Ursodeoxycholic acid in the prevention of gallstone formation after bariatric surgery: a meta-analysis
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CRD summary
This review concluded that ursodeoxycholic acid can prevent gallstone formation in morbidly obese patients with intact acalculous gallbladders after bariatric surgery. The conduct and reporting of this review were good and its conclusions should be taken to be reliable.

Authors' objectives
To determine the efficacy and safety of ursodeoxycholic acid (UDCA) in the prevention of gallstones after bariatric surgery.

Searching
MEDLINE (from inception), EMBASE (from inception), Cochrane Central Register of Controlled Trials (CENTRAL), LILACS, Australasian Medical Index and Health Research and Development Information Network (from 1906) were searched without language restrictions up to August/September 2007. Search terms were reported. Reference lists were searched and pharmaceutical companies and authors contacted to locate other trials.

Study selection
Double-blind randomised controlled trials (RCTs) that compared UDCA with placebo given after bariatric surgery in morbidly obese patients were eligible for inclusion. Outcomes of interest were the incidence of gallstone formation and adverse effects.

Mean age of participants in the included studies ranged from 33.5 to 38 years. The proportion of women ranged from 56% to 82%. UDCA dose ranged from 300mg/day to 1,200mg/day. Trial duration ranged from 3 to 24 months.

The authors did not state how studies were selected for the review.

Assessment of study quality
Study quality was assessed using the Jadad scale, a five-point scale covering randomisation, double-blinding and description of dropouts. Studies with a score of 2 or less were classed as low quality and those with a score of 3 or more as high quality.

Study quality was assessed by two reviewers independently. Disagreements were resolved by consensus.

Data extraction
Data on baseline comparability of groups, outcomes and treatment compliance were extracted by two reviewers independently. Disagreements were resolved by consensus. The relative risk (RR) and 95% confidence interval (CI) were calculated for dichotomous outcomes.

Methods of synthesis
Studies were pooled in a meta-analysis using the DerSimonian and Laird random-effects model. Heterogeneity was assessed using the I^2 statistic and values over 50% were taken as substantial heterogeneity. The impact of individual trial results on the pooled estimates were explored in sensitivity and subgroup analyses. Most of the trials reported results on an available case basis, so imputation of missing outcome data was used to perform analyses on an intention-to-treat basis. This assumed that any patients with missing outcomes did not experience the event of interest.

Results of the review
Five RCTs (n=521: 322 for UDCA and 199 for placebo) were included. All studies were classed as high quality (scores...
ranged from 3 to the maximum of 5). Only two studies had complete follow-up for all patients; the rest had missing data for between 17.2% and 31.7% of patients.

**Gallstone formation (five trials):** UCDA resulted in a significantly reduced risk of gallstone formation after surgery compared with placebo in both the available case analysis (RR 0.40, 95% CI 0.22 to 0.74, with substantial heterogeneity $I^2=58.9\%$) and the intention-to-treat analysis (RR 0.43, 95% CI 0.22 to 0.83, with substantial heterogeneity $I^2=61.9\%$). The trial with the greatest loss to follow-up and the worst patient compliance with treatment was the cause of most of the observed heterogeneity, but conclusions about UCDA remained the same when this trial was excluded.

**Adverse effects:** Two trials reported on adverse effects. One found comparable mild to moderate side effects between UCDA and placebo; the other reported that several patients dropped out because of vomiting or skin rashes, but that numbers were similar between treatment groups.

**Authors' conclusions**
Use of UDCA in patients with intact acalculous gallbladders can prevent gallstone formation after bariatric surgery.

**CRD commentary**
This review had a clear question and specification of the study inclusion criteria. The literature search was comprehensive, efforts were made to locate unpublished studies and there were no language or data restrictions. Most of the review methods (data extraction and validity assessment) were performed in duplicate, which reduced the risk of error in the process. The statistical analysis methods were appropriate and the authors investigated the impact of missing outcome data and reasons for the observed heterogeneity. In summary, the conduct and reporting of this review were good and its conclusions should be taken to be reliable.

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

**Research:** The authors stated that future trials should use intention-to-treat analysis and assess adverse effects of UDCA. A double-blind placebo-controlled trial of UDCA in morbidly obese diabetics who underwent bariatric surgery was needed.

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