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Monocomponent Insulin in Maturity Onset Diabetes Mellitus

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The problem of individuals suffering from maturity onset diabetes taking large doses of conventional insulin without satisfactory response is frequently met with. Many of these individuals respond well when they are put on a proper diet. In others, oral drugs may help to achieve good control. When these measures fail, management of diabetes becomes a problem. In such situations, the use of newer insulins have been a great boon.

Over the past several years attempts have been made to increase the purity of commercial insulin preparations, with the hope of eliminating the non-insulin contaminants. The potential antigens in commercial insulin are derivatives of insulin, pro-insulin and its intermediates, other hormones like glucagon, somatostatin, pancreatic polypeptide, vasoactive intestinal peptide and protamine and its contaminants. Since 1974, 'single' peak insulins are available which behave as molecules of uniform size. This contains 98% to 99% insulin as compared to 92% of standard insulin and is the purest and least antigenic form of insulin available today.

Monocomponent (MC) insulin is being used at the Diabetes Research Centre, Madras since 1976. This paper deals with the preliminary observations.

MATERIAL AND METHOD

The study group comprised 40 patients of maturity onset diabetes who were not responding to either large doses of conventional insulins (19 patients) or to insulin plus oral drugs (21 patients). Postprandial blood sugar more than 250 mg./100 ml. despite taking 80 units or more of conventional insulin was the criteria for selection of cases. There were 23 males and 17 females in the age group of 36 to 73 years.

The duration of diabetes in these patients is shown in Table 1.

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Table 1—*Showing Duration of Diabetes*

Duration	No. of patients
Less than 1 year	1
2 to 10 years	13
More than 10 years	26

Insulin antibody titres were measured in 30 patients at the start of the study by the method of Sebriakova and Little (1973) prior to treatment with MC insulin.

The dose of MÇ insulin was gradually increased wherever required to get the diabetes under control. The criteria for response is given in Table 2. The maximum dose of MC insulin employed was 80 units/day.

Table 2—*Showing Criteria and Degree of Response*

Criteria postprandial blood sugar (mg./100 ml.)	Degree of response	No of patients
< 180	Good	20 (50%)
180 - 250	Fair	12 (30%)
> 250	Poor	8 (20%)

The period of follow-up varied from 3 weeks to 2 years.

The measurement of antibody titres were repeated in 4 patients after changing over to MC insulin.

RESULTS

It was noticed that 32 patients (80%) showed satisfactory response to treatment with MC insulin (Table 2). The degree of response to MC insulin was not related either to the duration of diabetes or to the duration of previous insulin therapy.

Table 3 shows the mean fasting and post-

Table 3—*Showing Blood Sugar Values before and after MC Insulin*

	Pre-treatment	Post-treatment
Fasting blood sugar (mg./100 ml. ± SEM)	182.6± 6.8	121.7±5.8
Postprandial blood sugar (mg./100 ml. ± SEM)	312 ±11.6	196 ±7.5

prandial blood sugar values in the 40 patients, before and after treatment with MC insulin.

Table 4 shows the dose of MC insulin required for control of diabetes in 32 patients.

Table 4—*Showing Dose of MC Insulin Required*

	Dose in units			
	Up to 20	Up to 40	Up to 60	Up to 80
No. of patients	10(25%)	8(20%)	6(15%)	8(20%)

Follow-up—In patients who showed good response to MC insulin, the dose could later be reduced by at least 50%. In 12 patients, MC insulin could be withdrawn subsequently. These patients had hypoglycaemic symptoms even with small doses of MC insulin. The fasting and postprandial blood sugars were consistently under control after withdrawal of MC insulin and switching over to other modes of therapy. Of these, 2 patients could be maintained on conventional insulins, 8 on oral drugs and 2 on diet alone. This was interesting because initially all the patients had shown poor response to 80 units or more of conventional insulins.

Insulin antibody studies—The initial antibody titres measured in 30 patients showed wide variations ranging from 6 to 35.848 μu./ml. The data of 4 patients in whom the insulin antibody levels could be repeated is given in Table 5. There was an appreciable reduction in the antibody titres in all the 3 patients in whom it was raised initially.

Table 5—*Showing Follow-up Data of Insulin Antibodies*

No.	Antibody index μu./ml.		Period of follow-up	Dose of MC insulin in units per day
	Initial	Follow-up		
1.	1152	720	10 months	50
2.	591	37	2 months	20
3.	7920	5780	1 week	10
4.	12	10	4 months	20

DISCUSSION

A number of reports have appeared regarding the usefulness of MC insulin in resistant diabetes (Schlichtkrull *et al.*, 1972 ; Bruni *et al.*, 1973 ; Andreni *et al.*, 1974 ; Czyzyk *et al.*, 1974 ; Lithner, 1975 ; Teuscher, 1975). Most of these studies have been on young patients with insulin dependent diabetes. These studies have shown that in many cases, good response could be obtained with these insulins, and a 30-40% reduction in the requirement of insulin also has been reported.

The present study highlights the experience with MC insulin in patients with maturity onset diabetes where the problem of insufficient response to large doses of conventional insulins is occasionally met with.

Eighty per cent of patients who did not respond to conventional insulins showed satisfactory response to MC insulin. The requirement of MC insulin was also much smaller and 45% of patients in this study needed less than 40 units of MC insulin per day.

Insulin antibody titres measured in these patients showed that the titres were not raised in every patient who showed an unsatisfactory response to conventional insulins. There were wide variations in the initial antibody titres. However, in 4 patients in whom the authors could repeat the antibody levels after therapy with MC insulin, there was an appreciable reduction in the levels in 3 patients where it was initially raised.

An interesting observation noted in this study was that eventually in some of these patients the MC insulin had to be completely withdrawn because even small doses produced hypoglycaemia. Two of these individuals could be subsequently controlled with diet alone. A few of them responded to oral drugs and the others to conventional insulins.

Thus, in patients with maturity onset diabetes by switching over to less antigenic insulins for a period of time, it is possible to bring down or even break the immunogenic resistance.

SUMMARY

Monocomponent insulin was used in 40 diabetic patients of maturity onset type responding poorly to conventional insulins and/or conventional insulin plus oral drugs.

It was noticed that 80% of these patients responded satisfactorily to treatment with MC insulin. The degree of response was unrelated either to the duration of diabetes or to the duration of previous insulin therapy.

The dose of MC insulin used was considerably lower than that of conventional insulins and in 45% of the patients the dose needed was less than 40 units/day. In 12 patients, MC insulin could be withdrawn completely and the response maintained either with conventional insulins or oral drugs.

The response to MC insulin was unrelated to the initial insulin antibody levels. In 3 out of 4 patients in whom the antibody levels could be repeated while on MC insulin, they were found to be significantly reduced.

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