Impact of somatostatin analogs on the heart in acromegaly: a metaanalysis

Maison P, Tropeano A I, Macquin-Mavier I, Giustina A, Chanson P

CRD summary
This review assessed the effect of somatostatin analogues on cardiac outcomes in patients with acromegaly. The authors concluded that sustained somatostatin analogue treatment can improve structural and functional cardiac outcomes. Given the poor reporting of the review methodology, it is not possible to comment on the reliability of the results.

Authors' objectives
To synthesise the evidence of the effect of somatostatin analogues on the heart in patients with acromegaly.

Searching
MEDLINE, BIOSIS Previews and EMBASE were searched to June 2006; the keywords were listed. The proceedings of major cardiology meetings were handsearched to identify further studies that had only been published in abstract form.

Study selection
Studies of patients with acromegaly were eligible for inclusion. In the included studies, the mean age (where stated) ranged from 28 to 55 years and 47% of the participants were male.

Studies that evaluated somatostatin analogues were eligible for inclusion. The included studies explored various doses of either octreotide, long-acting release octreotide or prolonged-release lanreotide. Treatment duration ranged from 1 day to 18 months. It is unclear what the control was.

All study designs were eligible for inclusion. The designs of the included studies were not stated, other than that none of them were randomised controlled trials. Their size ranged from 5 to 30 patients.

Outcome inclusion criteria were at least one of the following: heart rate, interventricular septum thickness, left ventricular (LV) posterior wall thickness, LV end-diastolic dimension, LV end-systolic diameter, LV mass, LV mass index (per m² body surface area), LV ejection fraction, ratio of early to late mitral diastolic flow and exercise duration.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Two reviewers independently assessed validity on the basis of study design, blinding, statistical methods and losses to follow-up. Any disagreements were resolved by consensus.

Data extraction
Standardised effect sizes (weighted mean difference, WMD) were calculated as the mean difference between baseline and follow-up, divided by the variance at baseline. In one study this had to be estimated from the figures.

Two reviewers independently extracted the data and any disagreements were resolved by consensus.

Methods of synthesis
A fixed-effect meta-analysis was used to synthesise the results. Each study was weighted by the reciprocal of its variance. The authors stated that weighted least-squares meta-regression was used to investigate reasons for differences between the studies. Subgroup analysis was used to examine the effect of different forms of the drug, patients’ age, decline in insulin-like growth factor I and growth hormone levels and baseline LV mass. Publication and location bias were investigated using funnel plots. Statistical heterogeneity was assessed using the Q statistic. When significant heterogeneity was present, results from random-effects models were presented.

Results of the review
Eighteen distinct comparisons from 15 studies were included in the review. The total number of participants included was not clear: it was given as 290 in the text and 255 in Table 1. The authors stated that significant heterogeneity was found for most of the meta-analyses.

The authors stated that all of the studies were of a good quality. An assessment of publication bias suggested that this was only significant for one outcome (LV mass index).

Somatostatin analogue treatment was associated with a decrease in heart rate (WMD -0.47, 95% confidence interval, CI: -0.74, -0.19), LV mass (WMD -1.14, 95% CI: -2.06, -0.21), LV mass index (WMD -0.78, 95% CI: -0.97, -0.58), interventricular septum thickness (WMD -0.67, 95% CI: -0.95, -0.38) and LV posterior wall (WMD -0.50, 95% CI: -0.87, -0.14).

Somatostatin analogue treatment was associated with an increase in ratio of early to late mitral diastolic flow (WMD 0.43, 95% CI: 0.16, 0.70) and exercise duration (WMD 1.06, 95% CI: 0.43, 1.70).

No significant effect of somatostatin analogue treatment was seen for LV end-diastolic dimension, LV ejection fraction, systolic or diastolic blood-pressure, LV end-systolic diameter or fractional shortening.

The results for weighted mean change in each outcome were also reported in the review. No results of meta-regression analyses were presented.

Authors' conclusions
Sustained somatostatin analogue treatment can improve structural and functional cardiac parameters in patients with acromegaly.

CRD commentary
The review addressed a clear research question and inclusion criteria for the participants, interventions and outcomes were stated. Several relevant sources were searched and attempts were made to identify studies reported as abstracts, but no attempts to minimise language or publication bias were reported. However, statistical tests for publication bias were significant for only one outcome. The methods used to select the studies were not described, so it is not known whether any efforts were made to reduce reviewer error and bias.

The designs of the included studies were not adequately described, and the number of participants included in the review differed between the text and tables in the review. The authors stated that all of the studies were of a good quality, but in the absence of details about study design and validity criteria it is not possible to verify this. Analysis of multiple outcomes increased the probability that some results would be significant by chance. There was no discussion of how concomitant treatment might have influenced the outcomes.

There were several inconsistencies in the review, such as differences in the number of patients reported in the text and tables, the reporting of weighted mean change in outcomes in the results (although this was not mentioned in the 'Methods' section), and stating that meta-regression was used but not presenting results from this analysis.

Given the poor reporting of the review methodology and lack of sufficient details of the design and quality of the included studies, it is not possible to comment on the reliability of the results.

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

Research: The authors stated that larger trials or individual level patient meta-analysis is needed to investigate which sub-populations may particularly benefit from somatostatin analogue therapy.

Funding
Not externally funded.
Bibliographic details

PubMedID
17311857

DOI
10.1210/jc.2006-2547

Original Paper URL
http://jcem.endojournals.org/cgi/content/full/92/5/1743

Indexing Status
Subject indexing assigned by NLM

MeSH
Acromegaly /drug therapy /physiopathology; Adult; Blood Pressure /drug effects /physiology; Data Interpretation, Statistical; Exercise Test; Female; Heart /drug effects /physiopathology; Hormone Antagonists /therapeutic use; Human Growth Hormone /blood; Humans; Male; Middle Aged; Octreotide /therapeutic use; Peptides, Cyclic /therapeutic use; Randomized Controlled Trials as Topic; Sample Size; Somatostatin /analogs & derivatives /therapeutic use; Treatment Outcome

AccessionNumber
12007005710

Date bibliographic record published
01/09/2008

Date abstract record published
23/12/2008

Record Status
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.