EDITORIAL

DCCT:Truths and Consequences

First and foremost, kudos are in order for the investigators who participated in DCCT[1] for their patience and perseverance throughout the study period. The gratitude and fraternity as well as the lay community regarding the precise documentation of the importance of maintaining adequate metabolic control in delaying or preventing microangiopathic complications in IDDM,is evident by several editorials and reports published in various medical journals and even the lay press i.e., Reader's Digest.However,this concept has been appreciated all along by a majority of diabetologists.In fact ,many of them have advocated and promoted maintenance of adequate metabolic control because of some previous evidence suggesting the role of sustained hyperglycaemia in pathogenesis of microangiopathic long term complications as well as already known other sequelae of sustained hyperglycaemia, i.e.,cataracts,atherogenic lipid pattern causing macrovascular disease, neuropathy secondary to deposition of sorbitol in the neurilemmal sheaths and increased prevalence of infection[2-5].These physicians have perceived the present findings of the delay and/or prevention of 'microangiopathy' in prospective well designed long-term study as 'an added bonus'. But, several other controversies are posed by DCCT.

1. Many of the investigators participating in DCCT, expressed relief on the early termination of DCCT, either privately and some even publicly, during ADA Meeting in June 1993.It seems that the price they had to pay for the sacrifices involved i.e., changes in life styles, required for themselves and their loved one, were tremendously.Moreover,the fear of exhaustion and burning out was also expressed by many. If this was the prevailing attitude amongst most of the participants and that to in just over a period of 7 years, how are the medical community and the patients themselves, to cope with implementation of DCCT recommendations over the whole remaining life spans of both these participants in management of IDDM?

2. DCCT seems to indicate that the adequate metabolic control can be achieved by intensive insulin therapy alone. well as anecdotal experiences. Adequate metabolic control may be attained by conventional twice daily insulin therapy but with an intense recurrent education. Furthermore, even in DCCT,there must have been several patients in both groups, who achieved adequate metabolic control and others who did not, despite intensive therapy[1]. The data demonstrates a significant overlap of HbA_1C values between the two groups, one receiving intensive therapy and the other subjected to conventional treatment. Moreover, large standard deviations of HbA_1 C concentrations at all points during the period of the study in both groups also suggest this possibility. Thus, many subjects managed with conventional therapy also must have achieved metabolic control comparable to that noted in patients receiving intensive therapy. Therefore, the intensive therapy may not be universally needed and the actual appropriate therapy may vary in individual subjects.

3. The study concludes that tight metabolic control is responsible for delaying microangiopathic complications. However, in reality, the study actually assessed the influence of two different therapeutic approaches, the intensive therapy and the conventional treatment and not the degree of control. Thus, one could interpret that the intensive approach was responsible for favorable results since this group did better than the other group receiving conventional therapy. Therefore, the appropriate procedure should have been to establish a relationship between metabolic control on one aspect and the onset or progression of the severity of microangiopathic complications on the other, irrespective of the type of therapy. Such an analysis could be easily conducted from the presently available data. Furthermore, such an analysis alone may really assess the influence of tight metabolic control on incidence of microangiopathic complications.

4. Although DCCT did not reveal significant ill effects of the increased frequency and the severity of hypoglycaemic episodes, it must be realized that the participating subjects were relatively young and the premonitory symptoms of hypoglycaemia may be easily recognized in this population. However, as the population ages, the long term damage secondary to recurrent hypoglycaemia events could be more pronounced especially in the light of worsening

cerebrovascular and coronary atheroclerosis as well as the progressive lack of recognition of premonitory symptoms resulting in presentation of hypoglycaemia as a seizure or a syncope.

5. Finally, the DCCT study does not provide adequate data regarding the daily insulin dosage in the two groups. It is likely that the daily insulin dose was significantly higher in the group receiving intensive therapy when compared with the other group since the occurrence of hypoglycaemic episodes was three times higher and of greater severity in subjects managed with intensive therapy. Furthermore, a progressive rise in daily insulin dosage with the increasing duration of the disorder in most subjects with IDDM until the onset of nephropathy has been well documented. What could be the implications of therapy with larger insulin dosages over long duration of the disease in the light of the recent findings of exaggerated atherogenesis and increased incidence of hypertension in subjects with circulating hyperinsulinaemia induced exogenously or present endogenously?[8-10]

Therefore, in conclusion,DCCT may have opened many new questions requiring further long term assessment.

REFERENCES

1. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The New England Journal of Medicine 1993;329:977-86.
2. Klien R, Klien BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemologic study of diabetic retinopathy.II.Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. Arch Opthalmol 1984;102:502-6.
3. Chase HP, Jackson WE, Hoops SL, Cockerham RS, Archer PG, O'Brien D. Glucose control and the renal and retinal complications of insulin-dependent diabetes.JAMA 1989;261:1155-60.
4. Reichard P, Nilsson BY, Rosenquist U. The effect of long term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. N Eng J Med 1993;329:304-9
5. Lawrence A, Abraira C. New modalities in diabetes treatment. Am J Med 1988;85(suppl 5A);153-8.
6. Kabadi UM. Adjuvant therapy with tolazamide and insulin improves metabolic control in Type 1 diabetes mellitus. Diabetes Care 1985;8:440-6
7. Kabadi UM Birkenholz MR. Improved metabolic control in insulin-dependent-diabetes mellitus with insulin and tolazamide. Arch intern Med 1988;148:1745-9.
8. Stolar M. Atheroclerosis in diabetes: the role of hyperinsulinaemia .Metabolism 1988;37(suppl1):1-9.
9. Zavaroni I, Bonora E, Pagliara M et al. Risk factors for coronary artery disease in healthy persons with hypoinsulinaemia and normal glucose tolerance. N Engl J Med 1989;320:702-6.
10. Pollare T, Lithell H, Berne C. Insulin resistance is a characteristic feature of primary hypertension independent of obesity . Metabloism 1990;39:167-74.

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