Effects of somatostatin analogs on glucose homeostasis: a metaanalysis of acromegaly studies

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CRD summary
This review concluded that somatostatin analogue treatment may have a marginal clinical impact on glucose homeostasis in patients with acromegaly. The conduct of this review was generally good and the authors' conclusions are suitably cautious given that the evidence came from observational studies.

Authors' objectives
To assess the clinical impact of somatostatin analogues on glucose metabolism in patients with acromegaly.

Searching
MEDLINE was searched to the end of May 2008 for studies published in English. Search terms were reported. Reference lists of published trials, reviews and editorials, and international meeting abstracts were also searched.

Study selection
Eligible studies were randomised or non-randomised trials of at least three weeks of somatostatin analogues treatment in patients with acromegaly. Eligible studies had to provide numerical data for at least one of the following outcomes: fasting plasma glucose; fasting plasma insulin; glycated haemoglobin (HbA1c); and glucose concentration during an oral glucose tolerance test. Outcomes had to be measured before and after somatostatin analogues treatment; patients could not be selected by their biochemical response to somatostatin analogues.

The drugs under assessment in the included studies were octreotide, long-acting octreotide, lanreotide slow release and lanreotide Autogel, used singly or in combination. Median participant ages ranged between 31 and 61 years. The duration of treatment ranged from three weeks to 96 months.

Studies were selected by two independent reviewers with differences in opinion resolved in a meeting.

Assessment of study quality
The authors did not assess study validity.

Data extraction
The mean change in outcome from baseline to the end of treatment was extracted and used to calculate the effect size (ES), which was the mean change divided by the pooled standard deviation.

Data were independently extracted by two clinicians and two statisticians onto a standardised data extraction form; differences in opinion were resolved by a fifth reviewer who referred back to the original paper.

Methods of synthesis
A fixed-effect, inverse variance weighted model was used to pool the results. Statistical heterogeneity was assessed using Cochran's Q test (p<0.1) and the I² statistic (values over 50% were taken as high heterogeneity).

Meta-regression analyses were used to look at the impact of treatment duration, proportion of diabetic patients, and biochemical response to somatostatin analogues on the relevant outcomes.

Results of the review
Thirty-one studies were included in the review (n=619 patients, ranging from five to 90); 251 patients were treated with octreotide, 162 with octreotide long-acting release, 174 with lanreotide slow release, and 37 with lanreotide Autogel.
The included studies were mostly retrospective or prospective case series.

Somatostatin analogue treatment was associated with a statistically significant increase in the glucose response to an oral glucose tolerance test (ES 0.31, 95% CI 0.17 to 0.45; 12 studies; $I^2=53.5\%$). There was also a difference between types of somatostatin analogues, with lanreotide leading to a greater increase in glucose response (ES 0.83, 95% CI 0.50 to 1.16; 96 patients) compared with octreotide (ES 0.15, 95% CI -0.03 to 0.33; 212 patients). Fasting plasma insulin was significantly reduced with somatostatin analogue treatment (ES -0.45, 95% CI: -0.58 to -0.32; 16 studies; $I^2=68.8\%$), but there was no difference between different treatments.

Somatostatin analogue treatment did not have any effect on the change in fasting plasma glucose (18 studies) or HbA1c (15 studies), and there was very little between study heterogeneity.

There were also no differences between different types of somatostatin analogue treatment. Meta-regression analyses found no association between treatment duration, biochemical response or the prevalence of diabetes and any outcomes.

Other results were reported in the paper.

**Authors’ conclusions**
Somatostatin analogue treatment may have a marginal clinical impact on glucose homeostasis in patients with acromegaly.

**CRD commentary**
This review specified the inclusion criteria for study design, intervention, participants and outcomes. The search used only one database and was restricted to studies published in English, so relevant studies may have been missed. Two or more reviewers independently selected studies and extracted data, so steps were taken to minimise the risk of bias or errors.

There was no formal quality assessment. The evidence came from less reliable study designs, as most studies were case series, so the results are based only on changes within patients and not comparisons to a control treatment.

The conduct of this review was generally good and the authors' conclusions are suitably cautious given that the evidence came from observational studies.

**Implications of the review for practice and research**

**Practice:** The authors stated that more careful glycometabolic follow-up is needed in patients with difficult control of growth hormone hypersecretion compared with patients who are not resistant to somatostatin analogues.

**Research:** The authors did not give any recommendations for research.

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