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High-dose nifedipine use is associated with increased risk of out-of-hospital cardiac arrest: multi-country case-control study

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OnBehalf: ARREST

Introduction

Drugs that influence cardiac electrophysiological properties by impacting on cardiac ion channels have been associated with an increased risk of out-of-hospital cardiac arrest (OHCA) due to ventricular tachycardia/ventricular fibrillation (VT/VF). It is unknown whether dihydropyridines, which block L-type calcium channels, are associated with increased risk of OHCA.

Purpose

To determine whether the widely used dihydropyridines nifedipine and amlodipine are associated with increased OHCA risk.

Methods

We performed a multi-country case-control study using data from the Dutch Amsterdam Resuscitation Studies registry (ARREST, 2005-2011) and the Danish Cardiac Arrest Registry (DANCAR, 2001-2014). Both registries are community-based registries of all-cause OHCA and are part of the ESCAPE-NET consortium that studies OHCA across Europe. Cases were cardiac-caused OHCA patients with VT/VF, and controls (up to 5 per case) were non-OHCA individuals matched on age, sex and index (OHCA) date. Dutch controls were sampled from PHARMO Database Network and Danish controls from the general (Danish) population. We compared current use on the index date of the study drugs (prescription within 90 days before OHCA) to no use of any dihydropyridine, using conditional logistic regression analysis with adjustment for well-known risk factors of OHCA.

Results

We studied 2,503 cases and 10,543 controls in ARREST (median age 67.0 years, interquartile range [IQR] 57.0-77.0 years; 77.4% male), and 22,208 cases and 111,040 controls in DANCAR (median age 74 years, IQR 64-82 years; 62.9% male). In both registries, current use of high-dose nifedipine (≥60mg/day), but not low-dose nifedipine (<60mg/day), was associated with increased OHCA risk, compared to non-use of dihydropyridines (adjusted Odds Ratio [ORadj] 1.5 [95%CI 1.03-2.1] in ARREST, and 1.5 [95%CI 1.1-2.1] in DANCAR). Amlodipine use was not associated with increased OHCA risk in both registries; compared to amlodipine, high-dose nifedipine was associated with increased OHCA risk in both registries (ARREST: ORadj 2.3 [95%CI 1.5-3.5]; DANCAR: ORadj 1.6 [95%CI 1.2-2.2]).

Conclusion: Use of nifedipine ≥60mg/day, but not <60mg/day or amlodipine, is associated with increased OHCA risk.