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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# Table of Contents

Acknowledgements 5

Declaration 6

Abstract 7

Chapter 1: Introduction 9

1.1 Background 9

1.2 Aetiology and pathophysiology of diabetes 12

1.2.1 The incretin effect 17

1.3 Antihyperglycaemic agents 20

1.3.1 Biguanide 20

1.3.2 Sulfonylureas 21

1.3.3 Meglitinides 21

1.3.4 Thiazolidinediones 21

1.3.5 Alpha-glucosidase inhibitors 22

1.3.6 Sodium-glucose co-transporter-2 inhibitors 22

1.3.7 Insulin 23

1.3.8 Glucagon-like peptide-1 (GLP-1) analogues 23

1.3.9 Dipeptidyl peptidase-4 (DPP-4) inhibitors 24

1.4 Measures of beta cell function 25

1.4.1 Hyperglycaemic clamp technique 26

1.4.2 Measures of plasma connecting peptide (C-peptide) 27

1.4.3 Proinsulin to insulin plasma concentration ratio 28

1.4.4 Homeostasis model assessment (HOMA) 29

1.5 Measures of glycaemic control 31

1.5.1 Fasting plasma glucose 31

1.5.2 Postprandial plasma glucose 31

1.5.3 Glycated haemoglobin (HbA1c) 32

1.6 Diabetes related complications 33

1.6.1 Retinopathy 34

1.6.2 Neuropathy 36

1.6.3 Nephropathy 37

1.7 Why a systematic review is needed 38

1.7.1 Current evidence for the comparison between GLP-1 analogues and DPP-4 inhibitors on beta cell function and diabetes related complications in adults with type 2 diabetes 38

1.8 Review question 39
Chapter 2: Systematic review methods

2.1 Types of participants

2.2 Types of interventions and comparators

2.3 Types of outcomes

2.4 Types of studies

2.5 Search strategy
   2.5.1 Search method

2.6 Assessment of methodological quality

2.7 Data extraction

2.8 Data synthesis
   2.8.1 Data conversions
   2.8.2 Meta-analysis

Chapter 3: Results

3.1 Study inclusion process

3.2 Methodological quality

3.3 Description of included studies
   3.3.1 Interventions and comparators

3.4 Effects on pancreatic beta cell function
   3.4.1 HOMA-beta (%)
      3.4.1.1 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 26 weeks
      3.4.1.2 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 52 weeks
   3.4.2 Plasma proinsulin to insulin (P/I) ratio
   3.4.3 Plasma C-peptide levels

3.5 Effects on glycaemic control
   3.5.1 Glycated haemoglobin (HbA1c)
      3.5.1.1 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 26 weeks
      3.5.1.2 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 52 weeks
   3.5.2 Fasting plasma glucose
      3.5.2.1 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 26 weeks
3.5.2.2 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 52 weeks

3.5.3 Postprandial plasma glucose

3.6 Outcomes of diabetes related complications using GLP-1 analogue compared to DPP-4 inhibitor

3.7 Adverse events using GLP-1 analogue compared to DPP-4 inhibitor

3.7.1 Gastrointestinal adverse events

3.7.1.1 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 24 to 26 weeks

3.7.1.2 High dose and low dose GLP-1 analogue compared to DPP-4 inhibitor for duration of 52 weeks

3.7.2 Headache, infections, pancreatitis and mortality

Chapter 4: Discussion

4.1 General discussion

4.2 Limitations of included studies

4.3 Limitations of the review process

4.4 Implications for clinical practice

4.5 Implications for research

4.5.1 Cost effectiveness of adding GLP-1 analogues to metformin monotherapy

4.5.2 Use of GLP-1 analogue in prediabetes

4.5.3 Use of GLP-1 analogue in beta cell preservation and regeneration

4.5.4 Long term safety data for GLP-1 analogues

4.6 Conclusion

Appendices

I. Systematic review protocol

II. Search strategies

III. Joanna Briggs Institute (JBI) Critical appraisal tool

IV. Joanna Briggs Institute (JBI) Data extraction tool

V. Details of additional data obtained for included studies from study authors

References
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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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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.