Anti-anginal Drugs-Beliefs and Evidence: Systematic Review Covering 50 Years of Medical Treatment

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Abstract
Chronic stable angina is the most prevalent symptom of ischaemic heart disease and its management is a priority. Current guidelines recommend pharmacological therapy with drugs classified as being first line (beta blockers, calcium channel blockers, short acting nitrates) or second line (long-acting nitrates, ivabradine, nicorandil, ranolazine, and trimetazidine). Second line drugs are indicated for patients who have contraindications to first line agents, do not tolerate them or remain symptomatic. Evidence that one drug is superior to another has been questioned. Between January and March 2018, we performed a systematic review of articles written in English over the past 50 years English-written articles in Medline and Embase following preferred reporting items and the Cochrane collaboration approach. We included double blind randomized studies comparing parallel groups on treatment of angina in patients with stable coronary artery disease, with a sample size of, at least, 100 patients (50 patients per group), with a minimum follow-up of 1 week and an outcome measured on exercise testing, duration of exercise being the preferred outcome. Thirteen studies fulfilled our criteria. Nine studies involved between 100 and 300 patients, (2818 in total) and a further four enrolled greater than 300 patients. Evidence of equivalence was demonstrated for the use of beta-blockers (atenolol), calcium antagonists (amlodipine, nifedipine), and channel inhibitor (ivabradine) in three of these studies. Taken all together, in none of the studies was there evidence that one drug was superior to another in the treatment of angina or to prolong total exercise duration. There is a paucity of data comparing the efficacy of anti-anginal agents. The little available evidence shows that no anti-anginal drug is superior to another and equivalence has been shown only for three classes of drugs. Guidelines draw conclusions not from evidence but from clinical beliefs.

Keywords
Chronic angina, Anti-angina drugs, Beta-blockers, Calcium antagonists, Channel inhibitor, Ivabradine