Effect of Nicorandil in Patients with Refractory Angina and Advanced Coronary Artery Disease

Robert Avram*, Angela Nguyenb, Marie Gabrielle Lessard, E. Marc Jolicœura.

Background: Refractory angina (RFA) is a chronic morbid condition hampering the quality of life of thousand of Canadians and effective therapies are desperately needed. Nicorandil is a nicotinamide vasodilator with cardioprotective effects that has been shown to improve cardiac outcomes in patients with stable coronary artery disease (CAD). Nicorandil has never been studied in patients with refractory angina.

Methods: We investigated the safety and efficacy of nicorandil in patients with advanced coronary artery disease unsuitable for revascularization and persistent angina (CCS Class II to IV) despite maximal tolerable doses of two anti-angina agents, and compared it with similar control patients not exposed to nicorandil. Consecutive patients were selected from our RFA clinic from August 2009 to August 2013 and followed-up for at least 6 months. Nicorandil was available via the Health Canada’s special access program, and a pharmacist dedicated to the program monitored observance to nicorandil and the occurrence of drug-related adverse effects. We assessed the association between nicorandil and CCS angina class (1st endpoint) and cardiovascular outcomes (2nd endpoint) in patients with RFA.

Results: Forty patients treated with maximum orally tolerated dose of Nicorandil (up to 30 mg three times daily) were compared to 38 control patients (total n = 78). Baseline characteristics and cardiovascular status were similar in both groups. Over a median follow-up of 15 months, nicorandil was associated with a significant improvement in the functional status, as shown in the figure (p = 0.001). Patients receiving the active drug had 6-times higher odds of showing improvement in CCS class angina at their first visit as those in the control group, in a proportional-odds logistic-regression model (Odds ratio, 6.34; 95% confidence interval of 2.45 – 16.35, p = 0.0001). Moreover, in a multivariate cox-proportional analysis model, nicorandil failed to improve the combined occurrence of death or heart transplant + acute coronary syndrome + coronary revascularization + hospitalization rates at 1-year for angina compared to control patients (p = 0.28).

Figure title: Change in CCS Angina class in patients treated with vs. without nicorandil

Data presented as Mean ± SD; Intra-group comparisons performed with Wilcoxon Signed rank sum test; Intergroup comparison performed with ANCOVA adjusted for differences at baseline.
**Conclusion:** In patients with advanced coronary artery disease and RFA, Nicorandil is associated with an improvement in CCS class angina. Nicorandil failed to improve cardiovascular outcomes.

Authors affiliations: \textsuperscript{a}Department of Medicine, and \textsuperscript{b},Department of Pharmacy, Montreal Heart Institute, Université de Montréal, Québec, Canada.
No conflicts of interest.