Original papers

Eur J Pediatr (1993) 152:712–714

European Journal of
Pediatrics

Intravenous nicardipine in hypertensive children

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Received: 8 December 1992 / Accepted: 26 January 1992

Abstract. Fourteen hypertensive patients hospitalized in a paediatric intensive care unit were studied to evaluate safety and hypotensive efficacy of intravenous nicardipine. Systolic and diastolic blood pressure significantly decreased 1 h after the beginning of the treatment (1 μg/kg per minute). Mean decrease in systolic blood pressure during the first 24 h was between 9.9% and 13.4% of the initial value. Mean lowering of diastolic blood pressure was between 16.7% and 25.6%. Nicardipine did not significantly affect heart rate with dose of 1 μg/kg per minute. No clinical side-effects were observed. Nicardipine could be a first line drug for the treatment of hypertension in paediatric intensive care units.

Key words: Nicardipine – Children – Hypertension

Introduction

Nicardipine hydrochloride is a dihydropyridine calcium channel antagonist. Its properties, water solubility, short half-life, rapidity of therapeutic response and dose dependent reduction of blood pressure, have made it a first line drug for management of hypertensive episodes in adult patients with vital distress [8, 10, 15, 16]. To our knowledge, no data are available about utilisation of intravenous nicardipine in children. Our purpose was to assess the anti-hypertensive efficacy and safety of this treatment in a paediatric population hospitalized in an intensive care unit.

Patients and methods

Fourteen intensive care patients were included in the study. For all the patients, systolic or diastolic blood pressures were 10 mmHg above the 95th percentile for age and sex [12] on at least three separate examinations over 1 h. Mean age of the patients was 2.1 years (range 9 days to 10.9 years). There were 5 girls and 9 boys.

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Hypertension occurred after hepatic transplantation ($n = 3$), hepatic and renal transplantation ($n = 2$), small intestine transplantation ($n = 1$), surgical resection of coarctation of the aorta ($n = 5$), esocoloplasty ($n = 1$), aortic thrombosis ($n = 1$) and hypertension after extracorporeal lung support ($n = 1$). Pressures and cardiac frequency were measured oscillometrically by an automated blood pressure recording system (Dinamap Critikon). Blood pressures were registered at the onset of therapy and after 1, 2, 3, 4, 5, 6, 12 and 24 h. Initial infusion rate of nicardipine was 1 μg/kg per minute and was increased to 2 μg/kg per minute or 3 μg/kg per minute until therapeutic response. In one case, intravenous hydralazine was administered at the time of initiation of nicardipine therapy. Creatinine, sodium and potassium concentrations were measured before the onset of the infusion and after 24 h.

Results

At the beginning of the treatment, mean systolic blood pressure was 23.3 (± 13) mm Hg above the 95th percentile and mean diastolic blood pressure was 11 (± 7) mm Hg above the 95th percentile.

The course of blood pressure, with a dose of 1 μg/kg per minute is shown in Fig. 1 and 2. One hour after the beginning of the treatment, systolic and diastolic blood

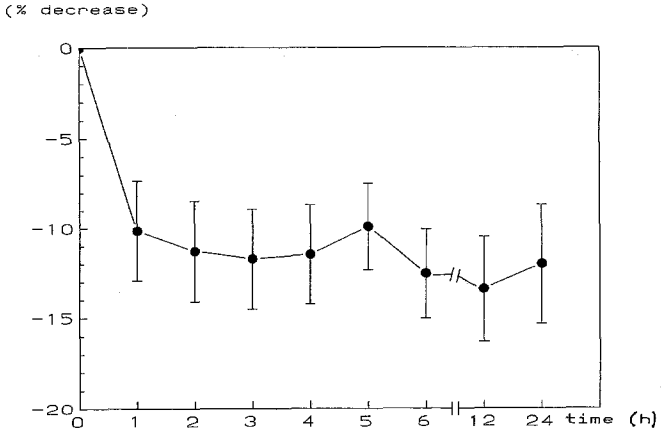

Fig. 1. Changes of systolic blood pressure over time in hypertensive children with intravenous nicardipine 1 μg/kg per minute (mean ± SEM)

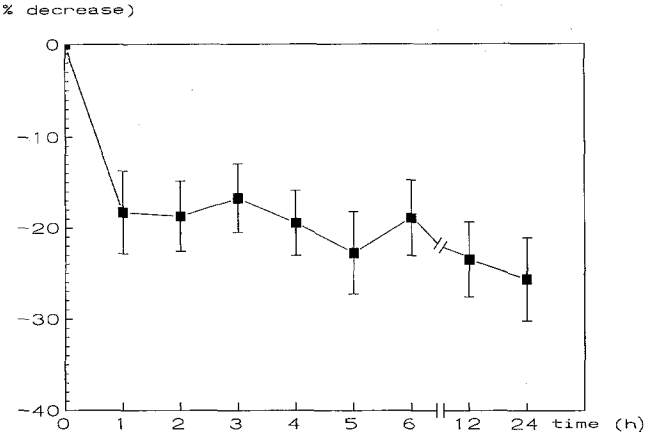

Fig. 2. Changes of diastolic blood pressure over time in hypertensive children with intravenous nicardipine 1 µg/kg per minute (mean ± SEM)

pressures were already significantly decreased ($P < 0.01$). Mean lowering of systolic blood pressure during the first 24 h was between 9.9% and 13.4% of the initial value (Fig. 1). Mean lowering of diastolic blood pressure was between 16.7% and 25.6% (Fig. 2).

In four cases, doses had to be increased from 1 to 2 µg/kg per minute and in 2 cases from 2 to 3 µg/kg per minute. Not enough patients received these doses to consider evolution of their blood pressures.

No clinical side-effects were observed. Mean cardiac frequencies did not vary significantly ($P > 0.05$). Sodium, potassium and creatinine concentrations after 24 h were not significantly different from the base-line levels.

Discussion

To our knowledge, this study is the first about the use of intravenous nicardipine in hypertensive children. Our results confirm studies in adults which have shown safety and efficacy of intravenous nicardipine [1]. Therapeutic response was excellent: with a constant infusion rate of 1 µg/kg per minute on effect was observed within 1 h. In a preliminary study we observed that a loading dose was useless and potentially dangerous in children. Consequently, in contrast to most studies in adult, we do not use a loading dose. None of the side-effects described with calcium channel blockers in adults (oedema, phlebitis, tachycardia) was observed. It was not possible to detect headache because our patients were very young.

Mechanism of action of calcium antagonists is to lower blood pressure by reduction of vascular resistance. They inhibit calcium entry into vascular smooth muscles, lowering systemic vascular resistance and blood pressure. They increase cardiac output, cerebral and renal flow [1, 2, 15]. Nicardipine has less negative inotropic effects and produces less tachycardia then the other calcium channel antagonists [13]. It reduces cardiac oxygen consuption [5] and has a myocardial protective effect [11]. These properties are especially important for management of hypertensive episodes in patients. Many other antihypertensive agents are used in intensive care units. All these agents have potential side-effects: cyanide toxicity with nitroprusside, increase of myocardial oxygen consumption with hydralazine and diazoxide, heart block and heart failure with labetotol and other β-adrenergic blocking agents. Angiotensin-converting-enzyme inhibitors might be ineffective in patients with non-renin-dependant hypertension. Diuretic agents are dangerous in patients with volume depletion, as a consequence of hypertensive crisis [4, 7].

Nicardipine metabolism is mainly hepatic. Therefore, doses have to be adjusted in case of liver disease but not in patients with renal insufficiency [9]. An interaction between cyclosporin A and calcium channel antagonist has been described [3]. The same cytochrome P450 (P450 IIIA) is probably involved in the metabolism of cyclosporin A and calcium channel antagonist [6]. Thus, calcium channel antagonists, especially nicardipine, increase blood cyclosporine levels by their inhibitory effect on the hepatic metabolism of cyclosporine [14]. Consequently, blood levels have to be carefully monitored and doses of cyclosporin A adjusted in case of co-administration of these drugs.

Because of its pharmacodynamic and haemodynamic properties nicardipine appears to be a first line drug for treatment of hypertension in paediatric intensive care units. We propose a very simple regimen for intravenous nicardipine treatment in children: an initial infusion rate of 1 µg/kg per minute which could be increased to 2 or 3 µg/kg per minute according to the course of blood pressure.

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