Effect of nicardipine on somatosensory evoked potentials in patients with acute cerebral infarction

Liping Yao, Deyun Ding

Abstract

We evaluated the effect of nicardipine, a calcium channel blocker, on somatosensory evoked potentials (SEP) in 26 patients with acute cerebral infarction. Post treatment, 58% (15/26) of the N20 and P25 latencies were prolonged in the affected hemispheres; 8% (2/26) were shortened; and 35% (9/26) did not change. The mean N20 and P25 latencies were significantly prolonged two hours post treatment in the affected hemisphere (N20, $P < 0.01$, P25 $P < 0.01$). Nicardipine (Ni) had no effect on SEP components in the intact hemispheres. Seventy five per cent of the 12 patients with hypertension had a decrease in blood pressure (BP) after taking nicardipine, but there were no undesirable side effects or worsening of neurological signs. Our study demonstrates that nicardipine prolongs the latencies of short-latency components of SEP in the affected hemisphere after acute ischaemic stroke and also decreases BP. These observations suggest that nicardipine therapy might impair neuronal function in the ischaemic zone.

Most studies evaluating the protective effect of Ca^{++} -antagonists on acute ischaemic stroke have been carried out on animal models. Only a few clinical studies have been reported and these results have been variable.¹ We evaluated the effect of nicardipine, a dihydropyridine calcium antagonist, on electrocerebrophysiological function in patients with acute cerebral infarction by means of somatosensory evoked potentials (SEP). The technique has been used in animal and human studies as a possible index of neuronal function after acute ischaemic stroke.^{2,3}

Materials and methods

Twenty six patients were included in the study. All patients had suffered their first acute cerebral infarction. There were 18 males and eight females, aged 50-78 years (mean: 64). All patients had CT scans within 10 days post-stroke. The maximal diameter of lesions on CT (8 mm slices) were as follows: 1 cm: 22

patients, 2-5 cm: two patients, normal CT: two patients. Internal capsule: 10 patients, parietal lobe: nine patients, frontal lobe: two patients, basal ganglia: two patients, thalamus: one patient. No patient was shown to have more than one infarct. All patients were conscious and had clinical manifestations of hemispheric involvement.

Needle electrodes were placed in Fpz, C3' and C4' (2 cm behind standard EEG C3 and C4), and the stimulating electrode was fixed to the skin over the median nerve at the wrist (electrode impedance 5 K). Stimuli were 0.2 ms square wave electrical pulses delivered with a frequency of 5 Hz and an intensity just above the thumb twitch threshold (current intensity 5-15 mA). The peak latencies of N20 and P25 components in the intact and affected hemispheres were recorded. At least three series of 256 responses were averaged for each side. The range of variability within individuals was less than 0.4 ms.

All patients had SEP examinations and 12 patients had blood pressure (BP) measured (cuff method) before and two hours after they had one 40 mg oral dose of nicardipine. Measurements were carried out between 24 hours and seven days post-stroke (table 1). No other vasoactive drugs were given at the time of SEP and BP recordings. The N20 and P25 latencies and BP before and after treatment were analysed by paired Student's *t* test.

Results

1 Effect of nicardipine on SEP (table 2)

Fifty eight per cent (15/26) of the N20 and P25 latencies were prolonged in the affected hemispheres, 8% (2/26) were shortened, and 35% (9/26) did not change post-treatment. The mean N20 and P25 latencies post-treatment were statistically significantly longer than pre-treatment in the affected hemispheres (N20 $P < 0.01$, P25 $P < 0.01$). There was no effect of nicardipine on SEP latencies in the intact hemispheres.

2 Effect of nicardipine on BP (table 3)

Two hours after receiving nicardipine, 75% of the 12 patients with hypertension had a decrease in BP. A statistically significant decrease in both systolic and diastolic pressures were observed.

Table 1 Post-stroke interval for SEP recordings

Day	24 hrs-2nd	2nd-3rd	3rd-4th	4th-5th	5th-6th	6th-7th
Number of patients	5	8	3	2	2	6

Department of Neurology, Second Affiliated Hospital of Zhejiang Medical University, Hangzhou, Zhejiang, People's Republic of China
L Yao
D Ding

Correspondence to: Dr L Yao, University of Pittsburgh Medical School, Anesthesia and CCM Research Laboratories, 1081 Scaife Hall, Pittsburgh, PA 15261, United States.

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Table 2 N20 and P25 latencies (ms) in affected and intact hemispheres before and after nicardipine

	SEP	N	Mean (SD)		P
			Before nicardipine	2 hours after nicardipine	
Affected hemisphere	N20	26	20.13 (1.45)	21.80 (2.08)	<0.01
	P25	26	26.31 (1.99)	28.00 (1.99)	<0.01
Intact hemisphere	N20	26	19.78 (1.26)	19.88 (1.33)	>0.05
	P25	26	26.68 (1.87)	26.29 (1.84)	>0.05

3 Effect of nicardipine on clinical manifestations

No undesirable side effects occurred and no patient had neurological deterioration after receiving nicardipine.

Discussion

The short-latency components of the SEP are closely related to neuronal metabolism and cerebral blood flow. Neuronal damage may result in abnormalities of the SEP such as prolonged latency, lowered amplitude, and even complete absence of the components.⁴ N20 and P25 waves are short-latency components of the SEP reflecting impulses transmitted to the thalamus and reaching the cortex through the primary sensory system. The N20 component may originate from thalamus, thalamocortical projections, or the primary sensory cortex.^{5,6} Absence or asymmetry of short-latency components of the SEP have been reported in 50%–75% of lacunar infarcts^{7,8} and such abnormalities have been particularly notable in thalamic infarcts or pure sensory stroke.³

Nicardipine is a potent second generation dihydropyridine calcium channel blocker. Plasma concentration of the drug is highest 20 minutes after administration, and BP is maximally decreased after two hours.^{9,10} This hypotensive effect has limited the amount of nicardipine which can be given in animal and human stroke studies.^{2,11} Grotta *et al*² evaluated the effect of nicardipine on the SEP in rats after four-vessel occlusion. The amplitude but not latency of short-latency components of the SEP were improved in treated animals, and CBF increased during reperfusion.

In animal studies, if Ca++-antagonists were given pre-ischaemia or immediately post-ischaemia, outcome measures such as histology, cerebrospinal fluid (CSF), electrophysiological function, learning ability, brain oedema, and mortality were often improved. However, when given post-ischaemia, the protective effect of Ca++-antagonists was absent and even negative results were observed.^{2,12–30} Although Vorstrup *et al* found that nimodipine actually decreased cerebral blood flow (CBF) in the area of infarction in patients with acute ischaemic stroke,³¹

Gelmers *et al*³² reported that recovery of patients receiving oral nimodipine started up to 24 hours after acute ischaemic stroke was better than in control patients.

Our results suggest that nicardipine possibly aggravated neuronal dysfunction in the affected hemisphere of patients when given one to seven days after ischaemic stroke. This result may have several explanations: 1) intracerebral “steal” of blood from ischaemic brain regions to areas of normal vascular reactivity where nicardipine causes vasodilation; 2) reduced CBF due to reduced BP and cerebral perfusion pressure; and 3) nicardipine therapy may have been given too late after stroke to reverse a transient ischaemic penumbra, or effectively limit calcium influx and its intracellular translocation.

In conclusion, our studies suggest that: 1) nicardipine prolongs the latency of SEP short-latency components in ischaemic hemispheres when given one to seven days after acute ischaemic stroke, and also decreases BP; and 2) SEP measures might be useful as a convenient means to evaluate the effect of therapy on electrophysiological function and to provide a quantitative outcome measurement for clinical studies.

According to the results in the literature, we consider that it is possible that patients with acute infarction might benefit from treatment with a calcium antagonist if treatment could be given before onset of the symptoms or within 24 hours after incident. The therapeutic use of calcium antagonist in acute ischaemic stroke needs more extensive experimental studies in various stroke models and clinical documentation in large-scale double-blind studies.

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Table 3 The effect of nicardipine on blood pressure (mm Hg)

N	Mean (SD)		P
	Before nicardipine	2 hours after nicardipine	
12	168/98 (14/10)	148/88 (22/12)	<0.01

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