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Effectiveness of Calcium Channel Blockers for Raynaud Phenomenon

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Clinical Question

Are calcium channel blockers (CCBs) effective therapy for Raynaud phenomenon?

Evidence-Based Answer

CCBs are modestly effective at reducing the frequency of attacks of primary Raynaud phenomenon. There is no evidence that attack severity or physiologic measurements are reduced by CCBs. Treatment is associated with adverse effects such as headache, flushing, and edema. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Primary Raynaud phenomenon is characterized by transient digital ischemia caused by vasoconstriction in response to cold or emotional distress (as opposed to secondary Raynaud phenomenon, which occurs in the setting of systemic disease and can be much more severe). Most estimates suggest that 3% to 5% of the general population experience primary Raynaud phenomenon.[1] Avoidance of precipitating factors has long been the primary treatment approach, with pharmacotherapy reserved for patients who have persistent or severe symptoms. There are no clinical practice guidelines for the treatment of primary Raynaud phenomenon.

CCBs are the most widely used medications for Raynaud phenomenon. Other agents, such as endothelin receptor antagonists, phosphodiesterase-5 inhibitors, vasodilators, and onabotulinumtoxinA (Botox), have been proposed as treatment for Raynaud phenomenon with minimal success.[2] A previous meta-analysis from 2005 concluded that CCBs moderately reduce the frequency of attacks by a mean of 5.00 per week (95% confidence interval, 0.99 to 9.02) and reduce the severity of attacks by 33%.[3] The criteria for inclusion of studies in the current meta-analysis were stricter than in the 2005 publication.

This meta-analysis included only persons with primary Raynaud phenomenon. Seven randomized trials of CCBs (either nifedipine [Procardia] or nicardipine [Cardene]) vs. placebo were included with a total of 296 participants. Three of the studies had six or fewer participants. The heterogeneity of these trials made quantitative pooling of data impossible for most outcomes, including severity of Raynaud phenomenon attacks. All seven trials were published before the introduction of the Raynaud's Condition Score, a validated outcome tool for Raynaud phenomenon.[4]

Pooled analysis of the frequency of attacks found a statistically significant reduction in attacks (i.e., 1.72 fewer attacks per week [95% confidence interval, 0.60 to 2.84]). This result was driven by the findings of the largest study, which was the only one to report a statistically significant benefit on its own.[5] In a sensitivity analysis, the results lost statistical significance after this study was removed from the meta-analysis.

No trial demonstrated a statistically significant improvement in physiologic responses to cold with treatment, such as finger systolic pressure, pulse amplitude of digital blood flow, finger skin temperature, and transcutaneous oxygen tension of the finger.

Adverse effects from CCB treatment were documented in all seven clinical trials. The incidence of headaches was significantly higher in the CCB treatment group than with placebo in four studies. Other adverse effects included flushing, edema, hypotension, vertigo, nausea, palpitations, tachycardia, and cutaneous rash.

Avoidance of inciting factors continues to be the mainstay of therapy for Raynaud phenomenon. Based on this review, CCBs can

provide limited benefit for most patients but are likely to cause adverse effects. However, there are few other medical options available for these patients. Because there are no treatment guidelines for physicians, a frank discussion of the benefits and risks should take place before prescribing CCBs to patients with Raynaud phenomenon.

SOURCE: Ennis H, Anderson ME, Wilkinson J, Herrick AL. Calcium channel blockers for primary Raynaud's phenomenon. *Cochrane Database Syst Rev.* 2014;(1):CD002069.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD002069.

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