EFFECT OF CALCIUM ANTAGONISTS ON SYMPATHETIC ACTIVITY

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ABSTRACT

To evaluate the effects of calcium antagonists on sympathetic activity in hypertensive patients, a MEDLINE search for English-language articles published between 1975 and May 1996 using the terms calcium antagonists, sympathetic nervous system, and catecholamines was conducted. Clinical studies only reporting the effects of calcium antagonists on blood pressure, heart rate and plasma norepinephrine (NE) levels in patients with hypertension were included. Data were combined and analysed according to class of calcium antagonist (dihydropyridine vs. non-dihydropyridine), their duration of action (short-acting [SA] vs. long-acting [LA]), and treatment duration. We identified 63 studies involving 1252 patients. In the short term, after single dosing, SA calcium antagonists decreased mean arterial pressure by 13.7 ± 1.1% and increased heart rate by 13.7 ± 1.4% and NE levels by 28.6 ± 2.5%. Short-term changes in NE levels correlated with change in heart rate ($r=0.59$, $P<0.01$) and inversely with change in arterial pressure ($r=0.46$, $P<0.05$) in patients taking dihydropyridine calcium antagonists . With sustained therapy, both classes of SA calcium antagonists increased NE levels. Whereas NE levels remained slightly elevated and heart rate unchanged with LA-dihydropyridine calcium antagonists, both heart rate and NE levels decreased with LA non-dihydropyridine calcium antagonists. SA calcium antagonists stimulate sympathetic activity when given acutely and over the long term, irrespective of their molecular structure. Sympathetic activation is less pronounced with LA dihydropyridine calcium antagonists and falls with LA non-dihydropyridine calcium antagonists. These data offer a possible pathophysiological explanation for the paradoxical increase in morbidity and mortality observed in some studies using SA calcium antagonists.