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Heart Rate Slowing versus Other Pharmacological Antianginal Strategies

Results of Comparative Studies

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Abstract

Relieving the symptoms of angina and improving the quality of life and functional status are important objectives in the management of patients with chronic stable angina. A high heart rate induces or exacerbates myocardial ischemia and angina because it both increases oxygen demand and decreases myocardial perfusion. β-Blockers are effective at reducing anginal symptoms largely by decreasing heart rate. Physician use and patient compliance may be limited by the side effects of β-blockers which include fatigue, depression and sexual dysfunction. Heart rate reduction can also be obtained by the calcium antagonists verapamil and diltiazem and by the new selective heart-rate-reducing agent ivabradine. Ivabradine (Procoralan) is a selective and specific I_f inhibitor that acts on one of the most important ionic currents for the regulation of the pacemaker activity of sinoatrial node cells. Ivabradine has demonstrated dose-dependent anti-ischemic and antianginal effects in a placebo-controlled study. The INITIATIVE trial is a large multicenter trial in which 939 patients with stable angina were randomized to ivabradine or atenolol. The noninferiority of ivabradine was shown in the INITIATIVE trial at all doses and for all criteria including time to limiting angina. The number of angina attacks per week was decreased by two thirds with both ivabradine and atenolol. In another trial of 1,195 patients, time to 1 mm ST segment depression was increased by 45 s with ivabradine 7.5 mg b.i.d. and by 40 s with amlodipine 10 mg daily. Unlike β-blockers, ivabradine is devoid of intrinsic negative inotropic effects and does not affect coronary vasomotion. A whole range of patients with angina may benefit from exclusive heart rate reduction with ivabradine, including those with contraindications or intolerance to the use of β-blockers and patients that are insufficiently controlled by β-blockers or calcium channel blockers.

Chronic stable angina is a common and disabling condition, affecting 30,000–40,000 per 1 million people in Europe and the United States. Angina results when myocardial perfusion is insufficient to meet metabolic demand.