Injected liraglutide is better than oral sitagliptin for blood glucose control in type 2 diabetes

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Injections of liraglutide are better than oral sitagliptin at controlling blood glucose levels in people with type 2 diabetes who have inadequate control on the standard treatment metformin. The findings appear in an Article in this week's *Lancet*, written by Dr Richard E Pratley, University of Vermont College of Medicine, Burlington, VT, USA, and colleagues.

An estimated 285 million people worldwide have diabetes at present, and 439 million are expected to have diabetes by 2030. Vascular complications are responsible for most of the associated morbidity, mortality, and excess costs. Although good glycaemic control can decrease the risk of microvascular, and possibly macrovascular complications, many people with type 2 diabetes are not achieving glycaemic goals, partly because of the low efficacy and adverse side-effects of available drugs.

Both liraglutide and sitagliptin increase secretion of the hormone insulin (which helps decrease blood sugar levels), and decrease secretion of the hormone glucagon (which prevents blood sugar levels increasing again). However, the two drugs have a different mechanism of action, and liraglutide requires injection, while sitagliptin can be taken orally. Liraglutide promotes weight loss, and causes nausea in some patients—while sitagliptin does not cause weight loss and rarely causes nausea. Data from direct in-patients comparisons of these two drug types

are scarce. Thus the authors compared the two directly in patients who had inadequate blood sugar control on metformin alone.

In this randomised trial, patients aged 18-80 year with type 2 diabetes mellitus who had inadequate blood sugar control (glycosylated haemoglobin [HbA1c] 7•5-10•0%)* on metformin (≥1500 mg daily for ≥3 months) were enrolled and treated at office-based sites in Europe, the USA, and Canada. Participants received 26 weeks' treatment with 1•2 mg (n=225) or 1•8 mg (n=221) injections of liraglutide once daily. or 100 mg sitagliptin orally once daily. The primary endpoint was change in HbA1c from baseline to week 26.

The researchers found greater lowering of mean HbA1c (8•5% at baseline) was achieved with 1•8 mg liraglutide (-1•50%) and 1•2 mg liraglutide (-1•24%,) than with sitagliptin (-0•90%). Estimated mean treatment differences for liraglutide versus sitagliptin were -0•60% for 1•8 mg and -0•34% for 1•2 mg liraglutide. Nausea was more common with liraglutide (59 [27%] patients on 1•8 mg; 46 [21%] on 1•2 mg) than with sitagliptin (10 [5%]). Minor hypoglycaemia (very low blood sugar levels) was recorded in about 5% of participants in each treatment group. But overall, both drugs were well tolerated.

The authors point out that in the UK Prospective Diabetes Study Group trial, a 1% reduction in HbA1c was associated with a 37% decreased risk of microvascular complications and a 21% decreased risk of death related to diabetes. They say: "These results suggest that the differences in HbA1c between liraglutide and sitagliptin that were recorded in our study are clinically relevant."

They conclude: "Liraglutide was superior to sitagliptin for reduction of HbA1c, and was well tolerated with minimum risk of hypoglycaemia. These findings support the use of liraglutide as an effective agent to add to metformin."

In an accompanying Comment, Dr André J Scheen, and Dr Régis P Radermecker, University of Ličge, Belgium, say that 1•2 mg liraglutide should be considered as the starting dose in most patients with type 2 diabetes, with recommendations for titration up to 1•8 mg if target HbA1c concentrations are not reached.

However they add: "Even though Pratley and colleagues recorded superior treatment satisfaction with 1•8 mg liraglutide than with sitagliptin, the gastrointestinal tolerance profile is better with sitagliptin than with liraglutide, and one pill of sitagliptin daily might be judged as easier to administer than one subcutaneous injection of liraglutide daily. The increased cost of liraglutide should be compared with the benefit provided by [its] improved glucose control and weight reduction."

Provided by Lancet

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