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SODIUM NITROPRUSSIDE FOR HYPERTENSIVE EMERGENCIES IN CHILDREN*

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Sodium nitroprusside (NaNP) is an effective drug for the emergency treatment of severe hypertension. Although NaNP is widely used as a hypotensive agent in adults[1,2], it has not been used much in the treatment of children[3-7]. Therefore, we have evaluated NaNP as a therapeutic agent in 13 episodes of hypertensive crisis in 9 children.

Material and Methods

Nine children, aged 6 to 14 years, 5 of them boys, were admitted to the Hacettepe University Institute of Child Health between September 1, 1983 and June 1, 1984 with intractable arterial hypertension. Diastolic pressure was above 120 mmHg in all patients and most of them presented with hypertensive encephalopathy characterized by headache, vomiting, drowsiness and convulsions. Cardiac failure was not observed.

On examination two of these patients were found to have acute poststreptococcal glomerulonephritis, in one there was renovascular hypertension, in four chronic renal failure, in one a hypoplastic kidney, and in another Takayasu arteritis.

NaNP was freshly prepared for intravenous administration by dissolving 500 mg in 100 ml of 5% dextrose solution (5000 µg/ml). From this solution, sufficient NaNP to provide 2 µg/kg/min for 4 hours was added to 120 ml 5% dextrose and infused at a uniform concentration of 2 µg/kg/min = 10 drops over 4 hours at a constant rate.

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All bottles and infusion sets were covered with carbon paper. Blood pressure was determined by auscultation using a standard mercury manometer with cuffs appropriate to the child's size. These measurements were obtained one hour before administration, just before infusion, at 5,10,15, and 30 minutes after infusion was begun, and at the end of the administration. Heart and respiration rates were recorded at the same time. All patients received the infusion in the supine position. Prior to NaNP infusion, all patients were on different antihypertensive regimens. Reserpine, hydralazine, methyldopa, propranolol, prazosin and furosemide were among the oral drugs used. During infusion, oral antihypertnesive regimens were rearranged.

Results

The rate of infusion (2 µg/kg/min) was constant in all but two patients. These two patients needed a dose of 3 µg/kg/min to control the blood pressure.

The mean blood pressure was 191.5 ± 29.4/140.2 ± 22.8 mmHg just before infusion. It decreased to 163 ± 19.3/117.3 ± 16.9 after 5 minutes ($p<0.01$); to 140.4 ± 12.8/100.5 ± 12.6 after 10 minutes ($p<0.001$); to 138.4 ± 10.7/ 90 ± 13.5 after 15 minutes ($p<0.001$); and to 130.4 ± 8.3/90 ± 8 mmHg after 30 minutes ($p<0.001$). No hypotension occurred at the end of the administration (Figures 1,2).

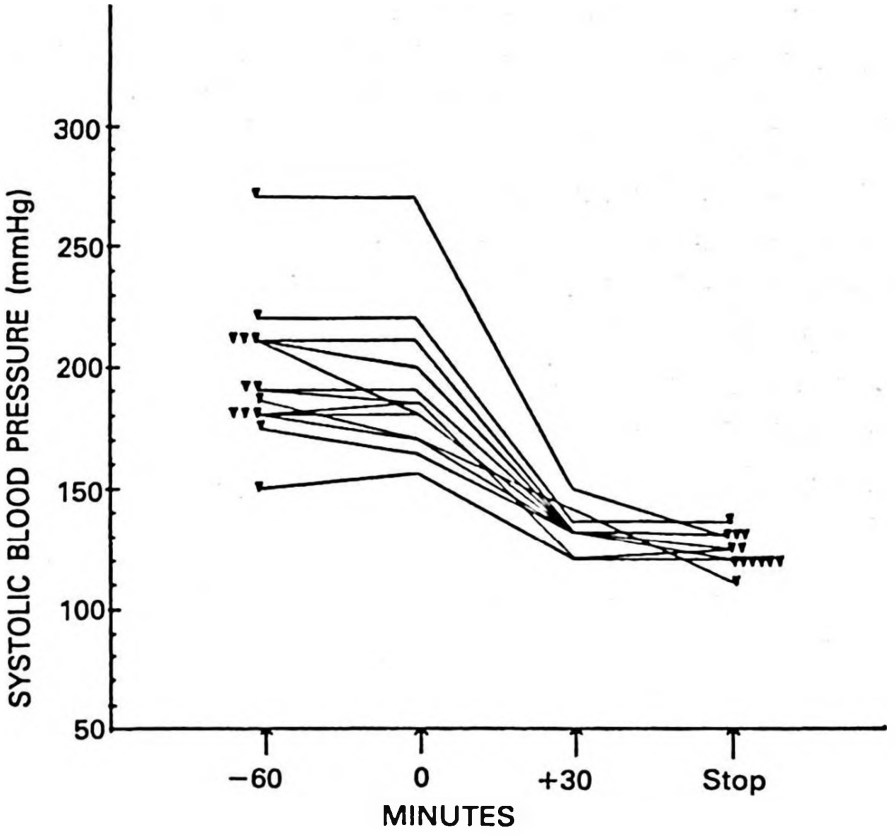

Figure 1

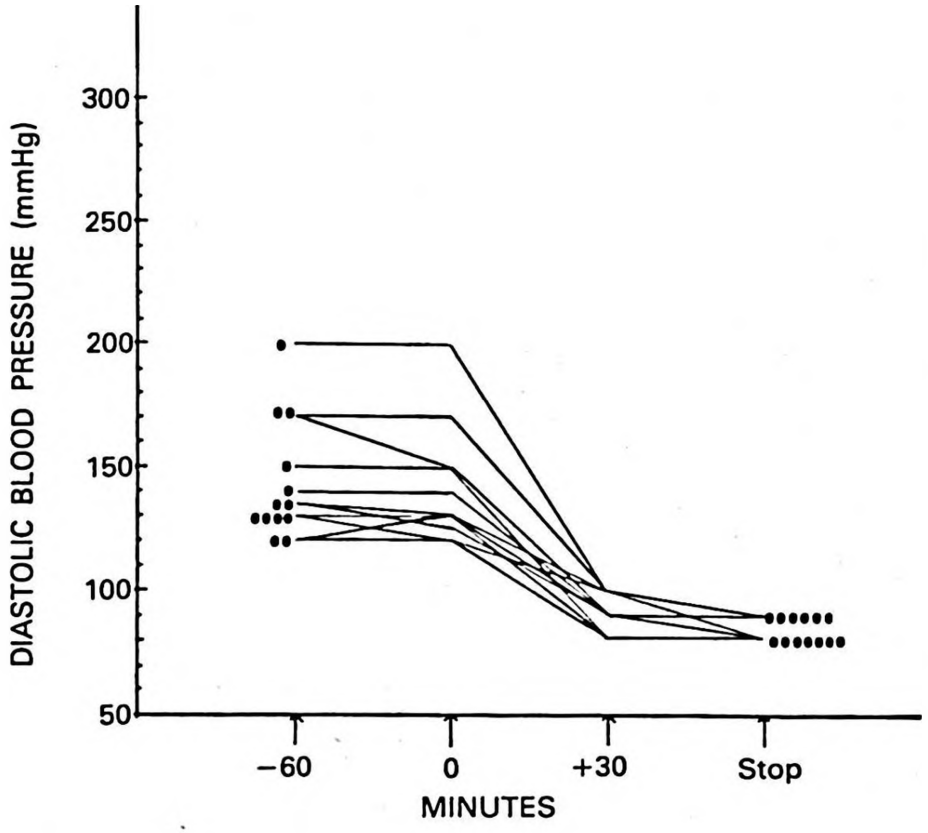

Figure 2

The heart rate decreased from 101 ± 9 to 85 ± 13 beats/min ($p<0.02$), and the respiration rate decreased from 24 ± 3 to 22 ± 2/min ($p>0.05$) during the infusion.

In all patients desired levels of blood pressure were obtained within five minutes of starting the infusion. The duration of NaNP infusion ranged from 12 to 48 hours with a mean of 22.6 hours.

Clinical symptoms subsided in all patients within 6-12 hours of infusion, thus permitting oral feeding. No unwanted effects were observed.

Discussion

NaNP was first used as a hypotensive agent in 1929 by Johnson[8]. Its effect is on the smooth muscle of the blood vessels. When infused, NaNP causes a very rapid fall in arterial and venous pressures[9]. Although the antihypertensive effect of nitroprusside is well described in adults, the experience in children has been limited and most reports are of sporadic cases[4-7].

The infusion rate of NaNP that we used in our clinical study was similiar to that used by others[3-5,7]. Both systolic and diastolic pressures were significantly decreased in all patients at the fifth minute of infusion ($p<0.01$). When we remember that all patients were on oral antihypertensive therapy before infusion,

the usefulness of NaNP becomes more obvious. However, it should be borne in mind that patients receiving oral antihypertensive drug therapy are more sensitive to the nitroprusside, as previously noted[9].

There is no reported condition in which the blood pressure cannot be reduced by NaNP. However, it is emphasized that if patients require progressively increasing doses, it is likely that the sodium nitroprusside-induced hypotension has led to an increased renin-angiotensin release, with consequent vasoconstriction, which opposes the hypotensive action of nitroprusside[10].

In order to obtain a constant and continuous response, the infusion rate of the solution should be regulated by continuous monitoring and by the use of an infusion pump[11,12]. Since the fall in arterial pressure is dose dependent[9], the blood pressure begins to rise immediately after cessation of infusion. In the absence of concurrently administered oral antihypertensives, blood pressure reaches the pretreatment level in 1 to 10 minutes[3,4,6] afer the infusion ends. Despite adjustments in the oral antihypertensive regimen of our patients, the hypotensive effect of NaNP was lost rapidly when the infusion stopped. Nonetheless, blood pressures never reached the pretreatment levels.

It is stated in a current pharmacological textbook[9] that it has not yet been established that NaNP can safely be used in children. However, since malignant hypertension may cause complications in children[13-16], similiar to those in adults[17,18], it should be treated immediately. Therefore, nitroprusside was used in our patients with malignant hypertension who did not respond to other antihypertensive drugs. Its use demonstrated that NaNP is effective in the treatment of children with hypertensive encephalopathy. Signs disappeared quickly when the blood pressure was controlled.

Nitroprusside can be quite a toxic agent in man when used for prolonged infusion in high doses[5,19,20]. Thus NaNP may result in death if the signs are not promptly recognised and immediately treated[13]. Toxicity is related to the accumulation of thiocyanate which is one of NaNP's end products. In general, when plasma thiocyanate reaches a potentially toxic level (5 to 10 mg/dl)[2], or the patient presents toxic manifestations such as fatique, nausea, vomiting, psychotic behavior, muscle spasms, hepatic necrosis, skin rashes, tinnitus, and hypothyroidism[1,2,8,9,21-23], nitroprusside therapy should be discontinued. It has been reported that treatment with dosages of less than 10 µg/kg/min for 3 days does not carry a high risk of complications in children[4,5,15,27]. During NaNP treatment in this series, we did not observe any side effects of this agent. Although NaNP therapy may cause tachycardia, the heart rate in our patients decreased from 101 ± 9 to 85 ± 13 beats/min ($p<0.02$). We could not find any reasonable explanation for this effect. If nitroprusside is used over a long-term, the patients should be monitored for measurements of serum thiocyanate or cyanide concentrations[2,4,5,19,24]. Thiocyanate levels were not measured in our

patients, however, no side effects or resistance to treatment have been observed in patients receiving NaNP therapy for a longer period of time than ours[4,5,24,25]. It is however advisable to measure thiocyanate levels particularly in patients receiving therapy for longer than 72 hours. If metabolic acidosis and severe hypotension occur, the infusion should be stopped. In this situation sodium bicarbonate[26], intravenous hydroxocobalamin (0.1 mg/kg)[27], an infusion of sodium nitrite (5 mg/kg/over 4 minutes)[28,29], or inhalation of amylnitrite[28,29] might be used. It has also been reported that rapid removal of thiocyanate can be achieved by hemodialysis[5].

Although other antihypertensive drugs are usually safe and effective in emergency situations[7-10,38], this is not always the case[33]. There is no reported case of a patient whose hypertension has not responded to NaNP. It can be safely used in children in a hypertensive crisis until the effect of other oral antihypertensive drugs can be felt.

Summary

Sodium nitroprusside (NaNP) in a dose of 2 µg/kg/min was used for the treatment of 13 episodes of hypertensive crisis in 9 children. Continuous intravenous infusion of NaNP significantly reduced the systolic and diastolic blood pressures in all patients from 191.5 ± 29.4/140.2 ± 22.8 mmHg initially to 163 ± 19.3/117.3 ± 16.9 after 5 minutes ($p<0.01$); to 140.4 ± 12.8/100.5 ± 12.6 after 10 minutes ($p<0.001$); to 138.4 ± 10.7/90 ± 13.5 after 15 minutes ($p<0.001$); and to 130.4 ± 8.3/90 ± 8 mmHg after 30 minutes ($p<0.001$).

The heart rate decreased from 101 ± 9 to 85 ± 12 beats/minute during the NaNP treatment ($p<0.02$). The respiration rate decreased from 24 ± 3 to 22 ± 2/minute ($p>0.05$). The mean duration of infusion was 22.6 hours. After cessation, the blood pressure increased immediately in all cases, but it remained lower than what it had been before infusion was started. This was attributable to the fact that oral antihypertensive drugs were rearranged at the time of infusion. No unwanted effects were observed. Thus, sodium nitroprusside has been found to be effective and safe in the management of hypertensive emergencies in childhood while awaiting the antihypertensive effects of oral medications to take over.

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