**Introduction**

Continued loss of beta cell function is responsible for progressive deterioration of plasma glucose control, and complications characteristic of type 2 diabetes. Research has indicated that a decline in beta cell function occurs early in the course of type 2 diabetes. (Figure 1.1)

There is increasing clinical evidence that the incretin hormone glucagon-like peptide-1 (GLP-1) can improve beta cell function, however clinical use of GLP-1 in its native form is hampered by its rapid, enzymatic inactivation by dipeptidyl peptidase-4 (DPP-4). Two classes of incretin-based antihyperglycaemic agents DPP-4 inhibitors and GLP-1 analogues utilise the biological potential of GLP-1 in two ways:

- GLP-1 analogues are resistant to DPP-4 inactivation and mimic the action of naturally occurring GLP-1.
- DPP-4 inhibitors block enzymatic DPP-4 action and thereby prolong the activity of endogenous GLP-1. (Figure 2.1)

**Aim**

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 on beta cell function and diabetes related complications.

**Method**

A search of PubMed, EMBASE and national and international clinical trials databases was conducted. Randomised controlled trials were included that compared GLP-1 analogues to DPP-4 inhibitors, either alone or in combination with metformin, in adults with type 2 diabetes. Primary outcomes of interest were:

- beta cell function measured by hyperglycaemic clamp technique, homeostasis assessment model (HOMA), measures of C-peptide and proinsulin to insulin plasma concentration ratio
- glycated haemoglobin (HbA1c)
- fasting and postprandial plasma glucose levels.

Secondary outcomes of interest were diabetes related complications (neuropathy, nephropathy and retinopathy) adverse drug events and mortality.

**Figure 2.** Schematic diagram explaining: (A) physiological secretion of GLP-1 from the gut, (B) its binding to GLP-1 receptors on the pancreatic beta cells and (C) its enzymatic degradation by DPP-4. GLP-1 analogue (D) binds to and activates GLP-1 receptors. DPP-4 inhibitors (E) prevent the degradation of biological GLP-1 and thereby enhance its activity on the pancreas. (Adapted from: Nauck M, Wibald T, Gallwitz B. Incretin-Based Therapies. Diabetes Care. 2009;32(Suppl:S23-S21).

A total of eight randomised controlled trials were included in the systematic review, including two unpublished studies and three multi-arm studies. Treatment duration ranged from eight weeks to 52 weeks. Four different GLP-1 analogues were used in the retrieved studies (lixisenatide, lixisenatide, dulaglutide and exenatide) while the same DPP-4 inhibitor (sitagliptin) was used as the active comparator throughout all included studies.

**Conclusion**

The findings showed that GLP-1 analogues had greater beneficial effects on pancreatic beta cell function, HbA1c and fasting plasma glucose levels than DPP-4 inhibitors, however caused more gastrointestinal adverse events.