Clinical reviews

Our panel of GPs review recent research papers in their specialist areas that may influence the way you practise

Reviewers

Addiction
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GP Leeds and Clinical Director Lifeline (North) RCGP regional lead substance misuse RCGP/British Liver Trust clinical champion for liver disease

Cardiovascular disease
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Diabetes
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Mental health
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Paediatrics
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Diabetes

Incretin-based diabetes therapy not associated with increased mortality

A recent meta-analysis, published in the *BMJ*, has shown no increase in all cause mortality in patients with type 2 diabetes using incretin-based treatments i.e. GLP-1 agonists and DPP-4 inhibitors.

The systematic review and meta-analysis reviewed randomised controlled trials that compared GLP-1 agonists or DPP-4 inhibitors with placebo, lifestyle modification, or active antihyperglycaemic drugs in patients with type 2 diabetes. The investigators searched Medline, Embase and the Cochrane Central Register of Controlled Trials, up to February 2017, for eligible studies.

Of 1,187 potentially eligible studies, 189 covering 155,145 participants met all eligibility criteria.

These included several large cardiovascular outcome trials where patients had, or were at high risk of, cardiovascular disease.

Of 189 trials reviewed, 77 reported no deaths at all. The other 112 reported 3,888 deaths among 151,614 patients, of which 3,592 (92%) were reported from the six large cardiovascular outcome trials.

Meta-analysis of the 189 trials showed no difference in all cause mortality between incretin drugs and controls (1,925/84,136 vs 1,963/67,478). Odds ratio 0.96 (95% CI: 0.90-1.02; $I^2 = 0\%$). The authors state this as moderate quality evidence.

The results suggest the possibility of a mortality benefit with GLP-1 agonists, but not with DPP-4 inhibitors, but the sub group analysis was not sufficiently robust to be certain of this.

All the included trials were funded by the pharmaceutical industry. However, the investigators state that their 'funnel plot and statistical test showed no evidence of publication bias'. Another limitation was that many of the trials had shorter follow-up periods than might be needed to detect mortality differences.

The authors conclude: 'Our results provide no support for the hypothesis that incretin-based treatments are associated with increased all cause mortality in patients with type 2 diabetes.'

'Additional large well designed randomised trials with adequate follow-up will be necessary to definitively establish or refute possible differences in the effect of GLP-1 agonists and DPP-4 inhibitors on all cause mortality,' they add.

The potential associated risks of diabetes drugs, which have been widely reported in the lay press and other media, have made it even harder for diabetologists and GPs to persuade patients of the need to comply with treatments for their condition. It is useful for us to be able to see meta-analyses such as this one.

DR MATTHEW LOCKYER

Liu J, Li L, Deng K et al. Incretin based treatments and mortality in patients with type 2 diabetes: systematic review and meta-analysis. *BMJ* 2017;357:2499

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