Does a reasonable daily dose of lactose cause symptoms in patients with self-reported lactose intolerance?

Evidence-Based Answer

Individuals who report lactose intolerance are usually able to ingest a daily lactose dose equivalent to at least 1 cup of milk (12 g lactose) without significant symptoms. (SOR: B, based on a meta-analysis and a systematic review with heterogeneity.) Daily doses of lactose equivalent to about 1.8 cups of milk (22 g lactose) can be tolerated if ingested with nutrients other than milk. (SOR: B, based on small RCTs with heterogeneity.)

A meta-analysis of 21 RCTs, with 862 total subjects, compared symptoms after the consumption of 7 to 25 g lactose with symptoms after the ingestion of placebo in men and women aged 13 to 74 who self-reported lactose malabsorption. To determine the severity and frequency of symptoms in this meta-analysis, the authors calculated pooled symptom effect sizes comparing lactose and placebo consumption.

The combined severity of abdominal bloating, abdominal pain, degree of diarrhea, frequency of bowel movements, and frequency of diarrhea after lactose consumption, calculated from 5 of the studies with 327 total subjects, had a pooled symptom effect size of 1.26 (95% CI, 1.00–1.51). However, the analysis revealed significant heterogeneity.

When one of the studies (which used a different rating system than the others) was excluded, the heterogeneity resolved in the data from the 116 remaining subjects and the pooled symptom effect size was no longer significant, at 0.12 (95% CI, −0.25 to 0.48). The only individual symptom found to have increased in frequency after lactose ingestion was flatulence, with a pooled symptom effect size of 0.51 (95% CI, 0.08–0.95). However, when this analysis was restricted to the 3 highest quality studies with 84 total subjects, the pooled symptom effect size was no longer significant, at 0.35 (95% CI, −0.12 to 0.82).

A systematic review summarized 20 small RCTs with 473 total subjects with either diagnosed lactose malabsorption or self-reported lactose intolerance (including 10 of the studies with 251 total subjects reviewed in the meta-analysis discussed above) to determine the maximum daily lactose dose tolerated.

The data were not pooled due to heterogeneity in patient populations, interventions, assessment methods, and outcome definitions.

However, 11 of 12 RCTs, which had subjects ingest lactose without nutrients other than milk, reported no or trivial symptoms with daily doses up to 14 g lactose, mild symptoms with 16- to 30-g lactose doses, and severe symptoms consistently found with 49 g lactose or higher. The remaining RCT reported minor symptoms only with 12 g lactose and more severe symptoms with 20 g lactose. The 8 RCTs that had the subjects ingest lactose with nutrients other than milk (173 total subjects) reported no symptoms with doses up to 22 g lactose.

Does proton pump inhibitor (PPI) therapy increase the risk of fractures?

Evidence-Based Answer

In the absence of other risk factors, PPI use is not associated with an increased risk of hip fractures, osteoporosis, or loss of bone mineral density (BMD) at the hip or spine. (SOR: B, based on case-controlled and cohort studies.)

A case-control study assessed the association between PPI use and hip fracture in subjects aged 50 to 79 years using data from the United Kingdom General Practice Research Database. Subjects (n=1,098) with a first-time recorded hip fracture, but no medical conditions that would predispose to hip fractures, were matched to controls (n=10,923) with no history of hip fracture.

Of the 132 subjects and 1,428 controls who had at least 1 PPI prescription before their index date, the estimated RR of hip fracture was 0.9 (95% CI 0.7–1.1), compared with subjects with no PPI prescriptions. When analyzed according to number of PPI prescriptions, there was no association between increased risk of hip fracture and increased numbers.
of PPI prescriptions (1 prescription: RR=1.0; 95% CI, 0.7–1.4; 2–9 prescriptions: RR=1.0; 95% CI, 0.7–1.3; 10–29 prescriptions: RR=0.9; 95% CI 0.6–1.4; ≥30 prescriptions: RR=0.5; 95% CI, 0.3–0.9). A nested case-control study evaluated the association between PPI use and risk of hip fracture using data from an integrated health services organization. Subjects with a history of hip fracture (n=33,752) were matched with controls (n=130,471) based on age, sex, duration of membership, first year of membership, and race. For those who had used PPIs for at least 2 years, the overall OR of experiencing a fracture was 1.30 (95% CI, 1.21–1.39) compared with nonusers. Fracture risk was also increased among individuals taking higher doses (0.75–1.49 pills per day: OR 1.30; 95% CI, 1.19–1.42; ≥1.50 pills per day: OR 1.41; 95% CI, 1.21–1.64) compared with nonusers. However, potential confounding conditions were also evaluated by contrasting odds ratios between models with and without confounding conditions. Associations between long-term use and higher doses and hip fracture were only found among subjects with at least 1 other risk factor (≥1 risk factor present: OR 1.25; 95% CI, 1.16–1.35; no risk factors present: OR 0.66; 95% CI, 0.38–1.12). Risk factors with a positive association included alcohol abuse, arthritis, diabetes, kidney disease, and use of a glucocorticoid.

Finally, a cross-sectional study and longitudinal study were conducted using the Population Health Research Data Repository and the Manitoba Bone Mineral Density Database to determine whether PPI use was associated with osteoporosis or decreased BMD. The cross-sectional study matched 2,193 subjects with osteoporosis of the hip with 5,527 controls, and 3,596 subjects with osteoporosis of the spine with 10,257 controls. After adjusting for potential confounders, no association was found between use of >1,500 standard doses of PPI and risk of osteoporosis at the hip (OR 0.84; 95% CI, 0.55–1.34) or spine (OR 0.79; 95% CI, 0.59–1.06). In the longitudinal study, 2,549 subjects underwent 2 BMD measurements separated by 2.31±0.5 years (mean±SD). Use of PPIs, even at a rate of >1.0 standard daily dose, was not associated with a significant effect on BMD at the lumbar spine (−0.08%±0.26%) or hip (−0.09%±0.21%; P>.2 for both). A 2007 RCT compared the effects on LDL levels from raw garlic, powdered garlic supplement (Garlicin®), aged garlic extract supplement (Kyolic®), and placebo. The trial involved 169 adults, aged 30 to 65 years with LDL level of 130 to 190 mg/dL. Participants were assigned either 4 g raw garlic (given as an average size clove crushed in a blender and mixed with condiments and served in a sandwich), 4 Garlicin tablets, 6 Kyolic tablets, or 4 to 6 placebo tablets that had a similar appearance to Garlicin, 6 days a week for 6 months. The study found no significant LDL reduction with any of the forms of garlic (mean 6-month net LDL change: raw garlic 0.4; 95% CI, −5.5 to 6.4; Garlicin 3.2; 95% CI, −2.2 to 8.7; Kyolic 0.2; 95% CI −5.3 to 5.7; placebo −3.9; 95% CI −9 to 1.2). The effects of garlic powder (2.1 g/d) on lipid levels on 84 overweight (BMI >24.5 kg/m²) patients, 40 to 75 years old, who also smoked (>10 cigarettes per day) were compared with placebo in a 2006 double-blind RCT. Over the 3-month study, no significant change was noted with garlic versus placebo in total cholesterol (0.9%; 97.5% CI, −5.5 to 7.8; P=.75), LDL (1.3%; 97.5% CI, −8.3 to 7.6; P=.076), or triglycerides (−2.8%; 97.5% CI, −17 to 14; P=.68).

A 2008 RCT with 42 men aged between 35 and 70 years compared time-released garlic powder tablets...