups respectively. In the MC insulin treated group, the percentage of patients showing deterioration in proteinuria was lower (11% vs 34%, P <0.05) and the percentage showing improvement was higher (48% vs 29%) compared to the conventional insulin treated group. Insulin antibody titres decreased significantly in the MC insulin group and serum C-peptide values decreased in both groups on follow-up.

Key words: Proteinuria, C-peptide, insulin antibody.

INTRODUCTION

Proteinuria is an early sign of kidney involvement in diabetic patients. Mild proteinuria (<500 mg/day) detected early is often reversible with control of hyperglycaemia.[1,2] The clinical course of diabetic nephropathy could also be influenced by the type of drug therapy.

Monocomponent (MC) insulins are more effective in the control of blood sugars than conventional insulins due to their purity and low antigenicity.[3-5] They also help to bring down elevated insulin antibody titres. However, it is not known whether these beneficial effects have any influence on the course of diabetic complications.

In this study, two matched groups of insulin requiring non-insulin dependent diabetic (NIDDM) patients with mild proteinuria (200 to 999 mg/day), one on MC insulin therapy and the other on conventional insulins were studied for a 3 year period. The aim of the study was to see whether there was any difference in the course of nephropathy in these two groups.

MATERIAL AND METHODS

All patients had NIDDM type of diabetes but required insulin for control of diabetes. All of them were treated initially with diet and oral hypoglycaemic agents for a minimum of 10 years and later with conventional insulin for a minimum of 2 years. Patients having urinary tract infection (UTI) were not included in the study. Baseline investigations included fasting and post pran-

dial plasma glucose (Glucose Oxidase – Boehringer Kit), HbAI,[6] blood urea and creatinine,[7] creatinine clearance and 24 hour proteinuria. Urine collection was done under careful supervision as an inpatient procedure. Urine protein was estimated using the sulphosalicylic acid method. Serum C-peptide[8] and insulin antibodies[9] were estimated by radioimmunoassay (RIA). Patients were randomly distributed to either the MC insulin treated group or to the conventional insulin group. Follow-up was done for 3 years and all the investigations were repeated annually.

Blood pressure measurements were recorded at each visit and antihypertensive drugs were prescribed for all hypertensive patients. If the proteinuria decreased to < 200 mg/day during the follow up, it was considered to have 'improved'; if it remained between 201 and 999 mg/day there was 'no change'; and if it increased to more than 1 g/day it was considered as 'deteriorated'.

Statistical comparisons were done using the Student's t test.

RESULTS

Fifty patients were selected initially in each group. In the MC insulin group, 15 and 6 patients dropped out in the first and second year of follow-up respectively. Two patients died of causes unrelated to diabetes. Among those treated with conventional insulins, one patient died of heart disease and 8 and 6 patients dropped out in the first and second year of the study respectively. Thus in the MC insulin group, 27 patients, and in the conventional insulin group, 35 patients, were available for the 3 year follow-up.

The two groups were well matched for age and duration of diabetes (Table 1). Severity of diabetes was also similar in both groups. Initial C-peptide and insulin

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antibody titres were not significantly different in the two groups.

The percentage of patients showing improvement in proteinuria is higher (13; 48%) in the MC insulin group compared to that in the conventional insulin group (10; 29%), though the difference is not statistically significant. However, the percentage of patients showing deterioration is significantly lower in the MC insulin group (3; 11% vs 12; 34% P < 0.05). Eleven (41%) and 13 (37%) patients in the two groups had no change in proteinuria (P:NS).

Table 2 shows the mean values of the various biochemical parameters in the three subgroups in the MC insulin and conventional insulin treated groups. Creatinine clearance decreased significantly in the 'deteriorated' groups. Serum creatinine also increased in this subgroup among conventional insulin treated patients. Post prandial blood glucose values (PPBG) and HbAI were similar in all subgroups.

Only 11 patients in the study groups had hypertension and their blood pressure was under control throughout the study. In 3 of them, the proteinuria reverted to normal and in the other 8 patients. it continued to be in the same range.

The insulin antibody titres decreased significantly in the MC insulin treated group, whereas it showed negligible change in the other group (Table 3). C-peptide values decreased in both groups during the follow-up.

DISCUSSION

Our results suggest that MC insulin treatment is more beneficial than the conventional insulin treatment in preventing the deterioration of proteinuria in diabetes. The changes are unlikely to be related to the plasma glucose as the glucose and HbAI values were similar in all subgroups. Changes in blood pressure could affect the protein excretion significantly.[10] In this study, changes in proteinuria were not related to the changes in blood pressure as this parameter was kept normal throughout the study in all patients.

A study by us has also demonstrated that MC insulin treatment is beneficial in the treatment of diabetic retinopathy.[11]

The exact mechanism by which purified insulins exert the beneficial effect is not clear. It has been consistently observed that treatment with MC insulin reduces the anti-insulin antibody titre.[12,13] This might have some beneficial effect by reducing the harmful contribution of the immune complexes. Andersen[14] observed deleterious influence of the complexes on the development of diabetic nephropathy. Long-term studies in larger groups of patients may throw more light on this aspect.

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NEWS

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