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What is the most effective first-line medical treatment of patients with primary Raynaud’s phenomenon?

Evidence-Based Answer

Nifedipine is the most effective calcium-channel blocker (CCB) for treating primary Raynaud’s phenomenon and is usually dosed at 5 to 20 mg 3 times daily. (SOR: B, based on a meta-analysis of lower-quality clinical trials.) Non-CCB vasodilators do not appear to be effective. (SOR: B, based on a meta-analysis of lower-quality clinical trials.)

In 2005, a meta-analysis of CCBs used in the treatment of primary Raynaud’s phenomenon evaluated 17 randomized, double-blinded, placebo-controlled studies including 348 patients. As a group, CCBs provided a weighted mean decrease (WMD) of −5 attacks/week (95% CI, −9.02 to −0.99; \( P<.01 \)) compared with placebo and also reduced severity of attacks by a WMD of −1.4 (95% CI, −2.2 to −0.58; \( P<.0001 \)) on a 10-cm visual analogue scale (VAS). When 2 trials were removed from the analysis to decrease heterogeneity, the effect was less robust (WMD for frequency, −2.8 attacks/week; 95% CI, −3.9 to −1.7; \( P=.01 \)).

When the analysis was limited to the 12 trials encompassing 215 patients comparing nifedipine with placebo, the effect was larger (WMD for frequency, −6.05 attacks/week; 95% CI, −11.19 to −0.19; \( P=0.04 \); and WMD for severity, −1.81 points on the VAS; 95% CI, −3.08 to −0.54, \( P=.005 \)). Doses of nifedipine ranged from 5 to 20 mg 3 times daily, with 1 trial using 30 mg nifedipine XL daily. Nifedipine use for primary Raynaud’s phenomenon was associated with adverse effects including edema, headache, flushing, palpitations, and tachycardia. Trials evaluating nicardipine and nisoldipine with placebo did not demonstrate a significant difference in either the severity or frequency of attacks.

A 2008 Cochrane review examined captopril, enalapril, and 5 vasodilators not currently available in the United States in 8 studies that included 290 patients with primary Raynaud’s phenomenon. The foreign medications included beraprost (inhibits platelet aggregation); dazoxiben (inhibits thromboxane synthetase); ketanserin (an antihypertensive and serotonin antagonist; and the nonclassified peripheral

vasodilators buflomedil and moxisylyte. CCBs were excluded from this analysis.

Captopril was associated with a nonsignificant difference in weekly attacks (95% CI, 0.43–1.16) in 2 studies with 25 patients. Enalapril was associated with a nonsignificant increase of 0.8 attacks weekly (95% CI, 0.43–1.17) in a study of 20 patients. There was no evidence of benefit for any of the medications studied; however, the authors concluded the studies were small and methodologically flawed.²

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Does oral immunotherapy reduce the risk of a hypersensitivity reaction to poison ivy?

Evidence-Based Answer

Oral administration of urushiol, the allergen in poison oak and poison ivy, can produce partial desensitization to poison ivy exposure. (SOR: C, based on inconsistent results and small studies.)

Researchers evaluated the response of 69 urushiol-sensitive participants to multiple oral urushiol dosing regimens. The participants were followed for 6 to 12 months. Skin test reactivity was scored from 1 (erythema and edema) to 4 (bullae). An improvement factor (IF) was calculated by multiplying the average decrease in score in a group by the percent of participants in that group who demonstrated improvement.¹

Oral urushiol exposure <100 mg was insufficient to alter skin test reactivity. Participants in the urushiol group who received a total dose of >250 mg achieved an IF of 1.11, compared with an IF of 0.14 for participants in the placebo group, although no statistical comparison was reported. While 6 of the 9 patients receiving urushiol reported improvement, no participants were fully desensitized.¹

A double-blind clinical trial randomized 42 urushiol-sensitive participants to oral urushiol at increasing doses up to a total dose of 300 mg or placebo over 3 to 6 months. A total of 21 participants receiving urushiol and 12 placebo controls completed the study. Most participants in the experimental group (15 of 21) became hyposensitized, compared with only 2 of 12 in the control group (P<.01).²

A third RCT included 87 urushiol-sensitive participants. Researchers administered oral pentadecylcatechol (PDC) and heptadecylcatechol (HDC)—forms of urushiol slightly modified to prevent it from binding to the skin. Forty-four participants received an oral 1:1 mixture using a 5-week induction phase with gradual escalating doses of this PDC/HDC mixture. Fourteen of the 44 participants went on to a maintenance phase with continual administration of the active compound for 24 weeks.³

Repeat skin testing revealed no statistically significant difference in hyposensitization between the experimental and control groups. Adverse reactions of pruritus ani and generalized pruritus occurred in several participants in the experimental group, and 2 participants dropped out of the study due these adverse reactions.³

At the November 2006 American College of Allergy, Asthma and Immunology convention, a study was presented in which 115 allergy clinic patients, with previously documented severe poison ivy dermatitis, were given sublingual urushiol extract (dose not disclosed). After the first year of treatment, 90% reported fewer and less severe episodes with shorter duration, and the antigen concentration required for a positive skin test increased 125-fold. After 7 years of therapy, the antigen concentration required for a positive reaction increased to 180-fold.⁴

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