Tight Control with Insulin in IDDM and NIDDM

Benefits and risks

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The goals of treatment of diabetes are outlined in Table I. Grossly uncontrolled diabetes could lead to coma due to ketoacidosis (50 per cent) hyperosmolar coma (32 per cent) or a mixed coma (18 per cent) with a related mortality of 26, 14 and 27 per cent respectively [1]. The role of early detection of diabetes and institution of appropriate therapy in preventing the acute complications is obvious to clinicians. Long term tight glycaemic control has been shown to reverse lipid abnormalities, abnormal haemorrheology and growth hormone levels. Whether it prevents or retards micro-angiopathy and whether the characteristic lesion – the capillary basement membrane thickening (CBMT) is due to genetic or metabolic factors [2,3] is still debatable. Long-term controlled studies in this area are not many. They result of diabetic control and complication trials, (DCCT) are eagerly awaited.

Table 1
Goal in the treatment of Diabetes

Children	Adults
Asymptomatic	Asymptomatic
Optimal growth and development	Acceptable weight
Normal physical activity, puberty/menarche and schooling	Normal working capacity
Potential for employment and marriage	Absence of acute complications
Absence of ketoacidosis	Minimal long term complications

With increasing experience in short term conventional and intensive insulin therapy (IIT), gratifying results have been obtained in many situations. Diabetes associated with pregnancy is one such situation [4]. In our own patients of 190 pregnancy and 196 infants, foetal survival was 92 per cent. The remaining 8 per cent had multiple congenital anomalies and/or neonatal complications: all of these were associated with either late detection and/or poorly treated diabetes. In a group of 54 IDDM patients under long-term follow up under our care, the outcome of those with acceptable glycaemic control in contrast to poor control is presented in Table 2.

Table 2
Two to sixteen-year follow up of 54 Diabetics below 20 years of age

	Acceptable*	Poor
Diabetes control	38	16
Growth and development	40	14
Gainfully employed	13**	2
Studying	21	6
School dropout	-	4
Girls married	4	-
Unemployed (girl)	-	1
Death	-	3***

* Seventy-five cent of blood sugar levels in a year were in acceptable range (see Table 3). Majority of these patients did not have glycohaemoglobin determination, as the test was not widely available 5-10 years ago.
** Two married and have become fathers
*** One was a married girl

Conventional mode of insulin therapy may not always achieve tight glycaemic control. Hence the need for adopting intensive insulin therapy (IIT) in some IDDM and NIDDM subjects at certain times.

The IIT is documented to achieve (1) acceptable glycaemic levels, (2) thinning of BM, (3) retinal function improvement, (4) correction of glomerular hyperfunction and arrest of the progress of early nephropathy, (5) improvement of nerve function [5 – 10] and (6) possibly better psychological function [11].

Indications for intensive insulin therapy are as follows:

1. Pregnancy especially during first trimester.
2. Unstable diabetes, wide excursions of blood glucose on a daily basis despite optimal insulin and dietary regimens.
3. Diabetic ketoacidosis especially those with a tendency for recurrence.
4. During major surgical emergencies or indolent infections.

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5. Impending vascular event, unstable angina, TIA, accelerated hypertension.

The monumental work of Jean Pirart lasting for 25 years during a time when IIT was not in vogue and adopting very liberal criteria for glycaemic control has clearly shown significant reduction in the incidence of nephro-retino-neuropathy in those with 'good control' of diabetes. [12]. Thus the experience gathered so far speak in favour of tight glycaemic control. The use of IIT is helpful in this regard. However IIT is not without, risk [13] (Table 4).

Table 3
Criteria fro Glycaemic control

Glycosylated Haemoglobin – 8% or less*				
Whole venous blood sugar (mg%)				
	Desirable		Acceptable	
	Pregnant	Non pregnant	Pregnant	Non pregnant
Fasting	100 or less	120 or less	120 or less	150 or less
Postprandial	120 or less	150 or less	150 or less	200 or less

*Normal values depend upon the method adopted.

Table 4: Risk of Insulin Therapy

Nonimmunogenic	**Immunogenic**
Hyperinsulinaemia	Allergy – Local/systemic
Atheroma	Lipoatrophy
Weight gain	Resistance
Insulin oedema	
Hypoglycaemia with or without	
Somogyi effect	
Dawn phenomenon	
Lipohyertrophy	

Hyperinsulinaemia due to exogenous insulin therapy has not clearly been shown to cause atheroma and hypertension [14]. Insulin oedema due to salt retention is only a temporary phenomenon. Somogyi effect can be prevented by reducing the insulin dose. Dawn phenomenon is yet to be completely understood. Allergy, resistance, lipohypertrophy and lipoatrophy have become infrequent with the use of purified insulin. Weight gain and severe hypoglycaemia are noted to be two disturbing events associated with tight control.

WEIGHT GAIN is attributable to chronic hyperinsulinaemia (HI) with or without hypoglycaemia. DCCT group has reported that patients with IDDM on IIT gained 5.1± 4.6 Kg compared with a gain of only 2.4 ± 3.7 Kg in those who continued on standard therapy [15]. In contrast weight gain in-patients with NIDDM, treated with IIT is usually modest, ordinarily not exceeding that observed in-patients managed with sulphonylurea. Minor dietary reduction and/or avoidance of excessive amount of insulin in a single injection seems to have prevented excessive weight gain [16].

HYPOGLYCAEMIA: High incidence of severe hypoglycaemia in children is confirmed by many investigators [17,18]. Grade 3 hypoglycaemia [19] characterised by unconscious state with documented low blood glucose and/or immediate response to glucose or glucagon, has been reported upto 34.2 per cent over a mean follow up of five years, Seizures has been reported in 42 per cent of episodes [20]. The occurrence of shown in Table 5. Severe hypoglycaemia is more common in subjects with non-detectable C peptide levels [22]. Elevated insulin antibody titres may be a further risk factor for severe hypoglycaemia. The mechanism may be diminished glucose counter-regulation which has been found to correlate with insulin antibody titre [22] Other factors that may contribute to hypoglycaemia include delayed or insufficient food intake, increased exercise without concomitant increase in calorie intake, incorrect insulin dose and inadequate insulin adaptation.

Table 5
Hypoglycaemia in DCCT Age 13 – 39 years

Therapy	
Standard	Intensive
9.8%	3.1 fold increase
	2.8 fold increase (Coma)

Increased risk in those with hypoglycaemia – unawareness and defects in counter- regulation

In conclusion, tight control for short period of time both in IDDM and NIDDM has been shown to be beneficial. It is tempting to believe that long term tight glycaemic control will significantly minimise micro-angiopathy. When standard conventional therapy fails IIT is useful in attaining good control.

The feasibility of IIT for long term use is yet to be determined. DCCT perhaps will throw some light in this regard. Close monitoring, however, is needed during IIT to adjust the insulin dose, diet and exercise so that severe hypoglycaemia, weight gain and possibly atherosclerosis and hypertension due to hyperinsulinaemia is avoided. In our country the cost of insulin compels us to be conservative in the use of IIT.

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