# Review: SAMe reduces symptoms in depression, osteoarthritis, and liver disease

Hardy M, Coulter I, Morton SC, et al. **S-adenosyl-L-methionine for treatment of depression, osteoarthritis, and liver disease.** Evidence Report/Technology Assessment no. 64. AHRQ publication no. 02-E034. Rockville, MD: Agency for Healthcare Research and Quality; Oct 2002. www.ahrq.gov/clinic/epcsums/samesum.htm.

## QUESTION

In patients with depression, osteoarthritis, or liver disease, is treatment with S-adenosyl-L-methionine (SAMe) effective?

## DATA SOURCES

Studies were identified by searching 25 biomedical databases for the year 2000, reviewing bibliographies of relevant articles, and contacting experts in the field.

## STUDY SELECTION

Studies published in any language were selected if they were randomized controlled trials (RCTs) or controlled clinical trials that compared SAMe with placebo or other drugs for treatment of depression, osteoarthritis, or chronic liver disease; or presented any historical or descriptive background information about SAMe and its use.

## DATA EXTRACTION

2 reviewers independently extracted data on study design, sample size, patient characteristics, intervention, study quality, and outcomes. Main outcomes included symptoms of depression measured by the Hamilton Depression Rating Scale (HDRS) or any other equivalent measure, pain (osteoarthritis), and pruritus and serum bilirubin levels (liver disease).

## MAIN RESULTS

47 studies (30 RCTs) of depression, 14 (11 RCTs) of osteoarthritis, and 41 (24 RCTs) of liver disease met the selection criteria. Meta-analyses were done using random-effects models. *Depression*: Reduction in HDRS scores was greater in the SAMe group than in the placebo group (Table). SAMe did not differ from other antidepressant drugs for decrease in HDRS scores (Table). *Osteoarthritis*: 1 large RCT showed a greater decrease in pain in the SAMe group than in the placebo group (Table). SAMe did not differ from nonsteroidal anti-inflammatory drugs for pain reduction (Table). *Cholestasis of pregnancy*: Decrease in pruritus and serum bilirubin levels was greater in the SAMe group than in the placebo group (Table). *Intrahepatic cholestasis for conditions associated with liver disease (other than pregnancy)*: Meta-analysis of 4 studies ($n$ = 393) showed a lower rate of unresolved pruritus in the SAMe group than in the placebo group (relative risk 0.45, 95% CI 0.37 to 0.55). Reduction in serum bilirubin levels was greater in the SAMe group than in the placebo group (Table).

## CONCLUSION

In patients with depression, osteoarthritis, or liver disease, S-adenosyl-L-methionine is effective for reducing symptoms, pain, and pruritus and bilirubin levels, respectively.

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**S-adenosyl-L-methionine (SAMe) vs placebo or other drugs for depression, osteoarthritis, and liver disease including cholestasis of pregnancy (ChP) and intrahepatic cholestasis (ICh) not associated with pregnancy at 14 to 31 days***

| Condition | Outcomes | NOS (NRCTs) | Comparison | Effect size (95% CI) |
|---|---|---|---|---|
| Depression | Decrease in HDRS scores | 11 (8)<br>14 (11) | SAMe vs placebo<br>SAMe vs other ADDs | –0.65 (–1.05 to –0.25)†<br>0.08 (–0.17 to 0.32) |
| Osteoarthritis | Decrease in pain | 1 (1)<br>8 (7) | SAMe vs placebo<br>SAMe vs NSAIDs | –0.2 (–0.39 to –0.02)†<br>–0.11 (–0.56 to 0.35) |
| ChP | Decrease in pruritus<br>Serum bilirubin (mg/dL) | 5 (4)<br>5 (4) | SAMe vs placebo<br>SAMe vs placebo | –0.95 (–1.45 to –0.45)†<br>–1.32 (–1.76 to –0.88)† |
| ICh | Serum bilirubin (mg/dL) | 5 (3) | SAMe vs placebo | –0.63 (–1.16 to –0.10)† |

*ADDs = antidepressant drugs; HDRS = Hamilton Depression Rating Scale; NOS = number of studies; NRCTs = number of randomized controlled trials; NSAIDs = nonsteroidal anti-inflammatory drugs. CI defined in Glossary.

†Significant differences favor SAMe (a negative effect size indicates that SAMe is associated with a decrease in the outcome at follow-up when compared with placebo).

## COMMENTARY

The review by Hardy and colleagues evaluated the effectiveness of SAMe for depression, osteoarthritis, or liver disease. SAMe has been available by prescription for > 20 years in many European countries. SAMe came to the North American market in 1999 and is sold as a dietary supplement, thus bypassing governmental regulation and entering the realm of alternative medicine.

SAMe is a critical metabolic intermediary, present in all human cells. It is the primary methyl donor in the central nervous system and increases hepatic concentrations of glutathione, the major hepatic antioxidant. Animal studies suggest that it has anti-inflammatory and analgesic effects that are not mediated by prostaglandins. Although information about side effects is not definitive, SAMe almost certainly has a different side effect profile from that of currently available medications for depression and osteoarthritis pain. Other important uses for SAMe probably await discovery.

It is surprising that such a potent medication is unregulated and available over the counter. It is misleading to consider SAMe a dietary supplement. This categorization deprives it both of the attention and the regulation that it warrants. Marked variability in commercially available preparations of SAMe makes routine clinical use problematic. An independent laboratory analysis of 13 commercially available preparations found that 6 of them did not contain the amount of SAMe claimed by the manufacturer (1). We can do better.

It is also misleading to think of SAMe as an "alternative" medicine. Possibly we should discard the dichotomy of alternative versus conventional medicine altogether and simply consider whether a treatment is effective. If it is proven to be effective, it should not be "alternative." If it is proven to be ineffective, then it is not medicinal. Whatever the outcome, it should be regulated.

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***Reference***

1. Product Review: *SAMe.* ConsumerLab.com, White Plains, NY; 2000. www.consumerlab.com/results/same.asp.