



## #EHRA2019: ESCAPE-NET study - nifedipine increases risk of sudden cardiac arrest



A new study by the European Sudden Cardiac Arrest network (ESCAPE-NET) has found that a widely used heart drug, nifedipine, is associated with an increased risk of out-of-hospital sudden cardiac arrest. Nifedipine is often used to treat high blood pressure and angina (chest pain). But ESCAPE-NET researchers urged caution when interpreting these results, citing the need to replicate the findings in other studies before action should be taken by doctors or patients.

The study, presented at EHRA 2019, examined if nifedipine and amlodipine, dihydropyridines commonly used for hypertension and angina, are linked with out-of-hospital cardiac arrest. The nifedipine doses most often used and studied in this study are 30 mg and 60 mg (90 mg is available but infrequently used) and the amlodipine doses are 5 mg and 10 mg. Standard practice is to start with a lower dose, then give the higher dose if blood pressure or chest pain are not sufficiently reduced.

The analysis was done using data from the Dutch Amsterdam Resuscitation Studies registry (ARREST, 2005-2011) and confirmed in the Danish Cardiac Arrest Registry (DANCAR, 2001-2014), both part of ESCAPE-NET. The network was established to find the causes, and help in the prevention, of cardiac arrhythmias (ventricular fibrillation and tachycardia). Patients with out-of-hospital cardiac arrest (OHCA) due to ventricular fibrillation/tachycardia were enrolled, plus up to five controls per patient matched for age and sex. Controls were from the Dutch PHARMO Database Network and the general population in Denmark.

Overall, the study included 2,503 patients and 10,543 controls in the ARREST analysis and 8,101 patients and 40,505 controls in the DANCAR analysis. The use of high-dose (>60 mg/day), but not low-dose (<60 mg/day), nifedipine was significantly associated with an increased risk of OHCA compared to non-use of dihydropyridines, with an odds ratio of 1.5 in ARREST and 2.0 in DANCAR.

In addition, high-dose nifedipine was associated with an increased risk of OHCA when compared with any dose of amlodipine, with odds ratios of 2.3 and 2.2 in the ARREST and DANCAR registries, respectively. There was no risk associated with amlodipine, the researchers noted.

Dihydropyridines act by blocking L-type calcium channels. A separate study in human cardiac cells showed that both drugs blocked these ion channels, thereby shortening the action potential of the cardiac cell. A shorter action potential can facilitate the occurrence of the fatal arrhythmias that cause sudden cardiac arrest. High-dose nifedipine (60 mg) caused more shortening of the action potential than high-dose amlodipine (10 mg).

"This study suggests that high-dose nifedipine may increase the risk of sudden cardiac arrest due to fatal cardiac arrhythmia while amlodipine does not. If these findings are confirmed in other studies, they may have to be taken into account when the use of either drug is considered," said Dr. Hanno Tan, ESCAPE-NET project leader and cardiologist, Academic Medical Centre in Amsterdam.

The findings come as a surprise considering that both drugs have been in use for many years and in many patients. A possible explanation why this discovery has only been made now is that OHCA is very difficult to study due to its rapid course, and requires dedicated datasets collected specifically for this purpose. Until now, there were insufficient patient records to test the impact of medications. ESCAPE-NET has made this possible by linking large cohorts across Europe, including ARREST and DANCAR.

Source: [European Society of Cardiology \(ESC\)](#)

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Published on : Wed, 27 Mar 2019