The effects of exenatide bid on metabolic control, medication use and hospitalization in patients with type 2 diabetes mellitus in clinical practice: a systematic review

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CRD summary
This review reported that exenatide initiation was associated with significant improvements in clinically relevant outcomes. Because of a lack of quality assessment and limitations in the conduct and reporting of the review, the reliability and generalisability of the authors' conclusions are uncertain.

Authors' objectives
To assess the effectiveness of exenatide twice daily in clinical practice.

Searching
PubMed was searched from January 2005 to May 2011. Only studies published in English were considered. Search terms were reported. The references of articles identified from the search were examined for additional studies.

Study selection
Retrospective or prospective studies of patients who initiated exenatide in clinical practice were eligible for inclusion. Studies had to include 100 patients or more per treatment group and report relevant outcomes. Studies such as randomised trials, reviews, case studies and articles that did not include at least one end point of interest were excluded.

The outcomes of interest were the effects of exenatide on haemoglobin A1C (HbA1C), fasting glucose, weight, systolic blood pressure, medication use, hospitalisation and cardiovascular disease outcomes.

Most studies were conducted in the United States. The authors stated that, compared with clinical trial populations, these exenatide-treated patients typically had a higher level of disease severity and comorbidities (such as, hypertension, hyperlipidaemia, obesity, history of cardiovascular disease). In some studies, patients were treated with exenatide in combination with the oral glucose lowering therapies metformin, sulphonylurea or thiazolidinedione with or without insulin. Comparators were other glucose lowering therapies, insulin, insulin glargine, NPH insulin (Neutral Protamine Hagedorn insulin) and sitagliptin. Some studies did not have comparator group.

The authors did not state how many reviewers were involved in study selection.

Assessment of study quality
The authors did not state that they assessed the study quality.

Data extraction
Data of patient characteristics, changes in haemoglobin A1C, fasting glucose, body weight, systolic blood pressure from baseline together with changes in medication, rates of hospitalisation and cardiovascular disease events were extracted.

The authors did not state how many reviewers were involved in data extraction.

Methods of synthesis
Results were presented in a narrative synthesis grouped by type of outcome.

Results of the review
Fifteen prospective and retrospective observational studies were included in the review (at least 60,000 participants treated with exenatide with sample size ranging from 102 to 39,275). In most studies, patient progress was followed for at least six months; the maximum follow-up was 27 months.

Haemoglobin A1C (nine studies) and fasting glucose (one study): Nine studies showed significant improvement in haemoglobin A1C when exenatide was initiated in combination with oral glucose-lowering medication. Patients who received exenatide in combination with oral glucose-lowering medication without insulin experienced significant
reductions in haemoglobin A1C of −0.5 to −0.9% (four studies). Patients initiating exenatide experienced a significant decrease in fasting glucose of −10 mg/dl.

**Weight Reduction (nine studies) and Systolic Blood Pressure (three studies):** Nine studies assessed weight loss and all reported significant weight loss with exenatide. Patients receiving exenatide in combination with insulin experienced weight loss, ranging from −2.3 to −11 kg. There was a statistically significant decrease of systolic blood pressure in patients initiating exenatide treatment with oral glucose-lowering medication, ranging from −1.9 to −11 mmHg.

**Medication Changes (five studies):** Statistically significant reductions in the use or dosage of either oral glucose-lowering medications or insulin after initiating exenatide treatment were found in every observational study that assessed medication changes.

**Hospitalisation and cardiovascular disease Events (four studies):** There were significantly lower rates of all-cause and cardiovascular disease-related hospitalisation and cardiovascular disease events in patients treated with exenatide than patients treated with other therapies overall.

**Authors’ conclusions**
Exenatide initiation was associated with significant reductions in clinically relevant outcomes. Improvements in haemoglobin A1C, fasting glucose, weight and systolic blood pressure in the observational studies in this review were consistent with improvements observed in controlled clinical trials.

**CRD commentary**
The review question and inclusion criteria were generally clear. The literature search was limited to one database and studies published in English so there was a high risk of publication bias and also a risk of missing relevant published studies from other databases. The authors did not report how many reviewers were involved in the study selection and data extraction, so reviewer's bias and error was possible. The authors did not report the quality of each included study, so it was difficult to assess the overall quality of the studies.

Only observational studies were included in this review and they were inherently at higher risk of bias than randomised trials. A narrative synthesis was appropriate but the synthesis presented did not distinguish clearly between different populations, glucose-lowering medications, disease severity and comorbidities and patient’s compliance on treatment regime.

Three authors were employees of Amylin Pharmaceuticals and one author had previously received grants from Amylin Pharmaceuticals; this could have been a conflict of interest.

Because of the lack of quality assessment and limitations in the conduct and reporting of the review (particularly the unclear synthesis), the reliability and generalisability of the authors’ conclusions are uncertain.

**Implications of the review for practice and research**
The authors did not state any implications for practice and further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.