Place of preoperative treatment of acromegaly with somatostatin analog on surgical outcome: a systematic review and meta-analysis

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CRD summary
The authors concluded that somatostatin analogues before surgery for acromegaly significantly improved surgical outcomes; centres without optimal surgical results should treat patients with a long-acting somatostatin analogue before surgery. Given the limitations of the evidence, potential for review bias, and unsupported recommendations by the authors, the conclusions are unlikely to be reliable.

Authors' objectives
To investigate the effects of preoperative somatostatin analogue on surgical outcomes when treating patients with acromegaly.

Searching
MEDLINE, EMBASE, The Cochrane Library and the Internet, using Google Scholar, were searched up to December 2011 for relevant articles. Search terms were reported. Reference lists of eligible studies and relevant reviews were manually searched.

Study selection
Eligible for inclusion were all studies that assessed the effects of treatment for acromegaly with preoperative somatostatin analogues, on postoperative cure rates. Eligible studies had to report sufficient data for meta-analysis. Abstracts were excluded, as were studies that did not report levels of insulin-like growth factor (IGF)-1 and studies without a control group.

The included studies were conducted between 1996 and 2010. The mean age of participants ranged from 40.6 to 47.5 years. Most studies administered short-acting octreotide, 100 micrograms every eight hours, for between three and an average of 36 weeks. The authors stated that IGF-1 levels before treatment were sometimes higher in the treated group than in the control group. Various criteria were used to define the cure rate. Tumour shrinkage, length of hospital stay, and surgical complications were reported.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
The authors did not state the criteria used to assess study quality, nor how many reviewers performed the assessment.

Data extraction
Two reviewers independently extracted the percentages of treated and non-treated participants who were cured, to calculate odds ratios and their 95% confidence intervals. Discrepancies between reviewers were resolved by discussion.

Methods of synthesis
Both fixed-effect and random-effects models were used to pool the odds ratios and their 95% confidence intervals; the data from the random-effects models are presented here. Separate analyses of randomised controlled trials (RCTs) only were performed. It appears that post-hoc regression analysis was performed to determine whether there was a relationship between surgical outcome and pre-treatment with somatostatin analogues.

Statistical heterogeneity was assessed using Galbraith and L'Abbe plots and Cochran Q. Sensitivity analysis was performed by removing each study one at a time. Publication bias was assessed using a funnel plot and Begg's and Egger's tests.

Results of the review
Ten studies (968 participants; range 24 to 286) were included in the review. Three were RCTs, two were non-
randomised controlled trials, and five were controlled retrospective studies. The authors stated that the studies were generally of good quality, and that few losses to follow-up were reported. Follow-up ranged from 12 to over 24 weeks, for nine studies; one study assessed some outcomes at one to two weeks and others at 48 weeks.

There was a borderline statistically significant effect on cure rates, favouring the treatment group (OR 1.62, 95% CI 0.93 to 2.82; 10 studies). The results were not significantly altered when sensitivity analysis was performed. Separate analysis of the three RCTs showed a statistically significant higher cure rate for participants receiving somatostatin analogues compared with controls (OR 3.62, 95% CI 1.88 to 6.96).

Regression analysis explored the relationship between the surgical performance of centres (cure rate in untreated patients) and benefit from pre-treatment with somatostatin analogues. This was briefly discussed in the review.

The mean volume reduction in tumour size ranged from 25% to 40%. Results for hospital stay were conflicting, and there were no differences between treatment groups in surgical complication rates.

There was no evidence of publication bias.

**Authors' conclusions**

Treatment with somatostatin before surgery for growth hormone-secreting pituitary adenomas significantly improved surgical outcome. In centres without optimal surgical results, all patients with these pituitary macroadenoma should be treated with a long-acting somatostatin analogue before surgery.

**CRD commentary**

The review question and supporting inclusion criteria were broadly stated. Several databases were searched without restrictions, reducing the potential for missed studies. The authors did not state whether study selection and quality assessment were performed in duplicate, which means that reviewer error and bias cannot be ruled out. The authors did not state how study quality was assessed, but stated that the included studies were of generally good quality. However, half the studies were retrospective; their samples were small; and treatment duration and follow-up were generally short.

Forest plots showed fairly wide confidence intervals and some evidence of inconsistency, but it was unclear how much statistical heterogeneity was present as the results were not reported. The authors acknowledged that the evidence was too limited to allow analysis for length of hospital stay and surgical complication rates.

There was potential for bias in the review, the evidence had limitations, and the overall findings were not statistically significant. The authors recommended long-acting somatostatin analogues for all patients in centres without optimal surgical results, but this was not fully assessed and was based on a secondary analysis. These limitations suggest that the authors' conclusions are unlikely to be reliable.

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

**Practice:** The authors stated that their results were mainly based on prospective studies of patients with macroadenoma, and should probably not be applied to patients with microadenoma.

**Research:** The authors did not state any implications for research.

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