The effectiveness of GLP-1 analogues compared to DPP-4 inhibitors for beta cell function and diabetes related complications among adults with type 2 diabetes: a systematic review and meta-analysis

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23rd December 2015

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Acknowledgements

It is with immense gratitude that I acknowledge my supervisors, Associate Professor Edoardo Aromataris and Dr Jared Campbell, for their advice and support. I would particularly like to thank Edoardo for his continuing patience and dedication, immense knowledge and tireless encouragement and enthusiasm. Without his guidance and mentorship this thesis would not have been possible.

I would like to take this opportunity to express my sincere appreciation to staff members at Joanna Briggs Institute for their help, support and friendly faces. In particular, I would like to thank Siang Tay for her assistance with copyediting the thesis chapters to assist with grammatical consistency and punctuation.

Finally, to my wonderful family, especially my husband, I thank you for coming on this journey with me, for supporting me during this challenging time, and for your company during the long, late nights of study. For this, I am eternally grateful.

Declaration

I, Susan Bellman, certify that this work contains no material that has been accepted for the award of any other tertiary institution, and, to the best of my knowledge and belief, contains no material previously published or written by any other person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and, where applicable, any partner institution responsible for the joint award of this degree.

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23rd December 2015

Abstract

Continued loss of beta cell function is responsible for progressive deterioration of plasma glucose control and complications characteristic of type 2 diabetes. Two classes of incretin-based antihyperglycaemic agents, dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide-1(GLP-1) analogues, have shown favourable effects on beta cell function. The aim of this systematic review was to provide a comprehensive synthesis of randomised clinical studies comparing the effectiveness of GLP-1 analogues to DPP-4 inhibitors in improving beta cell function and managing diabetes related complications.

A search of PubMed, EMBASE and national and international clinical trials databases was conducted for randomised controlled trials that compared GLP-1 analogues to DPP-4 inhibitors, either alone or in combination with metformin, in adults with type 2 diabetes. Methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist, and research data was extracted using the JBI data extraction tool. Outcomes included beta cell function (measured by homeostasis model assessment-beta [HOMA-beta], plasma connecting peptide [C-peptide] and proinsulin to insulin [PI/I] plasma concentration ratio) glycated haemoglobin (HbA1c), fasting and postprandial plasma glucose levels, diabetes related complications, and adverse drug events.

Seven randomised controlled trials including 2661 participants were included in this review. The overall quality of included studies was good. Treatment duration ranged from 24 to 52 weeks in the included studies and included a number of different dosages. Results of meta-analysis showed that GLP-1 analogues, at different dosages and duration, were associated with statistically significant improvements in beta cell function compared to DPP-4 inhibitors as measured by HOMA-beta; mean difference 23% and 25% for high dose GLP-1 analogues

after 26 and 52 weeks, respectively (p<0.00001); 18.5% and 16.7% for low dose GLP-1 analogues after 26 and 52 weeks, respectively (p<0.00001). Treatment with GLP-1 analogues showed a greater reduction in glycated haemoglobin (HbA1c) compared to treatment with DPP-4 inhibitors: a mean difference of -0.52% and -0.68% (-5.67mmol/moL and -7.41mmol/moL) for high dose GLP-1 analogues after 26 and 52 weeks, respectively (p<0.00001); and -0.38% and -0.45% (-4.14mmol/moL and -4.91mmol/moL) for low dose GLP-1 analogues after 26 and 52 weeks, respectively (p<0.00001). Treatment with GLP-1 analogues resulted in a greater reduction in fasting plasma glucose compared to DPP-4 inhibitors: a mean difference of -1.23 mmol/L and -1.47 mmol/L (-22.16 mg/dL and -26.49 mg/dL) for high dose GLP-1 analogues after 26 and 52 weeks, respectively p<0.00001); and -1.01mmol/L and -0.84mmol/L (-18.20mg/dL and -15.13 mg/dL) for low dose GLP-1 analogues after 26 and 52 weeks, respectively (p<0.00001). No studies reported outcomes for diabetes related complications. However, DPP-4 inhibitors were associated with fewer gastrointestinal adverse events compared to GLP-1 analogues. There were no differences in other adverse events such as headache and infection.

The findings showed that GLP-1 analogues had greater beneficial effects on pancreatic beta cell function and plasma glucose control than DPP-4 inhibitors, but caused more gastrointestinal adverse events. Longer term safety data is required to better identify the contribution of GLP-1 analogues in reducing diabetes related microvascular complications, and determine their long term pancreatic and cardiac effects.