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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.
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Exenatide update

The pharmacological action of exenatide and its potential role in the management of patients with type 2 diabetes (T2DM) were discussed in a previous E-bulletin 30(10). This E-bulletin will address some of the new evidence that has since emerged since for the use of exenatide.

A systemic review conducted in 2009 by Norris et al. evaluated 17 studies (4 active controlled; 4 placebo controlled, 9 non-randomised controlled) that assessed the efficacy of exenatide versus long acting insulin regimen, as well as to placebo. In the four active controlled trials, patients (average age 56) with BMI of 31-35kg/m^2 and average baseline HBA1c of 8.3-9% were followed for up to 52 weeks. This systemic review concluded that exenatide achieved similar improvements in overall glycaemic control compared to insulin in patients with T2DM that was sub-optimally controlled with oral therapy. Furthermore exenatide was associated with weight loss. The rates of hypoglycaemia were similar for exenatide and long acting insulin.

In previous studies comparing exenatide and long acting insulin, patients who received exenatide were found to have better postprandial blood glucose level (BGL) control, while those who received insulin had better fasting BGL profiles. A more recent study was published evaluating the use of exenatide in patients who are already treated with basal insulin, with the aim to evaluate the hypothesis that better overall BGL control can be achieved due to the complementary pharmacologic effects of exenatide and basal insulin on BGL profiles. The study was a 30-week, randomised, double-blinded placebo-controlled study conducted in 59 centres in five counties from Oct 2008 to Jan 2010. Study patients were type 2 diabetics who had been receiving insulin glargine of at least 20 units/day (average dose 48 units/day, alone or in combination with metformin and/or pioglitazone) for at least three months. These patients had an HBA1c level of 7.1% to 10.5% and BMI of around 34 kg/m^2. Patients were randomly assigned to receive exenatide or placebo. The primary study outcome was the change in HBA1c over 30 weeks from baseline, and secondary outcomes included changes in body weight, insulin doses, BGL profiles, hypoglycaemia and adverse effects. The study concluded that the use of exenatide with insulin glargine was associated with an additional 0.69% reduction of HbA1c (as well as weight loss) at the end of the 30-week period, compared to patients who only relied on titration of their insulin regimens for BSL control. Gastrointestinal side effects were more common in the exenatide group whereas the rate of hypoglycaemia was similar between groups (see summary below).

Change from baseline to wk 30	Exenatide group (n=137)	Placebo group (n=122)	Between group difference	P value
HbA1c level (%)	-1.74 (-1.91 to -1.56)	-1.04 (-1.22 to -0.86)	-0.69 (-0.93 to -0.46)	<0.001
Body weight (kg)	-1.78 (-2.48 to -1.08)	0.96 (0.23 to 1.7)	-2.74 (-3.74 to -1.74)	<0.001

Exenatide has available as a subsidised pharmaceutical benefit through the PBS since August 2010, but is only indicated to be used as dual or triple therapy in combination with metformin and/or sulfonylurea. It is believed that this recent study is not likely to change current practice at this early stage, mostly because of limitations associated with the study, including strict exclusion criteria. The data may not apply to patients who are treated with sulfonylureas; with a HbA1c of less than 7.0%; and those with a recent history of major hypoglycaemia. Further studies are underway to investigate the use of a weekly dosing of exenatide as well as the potential effects of exenatide on cardiovascular events.

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