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# PANCREATIC BETA CELL FUNCTION AND PERIPHERAL ACTIVITY OF INSULIN IN MATURITY ONSET DIABETICS—EVALUATION BY MATHEMATICAL APPLICATIONS

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## SUMMARY

**Evaluation of the Pancreatic beta cell function and peripheral activity of insulin in diabetics were done using recently described mathematical formulae. Diabetics in general, had decreased beta cell function as well as impaired peripheral activity of insulin. In diabetics with ideal body weight, the chief defect was diminished insuling output which was directly proportional to the severity of diabetes. In obese diabetics, the main defect was at the periphery, and except in those with severe diabetes, beta cell function was better maintained. Application of these mathematical formulae helps in a clearer understanding of the kinetics of insulin and pathogenesis of diabetes in various types of diabetics.**

## INTRODUCTION

The common parameters employed in assessing the functions of the beta cell of the pancreas are the insulin response to glucose load, the insulin/glucose ratio (I/G) and the insulinogenic index ($\Delta$ I/$\Delta$ G). Recently, it has been demonstrated by Sluiter and associates,[1, 2] that these parameters, being dependent on the absolute blood glucose levels are liable to gross variations even in the same individual. Based on certain mathematical deductions, these authors have put forth new parameters to evaluate the B cell function, the peripheral activity of insulin and also a glucose tolerance parameter, during oral G.T.T. They have demonstrated that these parameters are reproducible and provide a glucose-independent judgement of the Insulin response.

Applying the formulae propounded by the above authors we have tried to evaluate the B cell response and the peripheral activity of insulin in different groups of diabetics.

## MATERIAL AND METHODS

One hundred newly detected maturity onset diabetics attending the Diabetes Research Centre, Madras, were taken up for this study. There were 65 men and 35 women in the age group of 30 to 60 years. None of them had received any treatment for diabetes. 78 patients were of ideal body weight (IBW) and 22 were obese. (> 115% of IBW).

Twenty normal volunteers were taken as controls. An oral glucose tolerance test was done in every individual and at the same time samples were collected for radioimmunoassay of insulin. The glucose loads given were 50 gms, 75 gms and 100 gms depending on whether the patients were lean, of IBW or obese respectively. The blood sugar was estimated by the Ortho-toluidine method.[3] Immunoreactive insulin (IRI) was measured by the method of Herbert *et al*[4] using the radio-

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immunoassay kit supplied by the Bhabha Atomic Research Centre, Bombay.

The mathematical parameters applied were the following:

(a) *The corrected Insulin Response*: (CIR) This is an evaluation of the beta cell function.

$$CIR = \frac{II \times 100}{G\ (G - 70)}$$ where I is the insulin concentration in $\mu$g/100 ml. $\mu$u/ml and G, the glucose concentration in mg/100 ml.

In this study, we have calculated the CIR at the peak glucose level (CIRp) as it usually represents the maximum response.

(b) *Peripheral insulin activity*: (*A*)

$$A = \frac{10^4}{Ip\ Gp}$$ where Ip and Gp are the insulin and glucose values at the glucose peak in $\mu$u/ml and mg/100 ml respectively.

These parameters were applied and various groups of diabetics were compared.

## RESULTS

The severity of diabetes was graded as follows based on the G.T.T. (Table 1).

The values for the insulin response in diabetics, when compared to the controls showed that both the insulin output (CIRp) and the peripheral activity of insulin (A) were low in diabetics (Table 2). The difference was highly significant statistically ($P < 0.001$).

### *Effect of Body Weight*

Body weight is known to be a major factor influencing the beta cell function. Hence diabetics with IBW and obesity were studied separately. The results are shown in Table 3.

Significant lowering of CIRp was seen in the diabetics with IBW as well as in the obese diabetics ($P < 0.001$). However, obese diabetics had higher CIRp

TABLE 1.—*Gradation of Severity of Diabetes*

| Severity of Diabetes | Fasting blood sugar mg/100 ml | Peak blood sugar mg/100 ml |
|---|---|---|
| Mild | <120 | <200 |
| Moderate | 121 to 180 | >300 |
| Severe | >180 | <300 |

TABLE 2.—*CIRp and a In controls and Diabetics*

| Parameter | Controls Mean ± SD | Diabetics Mean ± SD | P value |
|---|---|---|---|
| CIRp | 1.7 ± 1.1 | 0.39 ± 0.4 | <0.001 |
| A | 1.14 ± 0.6 | 0.62 ± 0.66 | <0.001 |

TABLE 3.—*Effect of body weight on CIRp and A*

| Parameters | Controls (20) | Diabetics IBW (78) | Diabetics obese (22) |
|---|---|---|---|
| CIRp ± SD | 1.7 ± 1.1 | 0.32 ± 0.3 | 0.64 ± 0.7 |
| | | P <0.001 | P <0.001 |
| A ± SD | 1.14 ± 0.6 | 0.7 ± 0.7 | 0.34 ± 0.4 |
| | | P <0.01 | P <0.001 |

than those with IBW. This difference was also statistically significant ($P < 0.01$). This showed that obese diabetics had better insulin output than those with ideal body weight.

Similarly, the A values were also significantly lower in both groups of diabetics compared to controls. ($P < 0.01$ in IBW group, $P < 0.001$ in obese). Comparing the two groups of diabetics with ach other, the A value was significantly lower in the obese diabetics ($P < 0.001$) showing that the peripheral activity of insulin was greatly impaired in the obese group.

*Effect of Severity of Diabetes*

The effect of severity of diabetes on CIRp and A values was assessed separately in diabetics with Ideal body weight and obese diabetics. Table 4 presents the data in IBW patients.

The CIRp was low in all three subgroups of IBW diabetics ($P < 0.001$). There was a progressive fall in beta cell function with increasing severity of diabetes.

The peripheral activity of insulin, however, was not influenced by the severity of diabetes in the patients with IBW. Table 5 shows the effect of severity of diabetes on these parameters in obese diabetics.

In the obese patients, the beta cell function was maintained fairly well in the mild and moderate groups. However, in severe diabetics, the CIRp was very low.

The peripheral activity of insulin was very low in all obese diabetics, irrespective of the severity of the disease.

## DISCUSSION

In order to understand the kinetics of insulin and get a clear insight into the pathogenesis of diabetes, accurate assessments of beta cell function and peripheral activity of insulin are essential. Measurement of the IRI response to glucose stimulus alone does not provide much

TABLE IV.—*CIRp and A in relation to severity of diabetes In diabetics of IBW*

| Parameters | Control (20) | IBW Diabetics | | |
|---|---|---|---|---|
| | | Mild (37) | Moderate (24) | Severe (17) |
| CIRp ± SD | 1.7 ± 1.1 | 0.5 ± 0.16<br>P <0.001 | 0.14 < 0.12<br>P <0.001 | 0.035 ± 0.03<br>P <0.001 |
| A + SD | 1.14 ± 0.6 | 0.66 ± 0.39<br>P <0.01 | 0.85 ± 1.0<br>N.S. | 0.59 ± 0.6<br>P <0.01 |

TABLE V.—*CIRp and A in relation to severity of diabetes Iu Obese Patients*

| Parameters | Control | Obese diabetics | | |
|---|---|---|---|---|
| | | Mild (8) | Moderate (9) | Severe (5) |
| CIRp ± SD | 1.7 ± 1.1 | 0.96 ± 0.98<br>N.S. | 0.64 ± 0.44<br>P <0.001 | 0.18 ± 0.22<br>P <0.001 |
| A ± SD | 1.14 ± 0.6 | 0.26 ± 0.12<br>P <0.001 | 0.21 ± 0.44<br>P <0.001 | 0.4 ± 0.3<br>P <0.001 |

information as the IRI responses are highly variable. Moreover, it does not give a correct idea of the peripheral activity of insulin.

By applying the above mathematical formulae, it is possible to differentiate between the beta cell response and the peripheral activity of insulin.

In this study, application of these formulae in diabetics with different body build and severity has provided interesting information.

In diabetics with IBW the chief defect is impairment of the beta cell function as shown by low insulin output (CIRp). The insulin output is inversely proportional to the severity of diabetes. Though there is some decrease in the peripheral activity of insulin, it is not highly significant, nor is it related to the severity of diabetes, in these individuals.

In obese diabetics, the chief defect is at the periphery where there is considerable impedement to the action of insulin. The obese diabetics have a relatively better output of insulin than those with IBW, but in the severe diabetics, it is very low.

The mathematical applications are useful in quantitative and differential assessment of the beta cell response and the peripheral activity and thus aids in better understanding of the kinetics of insulin. It is well known that immuno reactive insulin (IRI) response to glucose load is influenced by the severity of diabetes and the body weight.[5-10] The mathematical derivations have helped to establish the relationships of these parameters more clearly.

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