Systematic review: effective management strategies for lactose intolerance

Shaukat A, Levitt MD, Taylor BC, MacDonald R, Shamliyan TA, Kane RL, Wilt TJ

CRD summary
The review assessed lactose intolerance and interventions to improve symptoms; it concluded that most individuals with presumed lactose intolerance or malabsorption can tolerate 12g to 15g of lactose. The authors' conclusions broadly reflected the evidence presented and appear likely to be reliable.

Authors' objectives
To assess the maximum tolerable dose of lactose and interventions for reducing symptoms of lactose intolerance among people with lactose intolerance and malabsorption.

Searching
MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), BIOSIS Previews, Global Health, Food Science and Technology Abstracts, and the Commonwealth Agricultural Bureau International databases were searched for studies published in English from 1967 to November 2009. Search terms were reported in the main report (see Other publications of Related Interest field). References of retrieved articles were also searched.

Study selection
Randomised controlled trials (RCTs) of participants older than four years with presumed lactose intolerance or malabsorption, that evaluated symptomatic response to single or multiple doses of lactose were included. Trials had to either blind participants to treatment, or use a design so that there would be no biased participant response. Trials of participants with irritable bowel syndrome and other probable causes of acute gastrointestinal symptoms were excluded. Comparison groups could receive placebo, usual care, no active treatment, or active control. The main outcome was symptoms of lactose intolerance.

Included participant populations had mean ages (where stated) ranging from 10 to 77 years. Four trials enrolled only children. Most RCTs were of participants with lactose malabsorption rather than lactose intolerance. The majority of trials used commercial lactase products or hydrolyzed milk (normally 0 to 2g, in a single serving) to deliver reduced lactose, but probiotics, colonic adaptation, and rifaximin were also studied. Comparator treatments varied, but most trials used normal milk.

Three reviewers independently selected studies for inclusion.

Assessment of study quality
Three reviewers independently assessed trial quality using the following criteria: allocation concealment; blinding (participant, investigator, or outcome assessor); use of intention-to-treat analysis; and losses to follow-up. The quality of evidence for primary outcomes across trials was graded as being high, moderate, low, or insufficient.

Data extraction
Three reviewers independently extracted data on symptom scores, with symptoms then classed as being none, trivial, minor, or severe (more details were reported on how this was done).

Methods of synthesis
A narrative synthesis was conducted, with results grouped by intervention.

Results of the review
Thirty-six RCTs were included in the review (the total sample size was unclear, but individual sample sizes ranged from 6 to 150 participants). Overall, the quality of trials was reported as being low; very few reported adequate allocation concealment.

Maximum tolerable dose of lactose (21 RCTs): Moderate evidence suggested that increasing doses of lactose produces
symptoms in patients with diagnosed lactose malabsorption, with or without self-reported symptoms, and the tolerable
dose may differ if lactose is consumed with (versus without) other nutrients. Most trials indicated that patients with
lactose intolerance or malabsorption could ingest 12g of lactose as a single dose with no or minor symptoms when
administered as a single dose without other nutrients; doses of 15g to 18g seemed to be well-tolerated when given as a
single dose with other nutrients.

**Efficacy of lactose-reduced and hydrolyzed formulations and lactase (28 RCTs):** There was insufficient evidence of
effectiveness in reducing symptoms of lactose intolerance (when compared with lactose). In trials of patients with
symptoms compatible with lactose intolerance, none of the four trials with control treatments of up to 12g of lactose
found a significant improvement in overall symptoms. Two of five trials reported significant reductions in overall
symptoms compared with control participants given more than 12g of lactose.

**Probiotics and yogurt (seven RCTs):** There was insufficient evidence of effectiveness at improving symptoms of lactose
intolerance.

Further results were reported.

**Authors' conclusions**
Most individuals with presumed lactose intolerance or malabsorption can tolerate 12g to 15g of lactose. Additional
studies are needed to determine the effectiveness of lactose intolerance treatment.

**CRD commentary**
The review addressed a clear question supported by appropriate inclusion criteria. Although numerous electronic
databases were searched, the restriction to published English language studies meant that some relevant trials may have
been missed. Suitable methods appear to have been used to minimise the risk of reviewer error and bias throughout the
review process.

Trial quality was assessed and was used in interpreting the review results. A narrative synthesis was conducted, which
appeared appropriate considering the clinical heterogeneity between trials. The authors highlighted the fact that most
trials were of patients with lactose malabsorption rather than lactose intolerance.

The authors' conclusions broadly reflected the evidence presented and appear likely to be reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that lactose intolerance should be excluded as the cause of symptoms in people who ingest
less than 15g of lactose with meals. They also stated that patients whose symptoms improve on a lactose-free diet can be
instructed to ingest limited quantities (one serving daily) of lactose-containing products, gradually increasing intake
until symptoms develop.

**Research:** The authors recommended that rigorous double-blind, placebo-controlled studies should be conducted to
evaluate treatment effectiveness in people with well-documented lactose intolerance. Studies should use standardized
diagnostic measures, interventions, and outcome reporting, with emphasis on clinically important differences. Rigorous
long-term safety data on these interventions, such as probiotics, are also needed.

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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.