Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review

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CRD summary
The authors concluded that glucagon-like peptide-1 and peptide tyrosine-tyrosine concentrations were usually higher and ghrelin levels were usually lower in participants undergoing Roux-en-Y gastric bypass surgery compared with various comparator conditions. Given the potential for error and bias in the review, the limited search and the unclear quality of included studies, the authors' conclusions should be treated with caution.

Authors' objectives
To investigate changes in gastrointestinal hormones and leptin following Roux-en-Y gastric bypass surgery.

Searching
MEDLINE was searched for English language articles; search terms were reported. Bibliographies of recent review articles were handsearched for additional studies.

Study selection
Studies that evaluated the impact of Roux-en-Y gastric bypass surgery on glucagon-like peptide-1, peptide tyrosine-tyrosine, ghrelin (gastrointestinal hormones) and/or leptin in participants with no previous weight loss surgeries were eligible for inclusion. Case studies and studies that did not differentiate between surgery types in their analyses were excluded.

The included studies compared Roux-en-Y gastric bypass with a variety of other gastrointestinal or anti-reflux surgeries in non-surgical lean, healthy, overweight or obese participants, or participants achieving weight loss through lifestyle modification. Within-subject study designs comparing pre- and post-surgery gastrointestinal hormone levels were also included. Most of the participants were female (where reported). Limb length ranged from 40cm to 150cm. Some studies included participants with diabetes. Outcomes were assessed using fasted blood samples, oral glucose tolerance tests, or plasma collection.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
A formal validity assessment was not conducted. For glucagon-like peptide-1, peptide tyrosine-tyrosine and ghrelin, a study was considered strong if it had a control group and/or sampled outcomes at multiple time points after meal consumption. For leptin, a study was considered strong if it had a control group.

Data extraction
The authors did not state how the data were extracted for the review.

Methods of synthesis
The studies were combined in a narrative synthesis.

Results of the review
Forty-six studies were included for review (n=1,247 participants). One articles reported on three studies, so it was unclear whether there was any overlap in these study populations. There was one double-blind randomised controlled trial (n=13 participants), 16 prospective or retrospective controlled studies (n=477 participants), 14 prospective uncontrolled studies (n=302 participants) and 15 cross-sectional controlled studies (n=455 participants).

Glucagon-like peptide-1 changes (16 studies, 14 articles): Five of the six studies comparing Roux-en-Y gastric bypass with weight-matched non-surgical participants found significant increases in glucagon-like peptide-1 in the surgery
group compared with the control group. Glucagon-like peptide-1 was also significantly greater in Roux-en-Y gastric bypass groups compared with participants undergoing other surgery or losing weight through diet (three studies). Four of the seven studies comparing hormone levels before and after surgery found significant increases in glucagon-like peptide-1 post-surgery.

**Peptide tyrosine-tyrosine changes** (twelve studies, eleven articles): Seven studies found significantly higher levels of peptide tyrosine-tyrosine following Roux-en-Y gastric bypass compared with lean (four studies), normal weight (one study), overweight (two studies), obese (four studies) or surgical (three studies) populations. Two studies that compared preoperative with postoperative peptide tyrosine-tyrosine hormone levels found significantly higher levels after surgery compared with baseline levels. One study found no significant differences in peptide tyrosine-tyrosine levels between participants undergoing Roux-en-Y gastric bypass and those receiving gastric banding surgery.

**Ghrelin** (25 studies): Ten studies reported that ghrelin levels were significantly reduced following Roux-en-Y gastric bypass surgery compared with lean (four studies), normal (three studies), overweight (two studies), obese (five studies) or other surgical (three studies) participants. Two studies found no significant differences. Eleven studies of weaker design reported conflicting results of the impact of Roux-en-Y gastric bypass on ghrelin.

**Leptin** (21 studies): Five studies found significantly lower fasting leptin concentrations with Roux-en-Y gastric bypass compared with normal weight (one study), overweight (one study) or obese control groups (three studies). Three studies found no significant differences between leptin and control groups. All eleven studies that compared pre- and post-surgery levels of leptin found significant decreases in leptin levels following Roux-en-Y gastric bypass.

**Authors’ conclusions**
Glucagon-like peptide-1 and peptide tyrosine-tyrosine concentrations were usually higher and ghrelin levels were usually lower in participants undergoing Roux-en-Y gastric bypass surgery compared with participants undergoing other surgical procedures, participants who were obese, overweight, healthy or lean, or those who lost weight by lifestyle modifications.

**CRD commentary**
The review addressed a clear question. Inclusion criteria were well-defined for intervention and outcomes, but broad for study design and participants. Only one database was searched, so relevant data may have been missed. The search was restricted to English articles; a search did not appear to have been carried out for unpublished data. Consequently, there was a risk of language and publication bias. The authors did not report using methods designed to reduce reviewer bias and error at any stage of the review process.

A formal validity assessment was not carried out, so it was not possible to determine whether studies deemed "strong" by the authors had methodological weaknesses. Many included studies were of a weaker design and all studies had small sample sizes. The decision to combine studies using a narrative synthesis was appropriate given the clinical heterogeneity between studies. However, the absence of statistical data made it difficult to determine the significance of the findings. There appear to be some discrepancies between information presented in the tables and that presented in the text.

In light of the potential for error and bias in the review, the limited search and the unclear quality of included studies, the authors’ conclusions should be treated with caution.

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

**Research:** The authors stated that further studies are needed measuring gastrointestinal hormone changes before and after meals. The micronutrient composition of these meals should be investigated to determine the response profile of gastrointestinal hormones to protein, carbohydrate or fat ingestion.

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