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### **Editorial:**

# IS STRICT GLYCAEMIC CONTROL BENEFICIAL?

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### Version española

Cardiovascular disease is one of the principle causes of morbidity and mortality, and diabetes mellitus is becoming one of the main risk factors. In fact, coronary disease is the principle cause of death in diabetic patients. Several studies on patients with type 1 diabetes showed that strict glycaemic control reduces coronary disease by more than 50%; but the data are not so clear in type 2 diabetes, as they usually have other underlying risk factors, such as high blood pressure, hyperlipidaemia and obesity. For these reasons, some authors doubt whether strict blood glucose control is necessary to reduce macrovascular events and total mortality in patients with type 2 diabetes mellitus.

Due to the negative results of several recent clinical trials, some experts suggest that the efforts to achieve strict glycaemic control in patients with type 2 diabetes should be relaxed. However, this could be wrong, as the microvascular benefits of strict blood glucose control are well established. It may be that all

these studies did not have sufficient power to detect a cardiovascular benefit, as the difference between the two comparison groups (standard and strict glycaemic control) was small, or the follow up period was too short. A recently published meta-analysis has shone new light on this subject (Ray et al. Lancet 2009; 373: 1765-72).

This meta-analysis combines the results of 5 recent clinical trials, with a total of 33,040 patients (including patients with stable type 2 diabetes) who were randomly assigned to standard or intensive diabetic treatment. The strict diabetic treatment was different in each study and was based on sulphonylureas, metformin, glitazones, insulin or a combination of several of them, with a mean follow up of 5 years.

The final analysis showed that strict hypoglycaemic treatment significantly reduced the incidence of myocardial infarction by 17% and coronary disease by 15%. However, no significant effect was found with stroke or overall mortality. Intensive treatment was also associated with a higher incidence of hypoglycaemic episodes (38.1% patients vs. 28.6% with standard treatment) and an increase in weight of 2.5 kg, which could limit the benefit gained over other cardiovascular risk factors.

It is important to point out that the results seem to be applied to the majority of the patients, regardless of the baseline glycosylated haemoglobin level. The mean reduction in HbA1c was 0.9% greater with the strict diabetic treatment, which shows us that better glycaemic control is achieved.

However, the cardiovascular benefits associated with glycaemic control are less than those obtained by a reduction in blood pressure or cholesterol. The results of this meta-analysis show us that each 1% reduction in HbA1c prevents around 3 coronary events per 200 patients treated for 5 years, a lower benefit than that obtained for each 1 mmol/l (38 mg/dl) of LDL-cholesterol or 4 mmHg in blood pressure (8.2 and 12.5 cardiovascular events prevented, respectively). Furthermore, the reduction in cholesterol with statins and blood pressure control decrease total mortality, which does not happen with strict glycaemic control.

Therefore, the overall cardiovascular risk of the patient must be assessed, and if there has to be a choice, controlling the hypertension and the dyslipaemia must be priorities, which does not mean that we have to forget to control the glycaemia the best we can. The doctor and the patient must weigh up the expected benefits with the will and ability of each individual patient to manage to control the main risk factors. A practical approach could be to gradually reduce the HbA1c, being careful to prevent severe hypoglycaemic episodes. Blood glucose control must begin as soon as possible.



#### **REFERENCE**

Ray KK, Seshasai SR, Wijesuriya S, Sivakumaran R, Nethercott S, Preiss D, Erqou S, Sattar N. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. Lancet 2009; 373: 1765-1772