

Irbesartan reduced heart failure in ACTIVE-I trial of patients with atrial fibrillation

The addition of irbesartan to the treatment of normotensive patients with atrial fibrillation in the ACTIVE-I study resulted in a significant reduction in hospitalisation for heart failure and an overall reduction in the number of days spent in hospital for any cardiovascular-related reason. While the increased risk of stroke is perhaps most feared in atrial fibrillation, heart failure is the 'neglected complication' of atrial fibrillation.

'Heart failure is a more common complication of atrial fibrillation than stroke', Dr Salim Yusuf of McMaster University and chief investigator of the ACTIVE trial programme noted in his presentation at the Hot Line session at the 2009 European Society of Cardiology congress in Barcelona. Prof John Camm of London supported this view and stated that atrial fibrillation increases the risk of heart failure 3.4-fold.¹

The ACTIVE-I trial included some 9 016 patients, mean age of 69.5 years, with documented atrial fibrillation, who had at least one other risk factor. They were drawn from the other two ACTIVE trials, which focused on antithrombotic aspects, comparing aspirin, clopidogrel and warfarin. Almost half of the total group was on warfarin and all patients were on antiplatelet therapy.

The mean blood pressure of patients at entry was 138/75 mmHg. The mean reduction in blood pressure in the irbesartan arm was modest (-2.6/-1.9 mmHg) compared to those on placebo. The placebo group of patients was well treated with regard to their blood pressure, reflect-

ing an increasingly common feature of current studies, as patients and their clinicians are positively influenced by the trial environment.

Irbesartan treatment did not reduce the risk of the first primary outcome, cardiovascular death, myocardial infarction or stroke (5.4% per year in each group), but with irbesartan there was a lower rate of the second primary outcome, cardiovascular death, myocardial infarction, and hospitalisation for stroke and heart failure (7.3 vs 7.7%, $p = 0.12$). This was chiefly due to a 14% reduction in the risk of hospitalisation for heart failure (3.2% per year in the placebo group vs 2.7% with irbesartan, $p = 0.018$).

A significant benefit for irbesartan was shown when the secondary endpoint of reduced hospitalisation for heart failure was considered alone. Dr Yusuf pointed out that there had never been a study on atrial fibrillation that could show a reduction in incidence of heart failure.

Subsequent *post hoc* analysis indicated a significant 13% reduction in the risk of the composite of stroke, non-central nervous system embolism and transient ischaemic attacks (3.4% per year in the placebo group vs 2.9% with irbesartan, $p = 0.02$). There were also consistently lower rates of each component of the composite.

The number of admissions to hospital (4 055 with placebo vs 3 816 with irbesartan, $p = 0.004$) and days hospitalised for cardiovascular reasons were also significantly reduced (39 941 for placebo vs 36 480 for irbesartan, $p = 0.0001$). Irbesartan was

well tolerated with similar rates of drug discontinuation compared to placebo.

Conclusions and relevance to South Africa

Dr Yusuf pointed out that it is important to focus on the whole patient. One must not strive to reduce only strokes, but also heart failure. 'From the results of the ACTIVE-I trial, it would seem reasonable to treat patients with atrial fibrillation with irbesartan, based on the reduced risk of heart failure complications and the reduction in the combination of stroke, transient ischaemic attacks and other embolic events', he concluded.

Of importance with regard to South Africa is a recently published study in local urban general practice, the I-TARGET trial, which showed that 2.7% of hypertensive patients included in the Treat-to-Target study had a history of atrial fibrillation and their mean age was only 60 years.²

As the South African population continues to age, non-valvular atrial fibrillation will become an ever more important cause of cardiovascular morbidity and mortality.

1. Stewart S, *et al.* A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med* 2002; **113**(5): 359-364.
2. Rayner B, Schoeman HS. A cross-sectional study of blood pressure control in hypertensive patients in general practice (the I-TARGET study). *Cardiovasc J Afr* 2009; **20**: 224-227.