measurements is uncertain. Further studies are also needed to clarify the potential role of medical management and also to assess informed patient preferences.

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EMLA Cream for the Débridement of Venous Leg Ulcers

Lok C, Paul C, Amblard P, et al. EMLA cream as a topical anesthetic for the repeated mechanical débridement of venous leg ulcers: a double-blind, placebo-controlled study. J Am Acad Dermatol 1999; 40:208-13.

Clinical question **How effective is eutectic mixture of local anesthetics (EMLA) cream in reducing the pain and decreasing the number of mechanical débridements necessary to treat venous leg ulcers?**

Background Mechanical débridement of venous leg ulcers is an accepted means of obtaining a clean ulcer and increasing healing rates. Débridement removes dead tissue and fibrinous plaques to allow the growth of granulation tissue. The effectiveness of EMLA cream as a local anesthetic for débridement has been demonstrated in previous studies.

Population studied A total of 69 patients from 9 departments of dermatology or phlebology who were scheduled for mechanical débridement of a venous leg ulcer were enrolled. The average age was 71 years for the intervention group and 73 years for the placebo group. Forty-nine of the participants were women. Ulcer areas were 5 to 50 cm^2, with debris and necrosis on 50% or more of the area, for which débridement was required 3 times a week for at least the first week. Patients had not used EMLA cream previously.

Study design and validity This was a randomized double-blind placebo-controlled trial. All patients were given a dose of 30 mg dextropropoxyphene and 400 mg acetaminophen an hour before débridement. A thick layer of either EMLA or placebo cream (maximum 10 g) together with an occlusive dressing (plastic wrap) was applied for 30 to 45 minutes. Débridement was started within 10 minutes of cream removal. After débridement, ulcers were dressed with sterile petrolatum dressing. After the first week, the frequency of continued débridement was determined by participating physicians. A maximum of 15 débridements was allowed during the study. An ulcer was defined as clean if 75% or more of its area was free from necrotic or fibrinous tissue. The number of débridements, the size of an ulcer, patient perception of pain during débridement, physician's assessment of quality of débridement, and local reactions were recorded.

Outcomes measured The primary outcome measured was the number of débridements needed to obtain a clean ulcer. Secondary outcomes included pain, duration and quality of débridement, ulcer area at study termination, local reactions, and plasma levels of the drugs and metabolites.

Results The type of ulcer, size of ulcer at admission and study termination, dose of cream and mean time between débridements were not statistically different between placebo and treatment groups. The median number of débridements necessary to obtain a clean ulcer was significantly lower in the EMLA group (11.5 compared with more than 15 in the placebo group, $P = .019$). The percentage of patients at the end of the study with a clean ulcer was significantly higher in the EMLA group (66.7% vs 33.3%, $P = .008$; number needed to treat = 3). Pain scores were decreased by 50% in the EMLA group compared with placebo ($P = .003$). There was no significant difference in the median duration of débridement (4 minutes with EMLA vs 3 minutes in the placebo group, $P = .253$). EMLA cream significantly improved the physician assessment of the quality of débridement. Local reactions were not statistically different between the 2 groups.

Recommendations for clinical practice **EMLA cream produces effective pain relief for the mechanical débridement of venous leg ulcers, reduces the number of débridements necessary, and results in a higher success rate of obtaining clean ulcers.**

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Omeprazole or Ranitidine for Intermittent Treatment of GERD?

Bardhan KD, Möller-Lissner S, Bigard MA, et al. Symptomatic gastroesophageal reflux disease: double-blind controlled study of intermittent treatment with omeprazole or ranitidine. BMJ 1999; 318:502-7.

Clinical question **Should omeprazole or ranitidine be used for intermittent treatment of gastroesophageal reflux disease?**

Background Gastroesophageal reflux disease (GERD) is a common diagnosis in primary care, but

optimal management is not well defined. Continuous treatment with H_2 blockers is the standard recommendation; however, in primary care settings, treatment is often intermittent. This randomized trial compared the use of omeprazole with ranitidine for intermittent treatment of GERD.

Population studied A total of 677 patients were enrolled from 56 European medical centers either following hospital consultation (54%) or directly from general practitioners (46%). These subjects had heartburn that interfered with normal activities for more than 2 days of each of the previous 2 weeks; endoscopy was used to confirm the diagnosis, and patients with severe erosions were excluded. Of those included in the study, 56% were male, and the median age was 47. Most patients were overweight (average body mass index = 27); 27% were smokers; 40% had evidence of *Helicobacter pylori*; and 76% had symptoms for more than 1 year. Thus, the population seems similar to that seen by US family physicians. The major difference is that all subjects had endoscopy-confirmed GERD and may have had more serious disease than is typical in primary care settings in the United States.

Study design and validity This was a randomized double-blind controlled trial. Patients were randomized to receive either ranitidine 150 mg twice daily, omeprazole 10 mg daily, or omeprazole 20 mg daily for 2 weeks. If patients remained symptomatic, the dose was doubled (except for the higher omeprazole dose) for an additional 2 weeks. Patients with no symptoms at 2 weeks or mild or no symptoms at 4 weeks entered the follow-up phase, during which they received treatment only when moderate or severe symptoms recurred. Follow-up rate was 71% over 1 year; intention-to-treat analysis was used, with the Cox proportional hazards statistic used to control for confounding causes.

This trial was of good quality. Weaknesses are relatively minor and include low follow-up rate, limited number of outcomes addressed, lack of information about clinical management including *H pylori* and smoking cessation management, and lack of control of important confounding variables, such as use of alcohol, nonsteroidal anti-inflammatory drugs, or promotility agents. In addition, the design of this trial did not allow a good assessment of the true effectiveness of intermittent therapy, since there was no comparison group receiving continuous therapy.

Outcomes measured The primary outcome was the number of patients successfully completing the study on intermittent treatment. Other outcomes included total time off treatment, number of relapses, and symptom control at 2 weeks. Endoscopic assessment of the effectiveness of therapy was not performed, and other important outcomes, such as patient satisfaction, level of symptoms, functional status (ie, impact on work and family), and cost were not addressed.

Results The groups were similar at baseline. After 2 weeks, 55% of patients taking 20 mg omeprazole were asymptomatic compared with 40% of those taking the 10-mg dose and 26% for ranitidine (P <.001; number needed to treat = 3.5 for 20 mg omeprazole vs 150 mg ranitidine twice daily). At completion, 47% were still receiving intermittent therapy; most patients had no relapses (32%), 1 relapse (24%), or 2 relapses (12%). Long-term outcome was not affected by initial treatment at randomization. Initial endoscopic grade of esophagitis, symptom duration, age, sex, body weight, and presence of *H pylori* did not influence outcomes.

Recommendations for clinical practice **This study provides good evidence that, compared with ranitidine, omeprazole provides faster relief of symptoms but no improvement in long-term success of intermittent treatment for GERD. The data also suggest that an intermittent treatment strategy for GERD may provide adequate symptom control with less medication for about half of patients. The study did not directly compare intermittent therapy with continuous therapy, and further study is necessary to show their equivalence.**

Clinicians choosing an intermittent strategy for treatment of GERD should consider omeprazole 20 mg if rapid reduction of symptoms is necessary, but they should keep in mind that there is little evidence that this agent is superior to ranitidine for long-term outcomes.

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Mediterranean Diet for Heart Disease

de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation 1999; 99:779-85.

Clinical question **Does the Mediterranean diet prevent recurrent myocardial infarction?**

Background The relatively low incidence of coronary heart disease experienced by coastal Mediterranean inhabitants has spurred interest in their dietary intake. The Lyon Diet Heart Study was designed to evaluate the Mediterranean diet as a way to prevent heart attacks in patients with pre-existing heart disease. The diet used in the study consisted of more bread, veg-