

## Review: S-adenosylmethionine treats osteoarthritis as effectively as nonsteroidal anti-inflammatory drugs with fewer adverse effects

Soeken KL, Lee W-L, Bausell RB, Agelli M, Berman BM. Safety and efficacy of S-adenosylmethionine (SAME) for osteoarthritis. *J Fam Pract.* 2002;51:425-30.

### QUESTION

In patients with osteoarthritis (OA), is treatment with S-adenosylmethionine (SAME) effective and safe?

### DATA SOURCES

Studies in all languages were identified by searching MEDLINE (1966 to September 2000), EMBASE/Excerpta Medica (1987 to 2000), CAMPAIN, Science Citation Index, International Pharmaceutical Abstracts, the Cochrane Complementary Medicine Field Registry, National Institutes of Health Office of Dietary Supplements Database, and Micromedex using the term arthritis and all synonyms for SAME. 3 rheumatology journals and relevant English-language and complementary medicine journals were hand-searched. Web sites, bibliographies of relevant studies, and books were examined, and manufacturers of SAME were contacted.

### STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that included patients with a diagnosis of OA; compared SAME with placebo or nonsteroidal anti-inflammatory drugs (NSAIDs); and reported

≥ 1 of the outcomes of pain, functional limitation, or adverse effects.

### DATA EXTRACTION

Data were extracted on study characteristics and quality, interventions, and outcomes. For pain and functional limitation, differences in mean responses between treatment and control groups were standardized to account for differences in the measurement scales across studies and expressed as a difference in effect size (ES), with a positive ES favoring SAME.

### MAIN RESULTS

20 studies were identified, and 11 (1442 patients, mean age 60 y, 70% women) met the inclusion criteria. The SAME dosage was 1200 mg/d orally in 6 studies, 600 mg/d orally in 3 studies, and 400 mg/d intravenously in 1 study; in 1 study, the dosage varied. Treatment duration ranged from 10 to 84 days. NSAIDs were used as active comparators in several studies, and placebo was used in 2 studies. SAME was more effective than placebo in reducing functional limitation (mean ES 0.31, 95% CI 0.098 to 0.52; 1 study) but not pain (weighted mean ES 0.22, CI -0.25 to 0.69; 2 studies, random-

effects model). SAME and NSAIDs did not differ for functional limitation (weighted mean ES 0.025, CI -0.13 to 0.18; 8 studies, fixed-effects model) or pain (weighted mean ES 0.12, CI -0.029 to 0.27; 8 studies, fixed-effects model). SAME was associated with fewer adverse effects than NSAIDs (weighted odds ratio 0.42, CI 0.29 to 0.61; 7 studies, fixed-effects model); adverse effects did not differ for SAME and placebo.

### CONCLUSIONS

In patients with osteoarthritis, S-adenosylmethionine (SAME) is as effective as nonsteroidal anti-inflammatory drugs in reducing pain and improving functional limitation and is associated with fewer adverse effects. Compared with placebo, SAME is more effective in improving functional limitation but not pain and does not differ for adverse effects.

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### COMMENTARY

OA affects > 50% of persons > 35 years of age (1), causing direct and indirect costs to the social system and dramatically reducing quality of life. Nonsteroidal anti-inflammatory drugs are standard therapy for relieving symptoms. The high costs and risks for adverse events (e.g., deaths caused by adverse effects at a rate similar to that of traffic accidents [2]) stimulate research for alternative treatments. In Germany, monthly therapeutic costs of EURO 100 to 300 (about US \$100 to \$300) for SAME, 400 to 1200 mg/d, have to be measured against the expected socioeconomic benefit.

The sample size in trials of the novel selective cyclooxygenase 2 inhibiting NSAIDs suggests the need for > 1442 patients in a meta-analysis to give sufficient power to detect clinically important differences compared with alternatives, such as SAME. The treatment of OA should be based on long-term data of safety and efficacy. Unfortunately, 1418 patients in the meta-analysis by Soeken and colleagues were treated and observed for < 1 month, a period without much clinical relevance for a chronic disease. Only 24 patients were treated for > 1 month.

Paracetamol (acetaminophen) is comparable to NSAIDs for control of symptoms of OA, with a lower risk for adverse effects and monthly costs of only EURO 6 (US \$6) for a daily dose of 2000 mg. Paracetamol has been accepted as a first-line drug in OA therapy (3).

SAME is up to 50-fold more expensive than paracetamol and should be superior to paracetamol in long-term efficacy and safety before being accepted as an alternative for OA. Weight reduction in obesity, physical training, and local therapy are effective and inexpensive in improving OA symptoms and prognosis and have lower associated risks than drug interventions (4). These treatments should be optimized before starting long-term drug therapy.

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### References

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