

The Role of Calcium Breaker in Coronary Diseases

(Calcium Channel Blockers as Anti-atherosclerotic Agents)

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Calcium channel blockers (CCBs) have been on the market for more than 30 years. Newer clinical applications are focused on three aspects:

1. Reduction in cell injury by blocking the calcium influx in ischaemic cells. Animal studies showed separately a reduction in infarct size in CCB treated groups in cerebral ischaemia and in myocardial ischaemia as compared with the placebo groups.
2. As an adjunct to angiotensin-converting enzyme inhibitors (ACEIs) in treating hypertension in diabetic patients. FACET (Frosinopril Amlodipine Cardiovascular Events Trial) using 380 diabetic subjects with hypertension and a follow up of 6 years showed that although there were more cardiovascular events in the Amlodipine groups (19.1%) as compared with the Frosinopril groups (7.6%), the events were much lower (3.7%) in the group on combined therapy. Given that diabetics require more aggressive management of hypertension and that the treatment goal is often not reached with monotherapy, CCBs and ACEIs would be an excellent combination.
3. As a regressive agent in atherosclerosis. Studies in cholesterol-fed rabbits showed that several CCBs decreased area of aortic atherosclerosis lesions (1980). Subsequent clinical studies including INTACT (International Nifedipine Trial on Anti-atherosclerotic Therapy, 1990) and Montreal Heart Study (1990) showed neutral overall findings but a subset analysis suggested a reduction in new lesions formation.

PREVENT (Prospective Randomised Evaluation of the Vascular Effects of Norvasc Trial, 2000) was a large multicenter trial involving 825 patients with coronary artery disease (CAD) and a three year follow up. The major findings were that although there was no significant difference between Norvasc and placebo on coronary lumen diameter as measured by quantitative coronary angiography (QCA), there was a significant reduction in major vascular procedure (43%) and hospitalization for unstable angina or congestive heart failure (35%). These encouraging results were in line with the slowing down of the progression of carotid atherosclerosis as indicated by the intimal-medial thickness measured by B-mode ultrasound.

According to Glagov's coronary remodeling hypothesis, arterial expansion may compensate for vascular thickening in the early stages of CAD. QCA which measures only luminal diameter may, therefore, underestimate the extent of disease. The protective effect of CCBs on the intimal-medial thickening thus provide healthier blood vessels and, therefore, less acute events and less new lesion formation.

In summary, CCBs are useful anti-atherosclerotic agents. Their clinical application in the treatment of hypertension provides additional benefit than just on blood pressure control alone. A reduction in acute cardiovascular events will be expected.