

## Oral Hypoglycemic Agents

**Q.** How does one recognize secondary failure to sulphonylurea. What is suggested line of management?

**A.** After initial successful therapy i.e., good glycaemic control, loss of effectiveness of oral drugs months or years later is referred to as secondary failure. This is probably indicative of progressive deterioration of beta cell function. There is another term now in usage, that implies sulphonylurea inadequacy, in that despite maximal sulphonylurea therapy, fasting blood glucose remains > 140 mg/dl

We employ a sulphonylurea sensitivity test that is if a dose of 10 mg of glibenclamide does lower the fasting blood glucose by 30% in 4 hrs, the patient is not likely to respond to sulphonylurea.

In literature, criteria of secondary failure include fasting blood glucose > 180 mg/dl, HbA1c > 9.5% and C-peptide post glucagons <0.6 mmol.

After excluding poor dietary and exercise compliance, poor response to maximal dosage of sulphonylurea calls for insulin therapy. Rarely a combination with biguanide may also bring about control of blood glucose. [ M.M.S.A.]

**Q.** What are the implications of combined therapy (Insulin + sulphonylurea) in IDDM and NIDDM.

**A.** In IDDM, combination therapy is not likely to be of any value. Only when there is evidence for presence of residual endogenous C-peptide, addition of reduction in the total daily dose of insulin (especially when it is above 80 units/24hr). Again in a few instances with frequent wide fluctuations of blood glucose combination therapy may be able to provide a better stabilization.

In NIDDM, a greater scope for achieving euglycaemia with combination therapy is being now reported. First lean NIDDM are often only partially responsive to oral sulphonylureas, some such individuals have islet cell antibodies and are in fact IDDM with late onset of the disease. Here

administration of insulin with or without sulphonylurea is indicated. NIDDM patients losing weight require insulin therapy as well.

There are a group of NIDDMs who have an increased hepatic glucose production and fasting hyperglycaemia. Late evening administration of ultrated insulin 6-8 units (as to provide basal level of insulin for 24 hr) will normalize the morning rise of blood glucose in these NIDDMs.

NIDDM with poor control or secondary failure require definite use of insulin. In combination with SU, the dose of insulin required may be 60-75% of actual requirement. This provides adequate control of blood glucose and HbA1c. Such patient may require twice a day regimen of pre-mixed or split mix regimen. The need for combined therapy may be only for a transitory period and after achieving a good control for 8-12 weeks, it may become possible to withdraw insulin and let the patient continue SU only. Again, NIDDM of very long duration (< 10-15 yr) progressively deteriorates as regards beta cell function and may require supplemental therapy with insulin along with SU.

There is no literature to indicate that side-effects of SU therapy or insulin (especially allergy or lipodystrophy) will be reduced if combined therapy is followed.[M.M.S.A]

### REFERENCES FOR FURTHER READING :

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