

Role of *S*-Adenosyl-L-Methionine in the Treatment of Intrahepatic Cholestasis

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Summary

Recent studies have established the clinical efficacy of *S*-adenosyl-L-methionine (SAME) in the treatment of cholestasis associated with hepatic diseases, pregnancy and the administration of estrogen-containing oral contraceptives. In 4 clinical trials involving a total of 639 patients with cholestasis due to acute or chronic liver disease, SAME in an intravenous dose of 800 mg/day or an oral regimen of 1.6 g/day for 2 weeks was superior to placebo in relieving the symptom of pruritus and in restoring serum total bilirubin and serum alkaline phosphatase towards normal. The drug is also effective in intrahepatic cholestasis of pregnancy (ICP), with intravenous administration of 800 mg/day for 2 weeks producing a substantial reduction in pruritus and an improvement in abnormal liver function indices. Moreover, SAME treatment decreases the incidence of premature labour. SAME appears to be the first safe and effective approach to the treatment of this syndrome, and also protects against the adverse hepatic effects of small doses of estrogen in patients with a history of ICP by normalising liver biochemistry and the oversaturated biliary lipid composition of the gallbladder bile.

In animal models, SAME reverses the pathological liver changes induced by xenobiotics such as tauroolithocholate and α -naphthyl-isothiocyanate (ANIT) and the antipsychotic chlorpromazine. Several cooperative mechanisms appear to underlie the anticholestatic action of SAME, the most important being the restoration of normal hepatocyte membrane fluidity and Na⁺, K⁺ ATPase activity, through a reversal of the reduction in phospholipid methylation produced by hepatotoxic agents. In addition, SAME may act by promoting trans-sulphuration pathway reactions and consequently improving the detoxifying capacity of this metabolic system.