Prevention of Non-insulin-dependent Diabetes Mellitus – an Emerging Challenge for India

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Why prevent NIDDM?

For a long time, non-insulin-dependent diabetes mellitus (NIDDM) has been regarded largely as a problem of the affluent countries [1]. However, there is now increasing realization that NIDDM is becoming a major problem in developing countries as well [2, 4]. There is reason to believe that urbanization and accompanying change from a traditional lifestyle to a more ‘westernized’ one may increase the risk of NIDDM [5, 6]. Migrant Indians in different parts of the world have a high risk of NIDDM [2, 7, 8] and within India people living in urban areas may have a higher risk than those living in rural areas [6,9].

NIDDM is a serious and chronic disease which is largely irreversible. It can lead to substantial disability and to premature death. Treatment for NIDDM may be costly and is often unsuccessful in preventing the consequences of the disease. Prevention of NIDDM is therefore worth considering seriously and is now receiving increasing attention all over the world. [4, 10, 11, 12].

In whom should NIDDM be prevented?

There are two broad approaches available for preventing any disease: a ‘population strategy’, which seeks to control the determinants of incidence in the population as a whole and a ‘high risk strategy’, which seeks to identify high risk susceptible individuals and to offer them some individual protection [13]. For a disease like NIDDM which is influenced by major life style and societal factors, a ‘population strategy’ may be the most effective way of delivering prevention, particularly, in communities where the incidence and prevalence of the disease is very high and the risk is spread broadly across most of the community. As Rose [13] points out, the ‘population approach’ offers a number of powerful advantages. "The first is that it is radical. It attempts to remove the underlying causes that make the disease common. It has a large potential – often larger than one would have expected – for a population as a whole". However, the evaluation of a ‘population strategy’ may not readily fall within the paradigm of classical randomized controlled trials. Therefore, it is believed that a randomized controlled clinical trial among high risk subjects may be the most acceptable way of finding out whether NIDDM is preventable and such trials are now being organized in a number of countries, including the US. [14].

Identification of high risk subjects for an NIDDM prevention study requires an understanding of the natural history of the disease. The development and course of NIDDM can be viewed as a number of arbitrary, but distinct stages [11, 15]. The first abnormality is believed to be genetic susceptibility, but knowledge of genetic factors is still rudimentary and except in rare circumstances, it is not possible to identify subjects at high risk for NIDDM by testing for genes [11]. After a variable time period, susceptible subjects may enter the second stage, which is referred to as impaired glucose tolerance (IGT). IGT is thought to be secondary to insulin resistance and is defined as hyperglycaemia during an oral glucose tolerance test (OGTT) which is not of sufficient degree for a diagnosis of NIDDM [16]. IGT is an easily recognizable condition and is a very strong predictor of NIDDM [17, 18]. Targeting subjects with IGT may therefore be an optimal strategy for selecting high risk subjects for an NIDDM prevention study. NIDDM without complications can be regarded as the third stage and the fourth stage is diabetes with micro and macro vascular complications.

A number of potentially modifiable risk factors including obesity, physical inactivity and a high-fat diet are thought to contribute to the progress from genetic susceptibility to IGT and from IGT to NIDDM [10, 19]. There is compelling evidence that obesity, particularly central obesity, is a risk factor for NIDDM [20, 21] and results of five prospective studies [22, 26] also strongly suggest that increased physical activity may have a protective effect on the development of NIDDM. However, the evidence concerning the role of dietary factors, which has been reviewed elsewhere [19], is not yet convincing, but there are reasons to believe that a low-fat diet may be useful in preventing NIDDM [27, 28].

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What are the interventions that can be used to prevent NIDDM?

As mentioned above, obesity is a major risk factor for NIDDM and measures aimed at obesity management, including the use of anorectic drugs, may be relevant strategies for prevention of NIDDM. In addition, there are behavioural modifications and pharmacological agents which may have a specific role in preventing NIDDM independent of their effect on obesity.

The main behavioural interventions are to increase physical activity and to promote a low-fat, high-fiber diet [10,11]. There are data which suggest that physical activity may independently reduce the risk of NIDDM over and above its effects through the reduction of obesity [25], but such evidence is lacking in the case of dietary factors. Nevertheless, promotion of a low-fat, high-fiber diet may be a worthwhile goal for NIDDM prevention. Behaviour modification is often difficult to deliver effectively and poses a number of special challenges. Eating and exercise behaviours are influenced by a whole range of social, cultural, economic and political factors [29] and in designing appropriate interventions, these factors will need to be considered. In addition, there are strong individual determinants of behaviour [30]. It is important to know what motivates an individual to behave in one way, or what factors motivate an individual to want to change a behaviour. The understanding of people’s perceptions is therefore central to delivering effective behaviour modification. The feasibility of behavioural interventions was tested in a clinical trial in Sweden and this study showed that it may be possible to reduce to half the five-year risk of progression from IGT to NIDDM [28]. However, because this was not a randomized controlled trial, the evidence is only tentative. More recently, preliminary results from the randomized clinical trial of behavioural interventions in adults in China with IGT were reported in an abstract [31]. In this study, 530 subjects with IGT were randomized into one of four groups: diet-only, exercise-only, diet and exercise and no intervention. At six years of follow-up, a significantly lower proportion of individuals in all three treatment groups progressed to diabetes (44%, 41% and 46% respectively) than in the control group (65%). The types of behavioural changes achieved in Swedish or Chinese societies may be very different from what could be achieved in other parts of the world and further studies in other populations are required. With a view to understanding the challenges of delivering behavioural interventions, we are conducting a feasibility study of life style interventions among adult, obese, normoglycaemic Pima Indians of the Gila River Indian Community (GRIC) of Arizona in the US. This is a randomized controlled trial in which 95 participants have been assigned to either a structured diet-exercise group or to a self-directed discussion group. The primary end points for this study are compliance and changes in diet and exercise behaviour. As secondary end points, a number of risk factors for NIDDM are also being measured. This study is intended to plan further diabetes prevention efforts in the GRIC and elsewhere.

Behaviour modification may be insufficient to prevent NIDDM in some individuals and a drug may also be required to overcome presumed genetic factors. Drugs that offer potential for prevention of NIDDM have been reviewed elsewhere [32]. Sulfonylurea drugs can decrease hyperglycaemia and appear to stimulate both insulin secretion and insulin action. Biguanides can inhibit intestinal glucose absorption and improve insulin action. Thiazolidinediones can improve insulin action. Acarbose is a glucosidase inhibitor and can decrease hyperglycaemia. Lastly, insulin can reduce hyperglycaemia and improve insulin secretion and action. Each of these drugs has its side effects and disadvantages and a choice may be difficult to make. There have so far been three studies that have evaluated the role of drug treatment in the prevention of NIDDM and a meta-analyses of these studies indicates little if any effect of drugs on the incidence of diabetes [32]. As each of these studies employed small sample sizes, the confidence interval was wide and the issue of whether NIDDM can be prevented with drug treatment remains unresolved. There is no justification for the use of such drugs in diabetes prevention activities unless their use can be incorporated into a research design so that their effects can be rigorously evaluated.

Current progress with NIDDM prevention trials

The National Institute of Diabetes and Digestive and Kidney Diseases is currently planning a national, multi-centre, randomized, NIDDM prevention clinical trial in the US. [14]. This trial will evaluate the efficacy of interventions designed to delay or prevent onset of NIDDM in individuals at high risk. This large trial is expected to recruit about 4000 subjects from 22 centres across the US.

Implications for India

NIDDM is no longer merely of concern to industrialized nations. It is an important emerging problem in India and in other developing countries [3]. NIDDM is potentially preventable and this potential is being currently evaluated in high risk subjects with clinical trials in the US. [14] and in...
other countries. While such studies will provide valuable insight into the causes of NIDDM and the feasibility of preventing the disease, the implications for implementing a preventive strategy will need to be addressed within the context of broader health policy, which will differ from country to country. As resources are always limited, the decision of whether or not to undertake a preventive strategy for NIDDM should consider the possible consequences and costs (including the opportunity cost of sacrificing the benefit that could have been derived form allocating the scarce resources to an alternative use) of such a program. Unfortunately, little is known about the costs and effectiveness of potential NIDDM prevention measurers. A population based strategy may be preferable for prevention of NIDDM because a high risk strategy would affect only a small proportion of all people who subsequently develop the disease [33]. Considering the high costs of even simple mass media campaigns in developing countries, it would appear difficult to justify population based prevention programs for NIDDM alone [3]. The links between diabetes, coronary heart disease, hypertension and other noncommunicable diseases have led to proposals in support of an integrated program for prevention and control of noncommunicable diseases [16, 34]. A broad strategy (stressing good nutrition, avoidance of obesity, increased physical activity and reductions in smoking and alcohol consumption) that tackles a wider range of emerging health problems makes sense for many developing countries [3]. Such a strategy will include modification of individual human behaviour, improvements in the health services, mass health education and selected government regulation and legislation. In deciding to implement such a strategy, each developing country will need to assess its own health needs and decide priorities appropriately. Good epidemiological studies of the natural history of diabetes, coronary heart disease, other chronic diseases and associated life style factors in countries such as India can provide valuable data to decide such priorities and also help improve the understanding of the causes and consequences of these conditions. Similarly, major collaborative long term studies in diverse populations within India, using different preventive strategies, are also essential for progress in prevention of diabetes [4].

REFERENCES


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