Efficacy and Tolerability of Felodipine and Amlodipine in the Treatment of Mild to Moderate Hypertension—A Randomised Double-Blind Multicentre Trial

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Summary

The purpose of this double-blind parallel-group study was to compare felodipine and amlodipine with respect to antihypertensive efficacy and tolerability. Patients with mild to moderate hypertension were randomised to 6 weeks' treatment with felodipine extended-release (n = 59) or amlodipine (n = 59) once daily. The starting dose of both drugs was 5mg, which after 2 weeks' treatment was increased to 10mg in patients whose blood pressure was still above 90mm Hg. Blood pressure measurements were performed approximately 24 hours after dose.

Both felodipine and amlodipine were found to lower blood pressure significantly compared with baseline. Seated blood pressure was reduced by 18/13mm Hg (systolic/diastolic) after 2 weeks and by 25/18mm Hg after 6 weeks in the felodipine group. Corresponding values in the amlodipine group were 16/12mm Hg and 23/17mm Hg. The differences in antihypertensive effect between treatments were marginal and not statistically significant. Pulse rate was not significantly affected by either treatment.

The proportion of responders (seated diastolic blood pressure < 90mm Hg) after 2 weeks' treatment was 59% for felodipine 5mg and 51% for amlodipine 5mg [nonsignificant (ns) between treatments]. After dose titration, at the end of the study, the response rates were 76% and 75% for felodipine and amlodipine, respectively (ns).

Both treatments were well tolerated. The numbers of patients reporting adverse reactions were 8 of 59 in the felodipine group and 11 of 59 in the amlodipine group. Headache, dizziness, flushing, and palpitations were the most common symptoms.

In conclusion, felodipine 5 to 10mg and amlodipine 5 to 10mg, once daily, were equally effective and well-tolerated antihypertensive treatments. Therefore, other factors such as degree of vascular selectivity and cost of treatment could be considered in the choice between these drugs.
Felodipine and amlodipine are 2 new dihydropyridine calcium antagonists, which have both been found to reduce blood pressure effectively and to be well tolerated (Murdoch & Heel 1991; Todd & Faulds 1992). Felodipine has, however, been shown to be highly vascular selective compared with amlodipine, which has a moderate degree of selectivity, similar to that of nifedipine (Cheng et al. 1991; Koolen et al. 1991; Ljung 1985; Nordlander et al. 1991).

Felodipine is provided in an extended-release formulation, and reduces blood pressure consistently over the 24-hour interval when administered once daily (Faison et al. 1991; Todd & Faulds 1992). It has been investigated as monotherapy in several studies, but also in combination with other drugs such as β-blockers, diuretics and angiotensin converting enzyme (ACE) inhibitors. In a series of studies, felodipine was found to be as effective or even more effective compared with a variety of standard regimens. A dose-response relationship in the range 2.5 to 20mg once daily has been demonstrated with felodipine, and 5mg is the recommended starting dose (Faison et al. 1991; Todd & Faulds 1992).

Similar to felodipine, amlodipine is given once daily and has been found to reduce blood pressure over 24 hours (Murdoch & Heel 1991). The anti-hypertensive efficacy of amlodipine has also been proven in a number of clinical studies comparing this drug to various standard regimens. A dose-response relationship in the same range as for felodipine has been shown and the recommended starting dose is 5mg (Frick et al. 1989).

Randomised double-blind comparative studies are necessary to determine the relative efficacies and tolerabilities of 2 drugs, and indirect comparisons of different studies can at best give some information on qualitative similarities or dissimilarities between drugs. To our knowledge, there are no previous direct comparisons between felodipine and amlodipine in the treatment of hypertension. The present study was therefore performed to compare the efficacies in lowering blood pressure, response rates 24 hours after dose, and tolerability of the 2 drugs.

Patients and Methods
Study Design and Patients

This was a randomised double-blind parallel group trial performed at 7 centres. After a drug-free period of at least 2 weeks, followed by a 2-week placebo period, patients with a seated diastolic blood pressure of 95 to 115mm Hg were randomised to 6 weeks of treatment with felodipine extended-release (Plendil®, Modip®, Flodil®; Astra) or amlodipine (Norvasc®, Istin®, Amlor®; Pfizer). The starting dose of both drugs was 5mg once daily, which after 2 weeks' treatment was increased to 10mg once daily in patients whose blood pressure was still > 90mm Hg 24 hours after dose. The study design is illustrated in figure 1. Since the formulations of the study drugs had different shapes, the double-dummy method was used for blinding purposes: thus patients took one dosage in the morning of active drug and one of placebo matching the other active drug. No other antihypertensive drugs were permitted during the study.

Patients with any of the following criteria were excluded from the study: secondary or malignant hypertension, impaired renal function (serum creatinine > 120 µmol/L), clinically relevant impair-