Fibrates consistently lower risk of cardiovascular events across high-risk groups

A recent meta-analysis of published clinical trials conducted over the past 50 years has confirmed that the administration of fibrates to a broad range of high-risk patients lowers the risk of cardiovascular events.[1]

The 10 to 13% relative risk reduction (RRR) found in this meta-analysis could be regarded as modest, but in high-risk patients, this contribution to the prevention of cardiovascular events is significant. Fibrates showed no benefit in this meta-analysis on stroke, all-cause mortality or sudden death.

The cardiovascular event reduction was highest in patients with a higher mean baseline triglyceride concentration (> 2 mmol/l), a finding that agrees with subgroup analyses done in several clinical trials, including the ACCORD trial.[2] No increased effect was seen in the subgroup of patients defined by a lower HDL cholesterol level in this meta-analysis. The ACCORD trial had placed patients with raised triglyceride and low HDL cholesterol levels in a subset, which showed greatest proportional risk reduction; such that only 20 individuals needed to be treated for five years to prevent one cardiovascular event.

Data from the ACCORD trial available in published form to the authors of the meta-analysis did not allow the low-HDL subgroup to be separated from the high-triglyceride subgroup. So currently, the role of fibrates in reducing cardiovascular events in a subgroup of patients with low HDL levels and triglycerides below 2 mmol/l should be the subject of further investigation.

This extensive meta-analysis included 45 000 individuals with a broad range of baseline characteristics. With regard to other cardiovascular conditions, the risk of heart failure was reported in three trials of 8 581 participants who had 584 heart failure events. Overall, there was no benefit of fibrates on heart failure. However, when the VA CO-OP Atherosclerosis trial,[3] which included patients with pre-existing cerebrovascular disease, was excluded from the meta-analysis, fibrates showed an 18% reduction in heart failure.

Three trials including more than 15 000 patients showed that fibrates reduced the risk of albuminuria by 14%. A very significant reduction of 37% was seen in the relative risk of diabetic retinopathy in two trials, which included more than 10 000 patients.[4,5]

J Aalbers, Special Assignments Editor

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Dabigatran launch *continued from p.173*

In the published literature, direct comparisons of rivaroxaban and dabigatran are not possible. However, in interpreting anti-coagulant data and comparing these drugs to enoxaparin as far as safety is concerned, it is clear that rivaroxaban with its superior efficacy carries a consistently higher bleeding risk. This view is supported by independent evaluations undertaken by the FDA and those done for the UK standard, NICE. 'The NICE technology guideline in fact comments that with regard to efficacy, the two agents are similar, but there is a tendency to increased bleeding with rivaroxaban', Prof Frostick said.

The availability of two doses of dabigatran is useful when dealing with more fragile patients such as the elderly (> 75 years) and those with moderate renal insufficiency. 'In the period of real-life clinical usage of these new entities, we need to do our own post-marketing surveys and we should not be complacent about any new clinical agents', Prof Frostick concluded.

The panel of South African experts added to the presentation with their experience of using dabigatran in the clinical trials locally, which increased patient numbers significantly in both the RE-MODEL and RE-NOVATE trials.

'Mobility in the older patient undergoing surgery is very important and we should understand the need for anti-coagulation in these patients for an extended period of time', Prof Barry Jacobson, head of haematology at the Witwatersrand University pointed out. 'The clinician should watch out for non-steroidal anti-inflammatory usage, and protease inhibitors for HIV treatment can also complicate the expected anti-coagulant action of dabigatran', he warned.

With regard to reversing the effects of dabigatran when required, activated charcoal and recombinant factor VIIA are useful, while in an emergency situation, the patient can be dialysed. The advantages of an oral medication such as dabigatran cannot be ignored as patients are now sent home very early after surgery, normally within three to five days.

J Aalbers, Special Assignments Editor

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