



WorldWIDE news

Successfully globalising the WorldWIDE initiative

2001 has been a successful year for WorldWIDE in raising awareness to enhance diabetes management through improved education. The launch of the WorldWIDE booth at EASD 2001, Glasgow, was very successful. Through this exhibition stand, WorldWIDE has begun to develop a network of people who are interested in enhancing education and knowledge of diabetes. Over 2000 EASD delegates attended the stand and 500 delegates from 78 countries registered with us for more information.

Discussion with fellow colleagues from other countries at the EASD WorldWIDE stand highlighted that there is a huge need for educational materials, especially in developing countries, and reinforced our belief that this type of initiative is worthwhile and long overdue. We were also given many ideas for future topics for discussion at forthcoming meetings and for educational materials that should be developed. We would like to thank you for your praise of the quality and usefulness of the materials

distributed at the booth and for your additional suggestions. Please help us to continue our initiative to provide access to educational materials and to expand the supportive global network by forwarding our details to colleagues who may be interested in joining the WorldWIDE mailing list.

Planned future initiatives for WorldWIDE include:

- Constantly updating and adding to the WorldWIDE website to provide an up-to-date learning tool that will eventually not only be aimed at clinicians, but also at students and patients.
- Publish educational literature and materials.
- Expand the global network of people interested in improving diabetes care through a booth at EASD 2002 in Budapest.

The WorldWIDE faculty is committed to continue this development in 2002 and we would welcome your continued support, feedback and suggestions on topics for WorldWIDE coverage.

Philip Home

WorldWIDE goes online

The WorldWIDE website (www.worldwidediabetes.com) was officially launched at EASD 2001 in Glasgow.

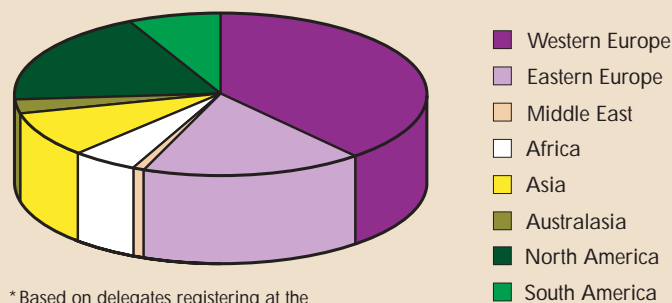
The website, which is updated on a regular basis, includes:

- Background to WorldWIDE
- A WorldWIDE slide resource
- Case studies
- Patient communication tools
- A viewpoint section
- The latest news from WorldWIDE
- Forthcoming congress information
- Links to diabetes resources

WINNER!

We would like to congratulate Dr M Szabo from Romania who was drawn as our first winner after completing our registration form at the WorldWIDE booth at EASD 2001 in Glasgow. Dr Szabo will receive free registration for EASD 2002 in Budapest.

Global distribution of WorldWIDE diabetes network*



* Based on delegates registering at the WorldWIDE booth at EASD 2001, Glasgow



An update on the UKPDS — the impact of ethnicity

Recent analyses from the United Kingdom Prospective Diabetes Study (UKPDS) confirm important ethnic differences in body weight, lipid profile and blood pressure, but not in glycaemic control, among people with Type 2 diabetes. Davis and colleagues (2001) described data from 2999 newly diagnosed people with Type 2 diabetes over a 9-year period. The ethnic composition of the study population was 83% Europid, 9% Afro-Caribbean and 8% Asian (of Indian origin). Assessments were made after 3, 6 and 9 years. Following a 3-month run-in period with dietary treatment alone, participants were randomised to either lifestyle only (diet) or lifestyle and therapy (sulphonylurea, insulin or metformin [obese only]) groups to improve glucose control.

Findings

- Baseline data at diagnosis showed significant ethnic differences in vascular risk factors. The Afro-Caribbean subpopulation had the highest HbA_{1c} levels and the lowest plasma insulin levels as well as the highest HDL cholesterol levels ($p < 0.01$ vs Europid and Indian). The Indian Asian group, on the other hand, had significantly lower body mass index compared with other ethnic groups, and Indian patients were significantly less likely to be hypertensive or taking antihypertensive therapy.
- During the 9-year study, there were no consistent ethnic differences in mean improvements of fasting plasma glucose or HbA_{1c} after adjusting for age, sex, baseline value, treatment allocation and change in weight — in other words, glycaemic control was similar between the groups.

- Body weight increased more in the Europid group (+ 5.0 kg) compared with the Afro-Caribbean (3.0 kg) or Indian (2.5 kg) groups.
- After adjustment for antihypertensive therapy, the increase in systolic blood pressure at 9 years was greatest in the Afro-Caribbean group, whereas diastolic blood pressure decreased progressively in all groups to a similar extent.
- Small, but generally beneficial changes in total and LDL cholesterol were noted by the end of the study that were comparable across the ethnic groups. However, significant differences were noted with respect to changes in HDL cholesterol and triglycerides. After 3 years, HDL cholesterol had increased significantly in the Afro-Caribbean group compared with the other groups — an effect that was maintained throughout the 9-year study period (Figure 1a) — while a matching decrease in plasma triglyceride levels was also greatest in this ethnic group (Figure 1b).

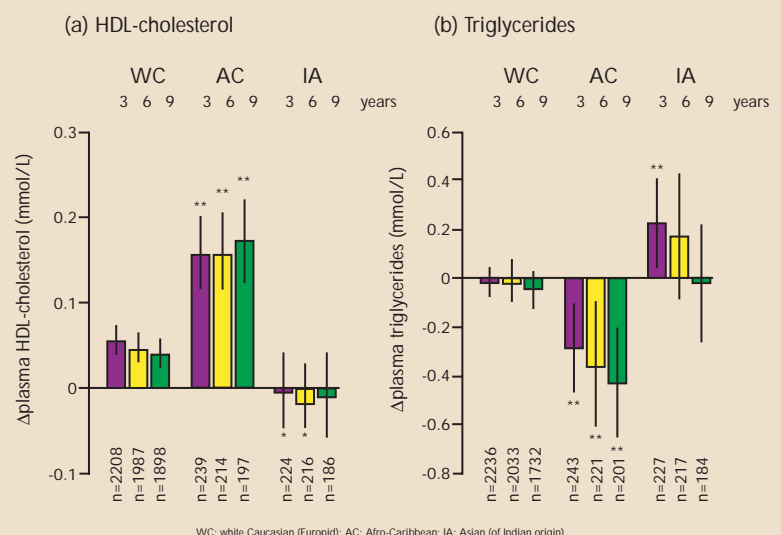
Conclusions

On the basis of these results, a focus on ethnicity-specific glycaemic control in Type 2 diabetes would appear to be unnecessary. However, the findings do not include true outcome data. Nevertheless, significant ethnic differences were evident for lipid profiles, both in baseline values and treatment-related changes. It is possible that the sustained increase in HDL cholesterol and reduction in triglycerides noted among Afro-Caribbean individuals in this study contribute to the reduced incidence of cardiovascular disease that has been reported in this population. The higher blood pressure is also consistent with other reports and the higher cerebrovascular risk. Furthermore, the low baseline blood pressure noted here in Indian individuals may belie the need for aggressive antihypertensive therapy in a group of people with a high incidence of diabetic nephropathy. Certain cardiovascular risk factors may, therefore, need to be considered separately among different ethnic groups.

References

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Figure 1: Ethnic differences in plasma lipid changes after 3, 6 and 9 years of the UKPDS



Myth or reality — is insulin therapy associated with cardiovascular disease?



Professor Jens Sandahl Christiansen

Early studies put forward the concept that hyperinsulinaemia was the common link between hypertension, obesity and glucose intolerance (Modan et al, 1985). Acute exogenous infusion of large doses of insulin has been shown to raise blood pressure by increasing renal sodium retention. However, in practice patients with endogenous (eg those with insulinoma) or exogenous (eg in Type 1 diabetes) hyperinsulinaemia have normal blood pressure and no signs of sodium retention. It is only in the presence of micro- or macroalbuminuria that changes are seen in these measures. Furthermore, the epidemiological evidence for an association between insulin levels and hypertension is not coherent; whereas the data appear irrefutable in the European population, they are less so in the Hispanic and black populations (He et al, 1999; Mitchell et al, 1992; Saad et al, 1991).

The clinical guidelines recently prepared by the US National Cholesterol Education Program (NCEP) Expert Panel (Adult Treatment Panel III [ATP III]) (reported in Issue 3 of this newsletter [NCEP, 2001]) highlight the strong association of diabetes (particularly Type 2 diabetes) with ischaemic heart disease (IHD) and the consequent need for aggressive therapy. Insulin insensitivity and its associated abnormalities (increased VLDL cholesterol and triglycerides, decreased HDL cholesterol, increased blood pressure and glucose intolerance) together comprise the metabolic syndrome (Syndrome X), which carries a high risk for ischaemic heart disease. However, it should be noted that hyperinsulinaemia per se has never been considered a part of this syndrome — it has been considered secondary to insulin insensitivity.

There are several famous studies that have assessed the relationship between insulin levels and IHD morbidity and mortality:

- The Helsinki Policemen Study found a strong association between post-glucose load insulin levels and IHD, although the association weakened with the length of follow-up (Pyörälä et al, 2000).
- The Paris Prospective Study, on the other hand, found no consistent association between post-load insulin levels and IHD, although fasting insulin was predictive of IHD (Fontbonne and Eschwege, 1991).
- In contrast, the Busselton study from Australia suggested that serum insulin is not a direct risk factor for IHD, although it may be a risk marker (in men, but not women) associated with other variables (Welborn et al, 1994).
- Likewise, the Bedford study found no association between baseline insulin and 10-year cardiovascular mortality or morbidity in people with borderline diabetes (note that these people would now be considered to have full diabetes) (Jarrett et al, 1982).
- A meta-analysis of studies assessing hyperinsulinaemia and cardiovascular disease found only a weak positive association (Ruige et al, 1998).
- A recent study in people with Type 2 diabetes did suggest an association in men, but not women (Lehto et al, 2000). However, whereas the predictive value of hyperinsulinaemia was independent of conventional IHD risk factors, it could not be separated from risk factors clustering with hyperinsulinaemia (high body mass index, raised triglyceride levels and low HDL cholesterol).

It should be noted that none of these studies distinguished hyperinsulinaemia from insulin insensitivity. One study that did measure both insulin and insulin insensitivity found no independent association between indicators of atherosclerosis and insulin levels, whereas an ethnicity-dependent association was reported for insulin insensitivity (Howard et al, 1996). If a pathophysiological connection is to be established between one measurement and another, it is generally agreed that coherent results from epidemiological studies are required. In the case of hyperinsulinaemia and IHD, this is clearly not the case. However, there is currently a desperate lack of prospective trial data. The UKPDS concluded that insulin therapy administered for up to 15 years is not associated with increased cardiovascular disease mortality or morbidity. Indeed, most of the evidence points away from such an association.

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Minimising the risk of hypoglycaemia in Type 2 diabetes



Professor Rüdiger Landgraf

'Mild' hypoglycaemia is common in people with Type 2 diabetes undergoing aggressive diabetes management (Miller et al, 2001). Severe hypoglycaemia, on the other hand, is rare, although in absolute terms more occurs in people with Type 2 diabetes than in those with Type 1 diabetes. However, its rarity should not obscure its inherent dangers — severe hypoglycaemia gives an increased risk of death (Campbell, 1985).

The problem of hypoglycaemia is one that is not exclusive to insulin therapy. A statement from the American Diabetes Association (ADA) in 1994 indicated that severe hypoglycaemia may be the most important complication of sulphonylurea treatment and that the elderly may be especially prone to hypoglycaemia through missed meals or renal impairment (Cryer et al, 1994). For instance, the Swedish study by Asplund and colleagues (1983) showed the incidence of hypoglycaemia with glibenclamide in the elderly to be 10–20%.

Other risk factors also appear to contribute with sulphonylureas. In a study from Switzerland, 21% of patients with severe hypoglycaemia had renal impairment and 80% of fatal cases had renal insufficiency (Berger et al, 1986). A recent study of hypoglycaemia among sulphonylurea-treated patients with end-stage renal disease found an association between hypoglycaemic events and a recent decline in energy intake (eg skipped meals due to anorexia), previous hypoglycaemic episodes, duration of diabetes and a history of cerebrovascular disease (Krepinsky et al, 2000).

Data from the relatively small Kumamoto study (Shichiri et al, 2000) showed a zero incidence of severe hypoglycaemia in people with Type 2 diabetes receiving intensive insulin therapy. This contrasts with the UKPDS and other studies where the incidence ranges from 2.3 to 7.8%. It is difficult to know whether this difference reflects insulin regimen, type of insulin or the ethnic group being managed.

There is also an association between alcohol consumption and hypoglycaemia (Rasmussen et al, 2001). However, such studies do not reflect real-life alcohol consumption habits. The risk may also be compounded by a reduced ability to detect the onset of hypoglycaemia. According to the study of Spyer et al (2000), hypoglycaemic counterregulation starts at higher glucose levels in people with Type 2 diabetes compared with controls. Hence, patients may feel hypoglycaemic even when glucose levels are normal/high and consequently learn to avoid taking medication.

Overall, it is clear that some data show severe hypoglycaemia can be a problem, albeit an infrequent one, in people with Type 2 diabetes, especially under certain conditions. The risk with sulphonylurea treatment is probably a far more substantial problem in the presence of these factors, although the risk may be lower with core drugs or fast-acting insulin secretagogues such as repaglinide. Any risk of hypoglycaemia associated with insulin can probably be reduced with appropriate attention to therapy and education, although there is, as yet, no randomised clinical trial evidence-base to support this view.

To conclude, when thinking about the risk of hypoglycaemia, one needs to consider a number of factors including the type of treatment, age, comorbidity (especially renal impairment), alcohol consumption and cognitive decline.

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Do you have a case history or discussion topic that may be of interest to your colleagues? We would like to hear from you. Although we cannot guarantee that your case history or topic will be discussed, we hope to be able to feature them in future issues of WorldWIDE News and on the worldwidediabetes.com website.

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Don't forget to include your contact details!

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