A comparison of the acute haemodynamic effects of nisoldipine and nifedipine during treatment with atenolol in patients with coronary artery disease

KIRSTEEN M. DONALDSON¹, KEITH D. DAWKINS² & DEREK G. WALLER¹

¹Clinical Pharmacology Group and ²Department of Cardiology, Southampton General Hospital, Southampton

- 1 The acute haemodynamic effects of intravenous nisoldipine (1, 2, 4 $\mu\text{g kg}^{-1}$) and nifedipine (2.5, 5, 10 $\mu\text{g kg}^{-1}$) were compared in a randomised, within-patient cross-over study. Fifteen male patients with stable angina pectoris treated with atenolol were studied after undergoing routine cardiac catheterisation.
- 2 Nisoldipine caused a dose-related fall in systemic vascular resistance (maximum 22%) associated with an increase in heart rate and cardiac index (18%) and a fall in mean arterial pressure (7%).
- 3 By contrast, nifedipine was associated with a significant increase in heart rate but systemic vascular resistance, cardiac index and mean arterial pressure remained unaltered.
- 4 At doses with equivalent effects on heart rate (2 $\mu\text{g kg}^{-1}$ nisoldipine; 10 $\mu\text{g kg}^{-1}$ nifedipine) acute dosing with nisoldipine caused a significantly greater fall in systemic vascular resistance and increase in cardiac index, whilst nifedipine caused a greater reduction in stroke volume index and left ventricular stroke work index.
- 5 The results suggest that, when combined with atenolol, acute dosing with nisoldipine may have a more complementary haemodynamic profile than nifedipine. The implications of this finding for chronic oral dosing in patients with impaired left ventricular function should be evaluated.

Keywords nisoldipine nifedipine atenolol haemodynamic effects

Introduction

The acute haemodynamic effects of the 1,4 dihydropyridine derivative calcium antagonist nifedipine are complex. In the isolated heart nifedipine has negative inotropic properties [1], although it also relaxes arterial smooth muscle resulting in a fall in systemic vascular resistance. *In vivo* cardiac output therefore increases due to a reflex tachycardia and an increase in stroke volume in response to the reduced afterload [2].

The combination of calcium antagonist and β -adrenoceptor antagonists has been shown to be beneficial in the relief of myocardial ischaemia in patients with chronic stable angina [3, 4]. However, acute studies have demonstrated that the reflex positive inotropic and chronotropic responses to nifedipine are attenuated by β -adrenoceptor antagonists [5]. Concurrent administration with β -adrenoceptor antagonists may unmask the direct negative inotropic action of nifedipine and

cause haemodynamic deterioration, particularly in patients with impaired left ventricular function [6].

Nisoldipine is a calcium antagonist chemically similar to nifedipine. *In vitro*, nisoldipine is 4–10 times more potent than nifedipine in inhibiting contraction of isolated smooth muscle. At concentrations that are equally effective in relaxing vascular smooth muscle, nisoldipine has substantially less negative inotropic activity [7]. It may therefore have more favourable haemodynamic effects than nifedipine *in vivo* and be safer in combination with β -adrenoceptor antagonists and in patients with impaired left ventricular function. Thus, Soward *et al.* [8] found no evidence of major myocardial depression in an acute study of nisoldipine in a group of patients, many of whom were also receiving various β -adrenoceptor antagonists.

No comparative studies of nifedipine and nisoldipine

in combination with β -adrenoceptor antagonists are available. The present study was designed to compare the acute haemodynamic effects of nifedipine and nisoldipine in a group of patients with proven coronary artery disease under treatment with atenolol.

Methods

Approval for this study was obtained from the local ethics committee.

Patients

Fifteen male patients (aged 39–63 years) undergoing routine cardiac catheterisation for the investigation of suspected coronary artery disease were entered after giving written informed consent. Symptoms had been present for a mean period of 23.4 months (range 3 months–10 years). Patients were excluded from the study if there was a history of cardiac failure, unstable angina or recent (within 3 months) acute myocardial infarction, significant valvular heart disease, atrial fibrillation, second or third degree atrioventricular block or if no evidence of significant coronary artery disease was found at catheterisation. Seven patients gave a history of previous myocardial infarction.

All patients were receiving long-term (greater than 3 months) treatment with atenolol (100 mg daily, nine patients; 50 mg daily, six patients) and sublingual glyceryl trinitrate as necessary. All other vasoactive medication was discontinued 3 days prior to participation in the study (nifedipine 5, diltiazem 1, oral or transdermal nitrates 8, chlorthalidone 1). Other concomitant therapy was discontinued the day prior to participation (cimetidine 1, indomethacin 1, frusemide with amiloride 1, bumetanide with potassium 1, aspirin 8).

Routine angiography was carried out immediately prior to participating in the study. Six patients had triple vessel disease; four double vessel disease and five single vessel disease. Left ventricular function was good in 13, reduced in one and poor in one. One patient had a mildly raised left ventricular end diastolic pressure (21 mmHg). Seven patients had abnormalities of regional wall motion (anterior in 2, inferior in 4, both anterior and inferior in 1).

Study design

A randomised, single-blind within patient cross-over design was employed.

On the morning of the study, patients were pretreated with atenolol, 50 mg orally, 3 h before the first haemodynamic measurement.

Cardiac catheterisation was performed with the patient fasting and without premedication using a right femoral artery approach and 8F sheath. During this procedure, the central aortic pressure was compared with a simultaneously recorded femoral artery pressure. A 7F Swan-Ganz thermodilution catheter was introduced via the right femoral vein under fluoroscopic control and positioned to provide high quality pulmonary capillary wedge and pulmonary artery pressure recordings.

Satisfactory ventricular pacing was established using the same route.

Baseline measurements were recorded at least 1 h after completion of the left ventricular angiogram. Heart rate was derived from the electrocardiogram. Femoral artery pressure, pulmonary artery pressure, pulmonary capillary wedge pressure and central venous pressure were measured using a Hewlett-Packard series 66 component monitoring system interfaced with Hewlett-Packard universal quartz transducers or a Hewlett-Packard 80300A monitoring trolley with Spectramed disposable transducers. All pressure measurements were derived from the mean of two consecutive readings. The appropriate correction was applied to calculate central aortic pressure from femoral artery pressure. Cardiac output was recorded using the thermodilution technique (mean of three measurements) with a Gould-Statham Spectramed SP1445 haemodynamic profile computer. The coefficient of repeatability of this technique, based on two consecutive determinations in each of 19 patients was 19.5%. The study therefore had a 90% power to detect changes in cardiac index of 15%. Pulmonary vascular resistance, systemic vascular resistance, cardiac index, stroke volume index and left ventricular stroke work index were calculated according to standard formulae.

These baseline measurements were repeated during ventricular pacing at a constant rate, usually 80 beats min^{-1} (one patient, who had a resting heart rate of 78, was paced at 95 beats min^{-1}).

The patients were then randomised to receive either intravenous nifedipine or nisoldipine with each dose infused over 1 min in increments to give cumulative doses of 2.5, 5, 10 $\mu\text{g kg}^{-1}$ nifedipine and 1, 2, 4 $\mu\text{g kg}^{-1}$ nisoldipine. Drugs were administered via a peripheral line to the first three patients. Both drugs caused local discomfort by this route and subsequent patients received the drugs via infusion into a central vein.

Five minutes after each dose, haemodynamic measurements were repeated in sinus rhythm and during ventricular pacing. Ten minutes were allowed to elapse between each incremental increase in drug dose (Figure 1).

The second drug was given at least 3 h after the last administration of the first drug. The anticipated delay between the first dose of atenolol and the start of the second haemodynamic study was 6 h. The elimination half-life of atenolol is approximately 8 h [9] and therefore

Figure 1 Study design (LV angio: left ventricular angiogram).

a second oral dose of 25 mg atenolol was given 2 h prior to commencing the second set of measurements. Before giving the second drug, the mean femoral artery pressure had to be within 15% of previous baseline values.

Statistics

Results are expressed as mean (s.d.). Baseline measurements were compared using Student's *t*-test. The actions of each drug were analysed separately for evidence of any dose-related trend as described by Wallenstein *et al.* [10]. The effects of equipotent doses of the two drugs were compared according to the method of Hills & Armitage [11] for two-period cross-over trials. This method of analysis enables any period effects to be analysed separately from treatment effects. In addition, it tests the assumption that the effects of each treatment are independent of the order of administration i.e. that there is no treatment-period interaction.

Results

One patient withdrew during the second part of the study (nisoldipine) due to pain at the peripheral injection site. The results from the first part of his study are included in the analysis of the effects of nifedipine but not for the comparison of the effects of the two drugs. Fourteen patients completed both parts of the study. The responses to treatment did not appear to depend on the route of administration (via peripheral or central line). There were no significant differences between baseline measurements for the two drugs. No significant period or order effects were detected in the actions of nifedipine and nisoldipine. No evidence of any treatment-period interaction was found. Patients with impaired left ventricular function appeared to respond to the two drugs in a similar fashion to those with normal ventricular function.

Nifedipine (Table 1)

Nifedipine caused a dose-related increase in heart rate ($P < 0.001$). Systemic vascular resistance was unaltered

and no significant changes were recorded in arterial pressure or cardiac index. The 15% increase in mean heart rate at the highest dose ($10 \mu\text{g kg}^{-1}$) was associated with reductions of 14% in stroke volume index and left ventricular stroke work index ($P < 0.005$ and $P < 0.01$ respectively). At constant rate ventricular pacing no significant changes were found in these parameters compared with measurements made during ventricular pacing prior to nifedipine treatment. All measurements on the low pressure system (central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, pulmonary vascular resistance) remained unchanged throughout the study.

Nisoldipine (Table 2)

Nisoldipine caused a dose-related fall in systemic vascular resistance during sinus rhythm, with a maximum fall of 22% at the highest dose used ($4 \mu\text{g kg}^{-1}$; $P < 0.001$). This was associated with dose-related increases in mean heart rate ($P < 0.001$) and cardiac index ($P < 0.001$) and a fall in mean arterial pressure ($P < 0.005$). Stroke volume index fell by 5.6% ($P < 0.05$) but left ventricular stroke work index was not significantly altered. The reduction in systemic vascular resistance following treatment with nisoldipine was correlated with the magnitude of the initial systemic vascular resistance ($r = 0.72$, $P < 0.01$). Similar results were obtained during constant rate ventricular pacing, with a maximum dose-related fall in systemic vascular resistance of 14% ($P < 0.01$). Central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure and pulmonary vascular resistance remained unchanged throughout the study.

Comparison between nifedipine and nisoldipine (Table 3 and Figure 2)

There were no significant differences between nifedipine and nisoldipine at baseline. At doses with equivalent effects on heart rate (nifedipine, $10 \mu\text{g kg}^{-1}$; nisoldipine, $2 \mu\text{g kg}^{-1}$), nisoldipine caused a significantly greater fall in systemic vascular resistance ($P < 0.02$) and increase in cardiac index ($P < 0.002$) than nifedipine, whilst nifedipine caused a greater fall in stroke volume

Table 1 Haemodynamic effects of nifedipine (mean (s.d.))

		Cumulative dose of nifedipine ($\mu\text{g kg}^{-1}$)				<i>P</i>
		0	2.5	5	10	
HR (beats min^{-1})	SR	56.8 (9.4)	61.6 (10.7)	63.2 (10.5)	65.5 (11.7)	$P < 0.001$
SVR (dyn s cm^{-5})	SR	1476 (263)	1516 (263)	1548 (319)	1468 (287)	NS
	paced	1620 (375)	1651 (383)	1731 (407)	1635 (351)	NS
MAP (mmHg)	SR	94.5 (11.8)	97.3 (10.9)	97.0 (11.0)	93.8 (10.8)	NS
	paced	94.1 (10.3)	94.8 (11.2)	95.3 (10.0)	92.5 (8.6)	NS
CI ($\text{l min}^{-1} \text{m}^{-2}$)	SR	2.52 (0.39)	2.53 (0.44)	2.47 (0.42)	2.52 (0.43)	NS
	paced	2.28 (0.37)	2.27 (0.40)	2.17 (0.41)	2.20 (0.34)	NS
SVI (ml m^{-2})	SR	45.2 (8.8)	41.6 (6.8)	39.6 (6.7)	39.0 (6.6)	$P < 0.005$
LVSWI (mmHg ml)	SR	4.01 (0.74)	3.82 (0.55)	3.61 (0.59)	3.44 (0.48)	$P < 0.01$
	paced	2.42 (0.45)	2.42 (0.54)	2.29 (0.57)	2.29 (0.49)	NS

Levels of significance relate to comparison of dose-related trends to zero.

Table 2 Haemodynamic effects of nisoldipine (mean (s.d.))

		Cumulative dose of nisoldipine ($\mu\text{g kg}^{-1}$)				
		0	1	2	4	
HR (beats min^{-1})	SR	55.9 (8.0)	62.5 (9.7)	66.4 (9.4)	69.6 (8.5)	$P < 0.001$
SVR (dyn s cm^{-5})	SR	1520 (328)	1424 (280)	1340 (256)	1192 (224)	$P < 0.001$
	paced	1672 (432)	1608 (472)	1528 (400)	1432 (416)	$P < 0.01$
MAP (mmHg)	SR	93.2 (11.5)	93.5 (11.4)	92.0 (11.7)	86.5 (10.0)	$P < 0.005$
	paced	94.2 (11.2)	91.1 (10.8)	91.3 (11.0)	87.0 (10.9)	$P < 0.02$
CI ($\text{l min}^{-1} \text{m}^{-2}$)	SR	2.45 (0.36)	2.59 (0.30)	2.74 (0.38)	2.90 (0.44)	$P < 0.001$
	paced	2.26 (0.39)	2.34 (0.53)	2.42 (0.53)	2.49 (0.47)	$P < 0.005$
SVI (ml m^{-2})	SR	44.3 (7.4)	42.1 (6.2)	41.7 (5.6)	41.8 (5.7)	$P < 0.05$
LVSWI ($\text{min}^{-1} \text{m}^{-2}$)	SR	3.79 (0.65)	3.68 (0.51)	3.62 (0.53)	3.39 (0.58)	NS
	paced	2.38 (0.46)	2.43 (0.65)	2.52 (0.76)	2.48 (0.68)	NS

Levels of significance relate to comparison of dose-related trends with zero.

Figure 2 The effects of increasing doses of nifedipine (○) and nisoldipine (●) on heart rate (a), systemic vascular resistance (b), cardiac index (c), mean arterial pressure (d), stroke volume index (e), and left ventricular stroke work index (f). Mean values are illustrated; bars represent the s.d. Levels of significance relate to comparison of the effects of $10 \mu\text{g kg}^{-1}$ nifedipine and $2 \mu\text{g kg}^{-1}$ nisoldipine.

index ($P < 0.05$) and left ventricular stroke work index ($P < 0.02$). The effects on arterial pressure did not differ significantly. During constant rate ventricular pacing similar differences were observed although these were less marked, only the effect on cardiac index achieving statistical significance (Table 3).

Unwanted effects

Three patients had episodes of hypotension and bradycardia after administration of the final dose of the second drug (nifedipine 1; nisoldipine 2), requiring treatment with atropine in 2 patients (following completion of data acquisition in 1, prior to completion of the final

set of measurements during ventricular pacing in the other). One of these had had a similar episode during the cardiac catheterisation. Other unwanted effects were generally mild, comprising headache (both drugs 2, nisoldipine alone 1); flushing (nifedipine alone 2); chest pain (nifedipine alone 2).

Discussion

The current study demonstrates that, in patients with coronary artery disease treated with atenolol, intravenous nisoldipine produces a dose-related fall in

Table 3 A comparison of the haemodynamic effects of nifedipine and nisoldipine (mean (s.d.))

		Nifedipine		Nisoldipine		
		Baseline	10 $\mu\text{g kg}^{-1}$	Baseline	2 $\mu\text{g kg}^{-1}$	
HR (beats min^{-1})	SR	57.4 (9.4)	66.7 (11.2)	55.9 (8.0)	66.4 (9.4)	NS
SVR (dyn s cm^{-5})	SR	1476 (263)	1468 (287)	1520 (328)	1344 (256)	$P < 0.02$
	paced	1620 (375)	1635 (351)	1672 (432)	1528 (400)	NS
MAP (mmHg)	SR	94.9 (12.1)	93.9 (10.8)	93.2 (11.5)	92.0 (11.7)	NS
	paced	94.0 (10.7)	92.4 (8.9)	94.2 (11.2)	91.3 (11.0)	NS
CI ($\text{l min}^{-1} \text{m}^{-2}$)	SR	2.56 (0.37)	2.56 (0.41)	2.45 (0.36)	2.74 (0.38)	$P < 0.002$
	paced	2.27 (0.38)	2.23 (0.33)	2.26 (0.39)	2.42 (0.53)	$P < 0.05$
SVI (ml m^{-2})	SR	45.4 (9.1)	39.0 (6.9)	44.3 (7.4)	41.7 (5.6)	$P < 0.05$
LVSWI (mmHg ml)	SR	4.08 (0.71)	3.48 (0.47)	3.94 (0.84)	3.68 (0.55)	$P < 0.02$
	paced	2.44 (0.47)	2.38 (0.46)	2.38 (0.46)	2.52 (0.76)	NS

Levels of significance relate to comparison between nifedipine 10 $\mu\text{g kg}^{-1}$ and nisoldipine 2 $\mu\text{g kg}^{-1}$.

systemic vascular resistance and improvement in cardiac function. This is similar to its effect following oral administration to patients with chronic stable angina pectoris receiving long term treatment with a β -adrenoceptor antagonist [12] and to its effect in untreated patients with coronary artery disease [13]. The magnitude of the reduction in systemic vascular resistance is directly correlated with the initial value, indicating that basal vascular tone is important in modulating the response to arterial vasodilatation, as has been reported previously for nifedipine [14]. By contrast, at the doses employed, nifedipine had no significant effect on systemic vascular resistance or cardiac index. This differs from its reported effects when used alone when it acts as an arterial vasodilator [15]. In these circumstances, the direct negative inotropic effects of nifedipine are counterbalanced by reflex sympathetic stimulation; the net result is an increase in cardiac output. Results of previous studies have suggested that the systemic vasodilatory effects of nifedipine are unaltered by the combination with a β -adrenoceptor antagonist [16–18], although this has been disputed [19]. Several factors should be considered in order to explain the apparent discrepancy between the findings of the present study and previous reports. These include the dose of nifedipine, the rate of administration, the timing of the measurements, the effects of vehicle and the extent of β -adrenoceptor blockade.

The highest dose of nifedipine used in the present study, 10 $\mu\text{g kg}^{-1}$, was equivalent to a mean total dose of 0.8 (0.09) mg. This is slightly lower than the dose employed in the study reported by Schanzenbacher *et al.* (1 mg) [18]. The mean maximum concentration after intravenous administration of 1 mg nifedipine is 26 ng ml^{-1} [20]. Although a concentration of at least 30–35 ng ml^{-1} is necessary to demonstrate a 20% improvement in exercise tolerance in patients with angina receiving atenolol, individual patients will respond to lower concentrations [21]. The dose of nisoldipine associated with symptomatic benefit in the presence of effective β -adrenoceptor blockade has not been determined. The intention of the present study was to compare the acute haemodynamic effects of equipotent doses of

nifedipine and nisoldipine. Since, for the reasons discussed below, nifedipine had no significant effect on mean arterial pressure at any dose tested, equipotent doses were identified by the magnitude of the reflex response as judged by their effects on heart rate. Equivalent doses were 10 $\mu\text{g kg}^{-1}$ nifedipine and 2 $\mu\text{g kg}^{-1}$ nisoldipine. This dose ratio (5:1) is consistent with previous *in vitro* clinical studies suggesting that nisoldipine is 4–10 times more potent than nifedipine in relaxing vascular smooth muscle [7]. There are no reported *in vivo* studies directly comparing intravenous doses of nisoldipine and nifedipine titrated to a similar steady state systemic effect in patients with normal cardiac function. In patients with impaired cardiac function, 0.17 $\mu\text{g kg}^{-1} \text{min}^{-1}$ nisoldipine and 0.58 $\mu\text{g kg}^{-1} \text{min}^{-1}$ nifedipine have similar hypotensive effects [22]. Using repeat coronary angiography, Jost *et al.* [23] reported that intravenous doses of 1 mg nisoldipine and 2 mg nifedipine were equipotent in dilating coronary vessels. The assumption that the doses compared in the current study are equipotent is supported therefore by the available clinical data.

The rate of input of nifedipine is an important determinant of its haemodynamic effects, more rapid administration causing a greater reflex sympathetic response with a larger increase in heart rate and a smaller fall in blood pressure than slower administration [24]. Two of the previous studies of nifedipine β -adrenoceptor antagonist combinations employed sublingual administration of the capsule formulation of nifedipine [16, 17]. It is likely that this is associated with a relatively greater vasodilatory effect and a lesser evoked sympathetic response than bolus intravenous administration. Receptor binding of nisoldipine is characterised by the slow onset of high affinity binding, the haemodynamic response following a hysteresis type relationship with plasma concentrations, the effect increasing slowly to a maximum over about 15 min [23]. This relatively slow onset of pharmacodynamic effect despite rapid bolus administration may provoke a lesser reflex sympathetic response than nifedipine. Peak plasma nifedipine concentrations are achieved a mean of 5 min after completion of the intravenous infusion of 1 mg nifedipine over 5

min [20]. The haemodynamic effects of nifedipine are linearly correlated with plasma drug concentration [23]. Schanzenbacher *et al.* [25] reported that the coronary vasodilatation and heart rate had returned to pre-infusion values within 6 min of initiation of a nifedipine infusion whilst the reduction in mean arterial pressure persisted for at least 12 min. Five minutes post-infusion would therefore appear to be the optimum time to record the maximum haemodynamic effects of nifedipine; the increase in heart rate in the present study confirms that the timing of the measurements was appropriate for the detection of haemodynamic changes. Following intravenous nisoldipine, the haemodynamic response is not linearly related to plasma concentration but follows a hysteresis type curve as discussed above [23]. It is possible therefore that nisoldipine had not produced its greatest effect when the measurements were recorded in the present study which might reduce the apparent difference between the two drugs.

The intravenous formulations of both nifedipine and nisoldipine include a vehicle comprising ethanol and polyethylene glycol in water. Walley *et al.* [15] have demonstrated that, at doses higher than those employed in the present study, the vehicle itself has transient vasodilatory effects and a direct negative inotropic effect. In the present study, a slightly lower volume of vehicle was administered with nisoldipine than with nifedipine. The effect of this would be to exaggerate both the vasodilatory and negative inotropic effects of nifedipine when compared with nisoldipine. The magnitude of this effect is likely to be small.

The increases in heart rate and myocardial contractility that usually occur during treatment with a dihydropyridine calcium antagonist are believed to be a consequence of reflex sympathetic stimulation and withdrawal of vagal tone secondary to afterload reduction. However, in the present study, an increase in heart rate occurred during treatment with nifedipine without any significant change in systemic vascular resistance. This could be explained by the presence of effective β -adrenoceptor blockade. In this circumstance, unopposed α -adrenoceptor stimulation would antagonise the peripheral vasodilatory effect of nifedipine which could explain the lack of change in systemic vascular resistance. The positive inotropic response to reflex sympathetic stimulation would also be attenuated by the presence of effective β -adrenoceptor blockade and antagonised by the direct negative inotropic effect of nifedipine. Overall, myocardial contractility was unaltered in the present study, as was shown by the unchanged stroke volume index at constant heart rate

and filling pressure. However, despite effective β -adrenoceptor blockade, heart rate could still increase as a consequence of reduction in vagal tone. The effectiveness of β -adrenoceptor antagonism has not been formally evaluated in previous studies of the vasodilatory effects of nifedipine during combination therapy. The resting heart rate was 54.4 (8.7) beats min^{-1} prior to treatment with a dihydropyridine calcium antagonist in the present study, although this is an unreliable guide to the extent of β -adrenoceptor blockade, which could only be confirmed by observing the inhibition of isoprenaline or exercise-induced tachycardia, measures which were not practical in the current study protocol. The resting heart rate was much higher in two of the earlier studies of combination treatment (70 beats min^{-1} [17]; 66 beats min^{-1} [18]), suggesting the possibility of less effective β -adrenoceptor blockade. Resting heart rate was not reported in the third study [16]. Nisoldipine is a more powerful vasodilator than nifedipine and the reduction in vascular resistance during nisoldipine treatment was probably sufficient to overcome α -adrenoceptor-mediated vasoconstriction.

Several mechanisms have been proposed to explain the anti-ischaemic effects of dihydropyridine calcium antagonists. A direct myocardial effect may lead to a decreased myocardial oxygen demand which will be offset by reflex sympathetic stimulation. The decreased afterload produced by a fall in systemic vascular resistance will reduce myocardial oxygen consumption whilst reduced coronary vascular resistance will result in increased coronary blood flow [18]. In the current study, at doses with equivalent effects on heart rate, nifedipine reduced stroke volume and therefore caused a greater reduction in left ventricular stroke work than nisoldipine. This should reduce myocardial oxygen demand. By contrast, the systemic vasodilator action of nisoldipine will reduce afterload and therefore myocardial oxygen consumption.

The findings from this study using intravenous dosing suggest that, at the doses employed in this study, when combined with oral atenolol, nisoldipine may have a more complementary haemodynamic profile than nifedipine. The implications of this need to be further evaluated during chronic oral dosing.

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