

Anticholinergics for COPD



Anticholinergics and cardiovascular safety

Two recent studies have raised concerns that the use of the anticholinergics ipratropium and tiotropium for COPD is associated with an increased risk of cardiovascular events. However, a large randomised controlled trial conducted over four years did not show an increase in cardiovascular risk when tiotropium was compared with placebo. The consensus is that tiotropium remains a safe and effective treatment for most patients with COPD.

Two studies showed an increased cardiovascular risk

The results of a large meta-analysis of randomised controlled trials suggests that ipratropium and tiotropium increase the risk of cardiovascular events in people with COPD compared with placebo, inhaled corticosteroids or beta-agonists.¹ The use of anticholinergic agents for more than 30 days was associated with an increased risk of cardiovascular events (RR 1.58, 95% CI, 1.21 – 2.06). The limitations of this study include the mix of treatments in the control arm and the fact that differences in cardiovascular risk factors (e.g. diabetes, smoking history, use of statins) was not accounted for. None of the randomised controlled trials included in the meta-analysis were designed to investigate differences in cardiovascular outcomes.

A case control study, published around the same time, showed that ipratropium was associated with an increase in all cause mortality and cardiovascular deaths compared with reference treatment (no treatment or short-acting beta-agonist).² The study can only show a possible association as there are a number of possible confounders. However, a well designed randomised controlled trial is required to investigate this association further. To date there have been no international or national recommendations to change the step one management of COPD, which is the use of a short-acting bronchodilator; either ipratropium or a beta-agonist.

A large long term trial showed no increased risk

The latest study (UPLIFT) was a randomised controlled trial which investigated almost 6000 patients given either tiotropium or placebo and then followed over four years.³ No significant differences in all cause mortality, myocardial infarction or stroke were found between the groups. The results of the UPLIFT study may provide reassurance of the cardiovascular safety of tiotropium.

Neither Medsafe or the Asthma and Respiratory Foundation are currently recommending any significant changes to practice in response to these study results. However, it is suggested that patients with ischaemic heart disease and unstable angina should have their anticholinergic treatment reviewed as they are already at very high risk of a cardiovascular event.⁴

Tiotropium is associated with fewer COPD exacerbations but does not slow decline in lung function

The UPLIFT study also looked at COPD exacerbations and the rate of decline in FEV1 compared with placebo. Patients treated with tiotropium experienced fewer exacerbations of symptoms than those on placebo (RR 0.86, 95%CI 0.81 – 0.91). However, over the four year study period, there was no difference in the rate of decline in FEV1 between the tiotropium and placebo groups. Smoking cessation remains the only intervention that can slow the rate of decline in lung function.

References

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4. Most COPD patients OK on inhaler. *New Zealand Doctor*. 22 October 2008:17