SUMMARY
Hypertension plays a central role in the pathogenesis of both CHD and stroke and is clearly one of the biggest challenges facing public health authorities and medical practitioners worldwide.

Five classes of drugs are currently recommended as first line agents for the management of hypertension by JNC VI 1997: Diuretics, beta-adrenoceptor blockers, calcium channel antagonists, alpha 1 adrenoceptor antagonists and ACE inhibitors /angiotensin II receptor antagonists.

Monotherapy was the cornerstone in the management of hypertension but was found to control BP in only one-half of the hypertensive population. Hence combination therapy has been proposed as a first choice alternative in the JNC VI guidelines.

Apart from better control of BP, combination therapy offers distinct advantage over monotherapy in terms of improved compliance, reduced pill burdens, cost benefits and markedly decreased incidence of adverse effects.

Amongst the several combinations listed, combination of a CCB and an ACE Inhibitor/Ang II receptor antagonist appears to offer some additional benefits over the other. No published data is available on the combined hemodynamic effects of amlodipine and losartan in normal human subjects.

Based on the facts the present study was planned where hemodynamic effects of amlodipine (CCB) 2.5 mg, 5mg and losartan
(Ang II, AT₁ receptor antagonist) 50mg/100mg were evaluated in healthy volunteers and in one female patient with mild hypertension. It was a randomised double-blind, placebo controlled, parallel group add on study of 5 weeks duration with an initial placebo run-in period of one week. The study in the patient was single blind. For two weeks the volunteer/patient received one active medication along with placebo of the second active medication and in the subsequent two weeks the second active medication replaced the placebo. Compliance was checked by carrying out pill counts, and adverse events were monitored throughout the study.

Monotherapy with amlodipine and losartan led to a fall in both SBP and DBP, and combination of these further complimented the fall. Fall in DBP was more in the group which received losartan initially followed by amlodipine add on. An order effect was thus observed with the combination.

On ambulatory blood pressure monitoring, a sustained and uniform fall in BP was observed in healthy volunteers and in a hypertensive patient.

No statistically significant effect was observed in ECG parameters and systolic time intervals in volunteers.

The drugs were, in general, well tolerated, though adverse events like headache, asthenia, thoracic pain were reported. All these adverse events were of mild grade and did not require any major
intervention. None of the laboratory parameters measured exceeded the prescribed normal range.

The study therefore establishes that the combination of amlodipine and losartan is indeed synergistic even in normal human subjects. Both these drugs belong to different classes and have a long duration of action which lasts for more than 24 hrs, so they are suitable for once a day dose which is deemed to be a very desirable property among antihypertensive drugs.

The combination of amlodipine and losartan thus appears rational and holds great promise in the treatment of hypertensives who are inadequately controlled with monotherapy or experience intolerable adverse effects with large doses of these drugs when used as monotherapy.