

exposure on child behaviour or intelligence could not be ruled out by the present study, but these effects, if real, are tiny compared with other factors which influence childrens' physical and mental development.⁶

We express our appreciation to the families of Walsall and their general practitioners, who allowed us to study the children, and to the health visitors based at Walsall Manor Hospital who carried out the field work for the survey. We also thank staff of the department of clinical chemistry, Walsall Manor Hospital and the department of haematology, Dudley Road Hospital, Birmingham for carrying out additional investigations.

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Sublingual nifedipine in acute severe hypertension

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SUMMARY Sublingual nifedipine was used for the treatment of acute severe hypertension in 12 children with renal disease. An average dose of 0.24 mg/kg was safe and proved effective on most occasions within 30 minutes with a median duration of action of three hours. There were no major adverse effects.

The current recommendations for the treatment of hypertensive crises in children advocate the use of intravenous infusions of labetalol or sodium nitroprusside.¹ Administration of these drugs has the disadvantage that they require parenteral administration and nitroprusside has to be protected from light to prevent decomposition. A drug that could be given orally that would act rapidly but would not cause profound hypotension would be an advantage. Nifedipine administered sublingually has been shown to be a safe and effective means of lowering blood pressure in adults.^{2,3} Its advantages are the ease of administration, absence of serious side effects, and the fact that it has been shown to increase cerebral blood flow thus reducing the risk of cerebral ischaemia.²

Over an 18 month period from February 1986 we have collected data on the use of nifedipine on 35 occasions in 12 children with severe hypertension.

Patients and methods

The 12 children with known renal disorders were all studied while inpatients (table 1). Their ages ranged from 6-15 years and weights from 16-60 kg. Eleven of the children were being treated with other antihypertensive drugs. Each child had an acute rise in blood pressure recorded on at least two occasions before treatment and needed urgent treatment. In each case the diastolic blood pressure was equal to or greater than 110 mm Hg. Children with features of hypertensive encephalopathy were not studied. Children below 30 kg body weight were given 5 mg nifedipine and children weighing 30 kg or more 10 mg. The dose range was 0.18 to 0.32 mg/kg with a mean dose of 0.24 mg/kg. The capsule was administered either by being cracked between the teeth and held under the tongue or by initially piercing the capsule with a needle and squeezing the contents out under the tongue. The blood pressure and pulse were measured before treatment, at 15 and 30 minutes, and then hourly for six hours. The blood pressure was measured with the child lying down by either one observer using a sphygmomanometer and an appropriate sized cuff covering at least two thirds of the upper arm, or an automated oscillometric device (Dinamap) when more than one observer monitored the blood pressure.

During the study period all other antihypertensive

drugs were withheld for six hours unless the diastolic blood pressure remained above 110 mm Hg. We used the following criteria to assess whether sublingual nifedipine was effective: a fall in the mean arterial pressure of at least 20 mm Hg or the diastolic pressure falling to below 100 mm Hg. The means and 95% and 99% confidence intervals were calculated for the falls in blood pressure observed and the appropriate *p* value determined using the *t* distribution.

Results

On 35 occasions (12 patients) the effect of sublingual nifedipine was studied over the first 30 minutes after administration. These results are shown in table 2. There was a highly significant fall ($p < 0.01$) in the systolic, diastolic, and mean blood pressures, the largest fall being observed in the diastolic pressure. Using each of our criteria for effectiveness they were fulfilled on 25 of the 35 occasions (71%). Two children (patients 4 and 10) failed to respond on three separate occasions. This was felt to be due to concurrent hypervolaemia. Two other initial non-responders did respond on other occasions. The

magnitude of the pretreatment blood pressure did not influence the size of the response obtained.

On 20 occasions (seven patients) the blood pressure was monitored hourly during a six hour period after the administration of nifedipine. The changes in the mean systolic and diastolic pressures are shown in the figure. On 17 occasions (six patients) the diastolic blood pressure fell below 100 mm Hg, and remained below this value from 30 minutes up to six hours (median duration of three hours). A variable duration of response was seen in those children who received the drug on more than one occasion. In those patients in whom nifedipine proved effective the lowest blood pressure was reached within the first hour. The minimum blood pressure recorded was 120/60 mm Hg and the maximum pulse observed was 140 per minute in a child who had a large fall in mean blood pressure of 50 mm Hg and complained of palpitations. Apart from this one occasion in one child, reflex tachycardia was not seen and there was no difference seen in the mean change in pulse rate whether the children were on β blockers or not.

Although nifedipine was well tolerated, most of the children commented on the unpleasant taste.

Table 1 *Clinical details of patients studied*

Patient No	Age (years)	Nifedipine dose (mg/kg)	Diagnosis	Other drugs taken
1	10	0.20	Chronic renal failure, CAPD*	Captopril, Nifedipine
2	14	0.27	Renal transplant	Metoprolol, nifedipine, enalapril
3	11	0.26	T cell lymphoma, renal insufficiency	Labetalol
4	14	0.20	Chronic renal failure, CAPD*	Hydrallazine, labetalol, enalapril
5	10	0.18	Renal transplant	Labetalol, nifedipine, hydrallazine
6	14	0.31	Renal transplant	Labetalol, nifedipine
7	14	0.29	Renal artery stenosis	Hydrallazine
8	15	0.22	Renal transplant	Metoprolol, prazosin
9	6	0.32	Chronic renal failure, CAPD*	Hydrallazine
10	12	0.22	Haemolytic uraemic syndrome	None
11	14	0.19	Chronic renal failure	Captopril, nifedipine
12	12	0.24	Reflux nephropathy	Labetalol, hydrallazine

*CAPD=continuous ambulatory peritoneal dialysis.

Table 2 *Effect of sublingual nifedipine on blood pressure after 30 minutes*

	Systolic pressure (mm Hg)	Diastolic pressure (mm Hg)	Mean arterial pressure (mm Hg)
Mean (SD) pretreatment blood pressure	164 (13.2)	118 (7.6)	133 (7.1)
Mean (SD) blood pressure 30 minutes after treatment	141 (13.7)	89 (13.5)	106 (12.4)
Mean change in blood pressure (95% confidence intervals)	-22.8 (-27.5 to -18.1)	-29.6 (-35.3 to -23.9)	-26.6 (-32.3 to -20.9)

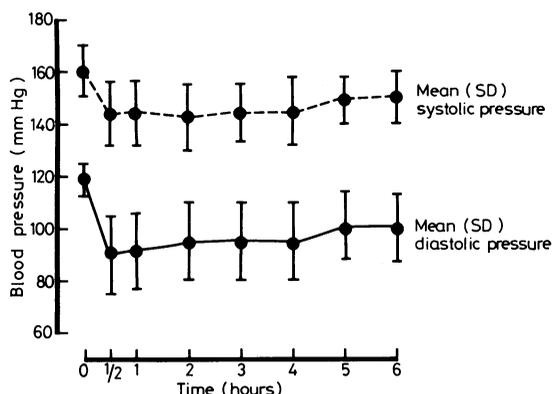


Figure 1 The effect of sublingual nifedipine on blood pressure over a six hour period (20 occasions in seven patients).

The only adverse effects were palpitations (two occasions), facial flushing (two occasions), headache (one occasion), and tiredness (one occasion). One patient vomited immediately after being given the drug and did not take part in the study. No patient complained of dizziness; symptomatic hypotension was not seen.

Discussion

The results of our study show that sublingual nifedipine in a mean dose of 0.24 mg/kg is a safe and effective drug that will rapidly lower blood pressure in children with acute severe hypertension. On 10 occasions (three patients), however, it proved not to be effective as judged by our criteria and the median duration of action was only three hours. Other studies in children have shown it to be effective on each occasion and the duration of action to last for six hours.⁴⁻⁶ These differences could be attributable to the slightly lower dose range in our study of 0.18–0.32 mg/kg as opposed to 0.25–0.5 mg/kg. We encountered no major adverse effects and generally

the drug was well tolerated and preferred to an intravenous drug. We consider the drug to be safe and have instructed selected patients to use it at home or on holiday if they have an episode of severe hypertension. We did not use the drug in children below the age of 5 years but it would be possible to use it on younger children by aspirating the contents of a capsule with a syringe and administering the required dose per kg body weight sublingually. The volume inside the 10 mg and 5 mg capsules is 0.34 ml and 0.17 ml, respectively (Bayer UK Ltd, personal communication). Precautions should be taken to protect the drug from light as it will degrade rapidly. Although we would not recommend it being used in hypertensive encephalopathy, where we favour the use of a drug which can be titrated such as intravenous labetalol, we believe that sublingual nifedipine has a role in the treatment of acute severe hypertension in children.

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