What are appropriate doses to use when switching hypertensive patients to amlodipine from lercanidipine or lacidipine?

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Background

Amlodipine is now available generically in the UK and is relatively inexpensive compared with other dihydropyridine calcium antagonists such as lercanidipine or lacidipine. This Q&A addresses the issue of appropriate doses to use if considering transferring hypertensive patients from lercanidipine or lacidipine to amlodipine. Lacidipine and lercanidipine are only licensed in the UK to treat hypertension and the treatment of angina is therefore not considered here.

A related question, Q&A 18.4, addresses how doses of amlodipine and felodipine compare for the treatment of hypertension or prophylaxis of stable angina.

Answer

Lacidipine compared with amlodipine

Two published trials have compared lacidipine with amlodipine. A third trial has compared lercanidipine, lacidipine and amlodipine. In addition, a further trial (1) involved treatment with hydrochlorothiazide in addition to the calcium antagonists and it was not to possible to determine the effect of monotherapy.

The first trial that compared lacidipine with amlodipine (2) was a 6-week crossover, double-blind double-dummy study in 65 patients with uncomplicated mild-moderate hypertension involved lacidipine 4mg daily with amlodipine 5mg daily. Doses could be increased after 2 weeks treatment if necessary, to lacidipine 6mg or amlodipine 10mg, for a further 4 weeks. 61 of the patients provided evaluable results. Comparable antihypertensive effects were found with the two drugs, with a reduction in systolic blood pressure of 19.2 ± 13.5mmHg for lacidipine and 22.3 ± 15.3mmHg for amlodipine. Diastolic pressure reductions were 13.3 ± 4.2mmHg for lacidipine and 12.3 ± 5.3mmHg amlodipine. The proportions of patients who achieved satisfactory blood pressure control was similar for the two drugs, 76% for amlodipine and 70% for lacidipine. Only a minority of the patients, 5 patients taking amlodipine and 7 taking lacidipine, were titrated to the higher doses and the results are not reported separately. The authors concluded that lacidipine 4mg and amlodipine 5mg were similarly effective in reducing blood pressure without significant increases in heart rate.

A second trial (3) compared 12 weeks’ treatment with lacidipine or amlodipine in 68 patients with mild-moderate hypertension. Results were based on the 62 who completed the trial. After initial treatment with either 4mg lacidipine or 5mg amlodipine for 6 weeks, the dose could be increased to 6mg or 10mg respectively. Eighteen patients (60%) in the lacidipine group and 12 (38%) in the amlodipine group required this dose increase. Blood pressure in those taking lacidipine fell from 161 ± 3 mm Hg systolic to 149 ± 3 and from104 ± 1 mm Hg to 95 ± 1 mm Hg diastolic. In those taking amlodipine 5mg daily, blood pressure fell during the first 6 weeks, from a baseline of 164 ± 3 mm Hg to 145 ± 3 mm systolic and 103 ± 1 mm Hg and 91 ± 1 mm Hg diastolic respectively. Falls in mean arterial pressure (MAP) were also presented, these were not statistically different; mean fall in MAP on lacidipine was -8 ±1% and for amlodipine was -11 ±1%. However in the high dose group the change in MAP was -7 ± 1% in those taking lacidipine and -12 ± 2% for those on amlodipine. This was a statistically significant difference, p<0.05, although the two drugs had similar effects on blood pressure. The authors concluded that although lacidipine 4mg daily provided similar blood pressure lowering to amlodipine 5mg daily, the lacidipine dose of 6mg daily was less effective than amlodipine 10mg daily.
The third trial (4) compared both lacidipine and lercanidipine with amlodipine in elderly hypertensive patients. This was a tolerability study in which 828 patients were randomised to double-blinded treatment with either lacidipine 2mg (n=208), lercanidipine 10mg daily (n=420) or amlodipine 5mg (n=200). If blood pressure control was unsatisfactory the dose of the medication could be doubled, or, as a further step, additional treatment with enalapril or atenolol (plus a diuretic if needed) could be added. Patients were treated for an average of 12 months, although over 25% in each group withdrew from the study in the first 6 months. Similar proportions of patients in all three groups were controlled on low dose monotherapy (47%, 52% and 56% for lacidipine, lercanidipine and amlodipine respectively) and high dose monotherapy (24% 22% and 23%). After 6 month’s treatment, sitting systolic and diastolic BP were significantly reduced by lacidipine (29.4 ± 1.0 /14.0 ± 0.6 mmHg) lercanidipine (29.6 ± 0.7/14.3 ± 0.4 mm Hg) and amlodipine (29.7 ± 1.1/14.5 ± 0.6 mmHg), with no significant differences between treatment.

In conclusion therefore, the trials indicate that 2mg or 4mg lacidipine were similarly effective to 5mg amlodipine; one trial suggested that 6mg lacidipine is less effective than 10mg amlodipine in reducing mean arterial pressure, though blood pressure reductions were similar.

Lercanidipine compared with amlodipine

Five trials were located that compared the antihypertensive effects of lercanidipine with amlodipine. The first of these (5) involved treatment of hypertensive patients (grade 1 or 2 essential hypertension) for 4 months with a calcium antagonist. Of the 110 recruited to the trial, 15 were randomly assigned to lercanidipine 10mg daily and 20 to amlodipine 10mg daily. The study involved Fourier analysis of 24-hour blood pressure profiles, but mean reductions in blood pressure (taken between 2 to 6 hours after the dose) were also presented. Lercanidipine produced a mean peak reduction in blood pressure of 16mm Hg systolic and 18mmHg in diastolic pressure. Corresponding figures for amlodipine treatment were 19mm Hg systolic and 15mm Hg diastolic pressure.

A second study, described above (4) involved 828 patients over 60 years of age with hypertension in a multicentre double blind parallel group trial. Patients were randomised to lacidipine 2mg/day (n=208), lercanidipine 10mg/day (n=420) or amlodipine 5mg/day (n=200). During the 12 month study, the doses of antihypertensives could be doubled if control was unsatisfactory, and further antihypertensives added if hypertension remained uncontrolled subsequently. Blood pressure was equally and effectively controlled in all three groups, with 47%, 52% and 56% of the groups respectively being controlled on low dose monotherapy and 24% 22% and 23% controlled on high dose monotherapy. The authors concluded that lercanidipine 10mg/day and amlodipine 5mg/day produced comparable blood pressure control.

The third study (6) was a small randomised double blind crossover study involving 20 patients with mild-moderate hypertension (16 completed the study). They were given either lercanidipine 20mg or amlodipine 10mg daily for 4 weeks, with a 2 week washout period before starting the treatment with the second drug. The 24-hour ambulatory blood pressure monitoring trace was similar for both drugs. After the first 4 week period, 86% of those taking lercanidipine and 56% of those taking amlodipine were considered to have controlled blood pressure. After the second 4 week period, the figures were 67% and 86% respectively, indicating that blood pressure control was comparable between the two treatments.

The fourth study (7) involved 22 middle aged men (aged 48± 5 years) with mild-moderate hypertension. This was a single blind crossover study, treatment with each agent lasted 2 weeks and there was a 2-week washout period in between. Falls in blood pressure were slightly greater in the group taking amlodipine 10mg daily (mean systolic fall of 11mm Hg, diastolic fall of 11mm Hg), compared with those taking lercanidipine 20mg daily (8mmHg systolic and 7mmHg diastolic). The authors did not test for any statistical significance between these effects.

A further study (8) in 92 postmenopausal hypertensive women investigated the effect of lercanidipine 10mg daily and amlodipine 5mg daily over 4 weeks, after which the dose of both drugs was doubled. They found comparable blood pressure lowering activity of the two drugs. The mean (±SD) change in systolic pressure was -22.4 (±1.6) mm Hg for lercanidipine versus -24.6 (±1.7) for amlodipine; the
mean (±SD) change in diastolic pressure was -10.7 (±1.1) for lercanidipine and ±13.3 (±1.2) for amlodipine. The percentage of patients whose blood pressure was normalised to systolic and diastolic below 140/90 mmHg was also not significantly different in the two groups, 56% for lercanidipine and 67% for amlodipine (P = 0.343).

In summary therefore one trial (the largest, with more than 200 in each group) found that amlodipine 5mg daily produced a similar blood pressure lowering effect to lercanidipine 10mg daily. Smaller trials found similar antihypertensive effects using lercanidipine 20mg daily and amlodipine 10mg daily (3 trials), and amlodipine 10mg and lercanidipine 10mg daily (one trial).

**Summary**

- Lercanidipine and lacidipine are relatively expensive calcium channel blockers used to treat hypertension. A similar antihypertensive effect may be expected if people taking these agents are transferred to amlodipine.

- Lacidipine 2 or 4mg daily is similar in effect to 5mg amlodipine; 6mg lacidipine daily may be slightly less effective than amlodipine 10mg daily.

- Lercanidipine 10mg daily has a similar effect to amlodipine 5mg daily; amlodipine 10mg daily is approximately similar in effect to 20mg lercanidipine, although there is limited evidence that 10mg of each of the agents are similar in antihypertensive effect.

**Limitations**

Trials of antihypertensive agents generally involve patients with mild-moderate hypertension who are taking only one or two antihypertensive agents. The information contained here should therefore be treated with caution when considering treatment of patients with severe or secondary hypertension or with renal impairment or other chronic disease.

**References**

Quality Assurance

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Search strategy
Please specify which of these are used if appropriate, (whether or not all of them yielded useful information) and add others if necessary:

- Embase: [lercanidipine/ or lacidipine/ + amlodipine/ ]
- Medline [lercanidipine (ti,ab) + amlodipine/; lacidipine (ti,ab) + amlodipine/]
- IDISweb [lercanidipine + amlodipine]; [lacidipine + amlodipine]
  (Searches repeated May 2012)