ACUTE TREATMENT OF HYPERTENSIVE CRISIS WITH NIFEDIPINE

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Ten patients with a hypertensive crisis and a decreased renal function were treated with 10 ($n=7$) or 20 ($n=3$) mg nifedipine sublingually. Blood pressure was reduced in 60 min from $211 \pm 4/134 \pm 5$ to $172 \pm 6/107 \pm 6$ mm Hg. The decrease of blood pressure was accompanied by a rise in heart rate from 83 ± 6 to 98 ± 5 beats/min. In all seven patients with an encephalopathy signs of this complication were reduced. No serious side-effects were observed.

Keywords nifedipine hypertensive crisis

Introduction

In comparison with other calcium antagonists nifedipine has potent vascular smooth muscle relaxing effects, especially in coronary arteries. Therefore, its use has particularly been advocated in Prinzmetal's angina (Zsotér, 1980). In recent years it has also been tested in patients with hypertension (Bailey *et al.*, 1982; Yoshimura *et al.*, 1983). Most of the patients investigated until now had a normal renal function. Nifedipine has been used in only a few cases of hypertensive crisis (Murakami *et al.*, 1972; Ueda *et al.*, 1979; Bertel *et al.*, 1983). We report here on our positive experience with the use of nifedipine in 10 patients with a hypertensive crisis and decreased renal function.

Methods

We treated 10 patients with a hypertensive crisis with nifedipine capsules sublingually. Their clinical data and the dose of nifedipine administered are summarized in Table 1. Hypertensive crisis was defined as a diastolic blood pressure of over 130 mm Hg and a retinopathy grade III or IV, or as a diastolic blood pressure above 100 mm Hg with manifestations of hypertensive encephalopathy. Soft gelatin capsules containing a solution of nifedipine in polyethylene-glycol were used. The patients were instructed to bite the capsule and to keep it fixed under the tongue for 10 min. During the study, the patients were in the supine position and their blood pressures were recorded every 2 min with an automatic device (Arter-

iosonde 1217) from 30 min before until 60 min after the administration of nifedipine. With this device diastolic pressure is determined at a level comparable to Korotkoff sound V. Heart rates were calculated from ECG-strips taken immediately before and at 10 min intervals during 1 h after the nifedipine administration.

Blood pressure values given are the means of five consecutive readings before, and of three at the indicated time after the intake of the drug. If the time is not indicated, the data given concern the changes of blood pressure or heart rate at 60 min. Mean arterial pressure was calculated as the sum of the diastolic blood pressure and one third of the pulse pressure. Mean values $\pm$ s.e. mean are given. Statistical analysis was made with Student's *t*-test for paired observations. A *P*-value of 0.05 was considered as the level of statistical significance.

Results

Figure 1 shows the gradual decreases of the blood pressure induced by nifedipine. This decrease was already significant at 10 min and did not change significantly any more from 30 min after administration of the drug. Heart rate rose concomitantly by $11.5 \pm 3.8\%$. The decrease of MAP was $-16.7 \pm 2.5\%$ after 10 mg ($n=7$) and $-25.2 \pm 2.2\%$ after 20 mg of nifedipine ($n=3$). The individual data on the blood pressure before and after nifedipine treatment are given in Table 1. The maximal decrease of MAP was obser-

Table 1 Clinical data of 10 patients with a hypertensive crisis treated with nifedipine sublingually

Patient	Dose of nifedipine (mg)	Age (years)	Sex	Retino pathy ¹ (grade)	Encephalo-pathy	LVH ²	Origin of hypertension ³	ECC ⁴ (ml/min)	Concomitant therapy	BP ⁵ (mm Hg) A	BP ⁵ (mm Hg) B
1	10	19	F	IV	-	+	N	2	-	201/134	178/117
2	10	30	F	III	+	+	N	61	frusemide	218/148	176/130
3	10	27	M	IV	+	-	N	20	triamterene	196/111	175/84
4	10	53	F	III	+	+	S	96	-	225/114	185/100
5	10	48	M	III	-	+	N	25	α -methyldopa	230/149	210/127
6	10	26	M	III	+	+	N	12	chlorthalidone	227/133	147/99
7	10	38	F	III	+	+	E	52	propranolol	209/152	166/130
8	20	49	F	III	-	-	E	65	diazoxide	212/130	150/91
9	20	18	F	0	+	-	T	27	metoprolol	189/117	148/85
10	20	33	M	I	+	-	N	21	frusemide	199/146	180/110

¹) According to the criteria of Keith *et al.* (1939) ²) Left ventricular hypertrophy according to the criteria of Romhilt & Estes (1968) ³) N = nephrogenic, S = scleroderma, E = essential and T = renal transplant rejection ⁴) Endogenous creatinine clearance ⁵) Blood pressure before (B) and 60 min after (A) administration of nifedipine.

ved in patient 6, being -30.0% at 50 min after the intake of nifedipine. One h after the administration of nifedipine the signs of encephalopathy had clearly diminished in patients 2, 3, 4, and 7, and had completely disappeared in patients 6, 9, and 10. In patients 4 and 8 treatment was continued successfully with nifedipine 10 mg six times daily after addition of chlorthalidone 50 mg daily and metoprolol 100 mg three times daily, however without achieving completely normal blood pressures. In the eight remaining patients treatment was successfully continued with captopril or with a combination of diazoxide, a β -adrenoceptor-blocker and a diuretic agent. No serious side-effects of nifedipine were observed in the hour after its administration. Two patients complained of flushing and one of palpitations. In none of the patients was an increase of the P-R interval observed.

Discussion

In the 10 patients with a hypertensive crisis described here, nifedipine administered sublingually lowered blood pressure effectively, also in those patients with a low endogenous creatinine clearance. In all seven patients with an encephalopathy, nifedipine reduced or completely suppressed the symptoms of this condition. Although we did not observe exaggerated falls

Figure 1 Effect of nifedipine administered sublingually at $t = 0$ min, on blood pressure and heart rate in 10 patients with a hypertensive crisis.

in blood pressure in our patients, the risk of cerebral and myocardial ischaemia cannot be excluded. An extra advantage of a calcium antagonist in comparison with other vasodilators might be, that it selectively increases cerebral and cardiac blood flow as has been shown in animal experiments (Aboul-Khair *et al.*, 1981). Recently, Bertel *et al.* (1983) demonstrated in five patients with severe hypertension, that cerebral blood flow remained constant or increased after emergency treatment with nifedipine.

The observed increases in heart rate and the absence of an increase of the P-R interval were somewhat unexpected, since nifedipine has a direct negative chronotropic effect. However, this effect is probably outweighed by a reflex adrenergic stimulation (Low *et al.*, 1982) and perhaps also by withdrawal

of parasympathetic tone (Millard *et al.*, 1982), which occur as a consequence of vasodilation. Not only the rise in heart rate, but also the occurrence of flushing and palpitations fits with the concept that nifedipine exerts its antihypertensive effect by direct vasodilation.

In conclusion, nifedipine can be a useful drug in the treatment of hypertensive crisis, which deserves a more extensive evaluation in this condition. It seems even suited to be used as a first drug in the treatment of this condition, since it is so easy to administer, it has a rapid onset of action and it did not induce exaggerated falls in blood pressure.

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