CLINICAL IMPORTANCE OF NON-INVASIVE INTRACRANIAL PRESSURE MONITORING IN EARLY PREDICTION OF HEMATOMA ENLARGEMENT FOLLOWING HYPERTENSIVE INTRACEREBRAL HAEMORRHAGE

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[Monitoraggio non invasivo per l'allargamento dell'ematoma]

ABSTRACT

Objectives*: To evaluate the clinical importance of the non-invasive intracranial pressure monitoring in early prediction of hematoma enlargement in patients with hypertensive intracerebral haemorrhage.*

Methods*: Dynamical monitoring was prospectively performed in 158 patients with non-invasive intracranial pressure. Cranial CT was employed to determine whether the hematoma was enlarged (HE group) or stable (HS group). The non-invasive intracranial pressure, cerebral perfusion pressure, the difference of non-invasive intracranial pressure between two hemispheres and the score in Glasgow Outcome Scale were compared between two groups.*

Results*: Hematoma enlargement was found in 59 patients (37.34%) of whom 91.52% developed hematoma enlargement within 12 h. The non-invasive intracranial pressure and difference in the HE group were significantly higher than those in the HS group. In the cerebral perfusion pressure in HE group and the non-invasive intracranial pressure, cerebral perfusion pressure and difference in the HS group were similar to those on admission (P>0.05). There was no significant difference in the number of patients with difference of ≥1.3 mmHg on admission. However, subsequently the number of patients with difference of ≥1.3 mmHg was 51 (86.44%) in the HE group and 44 in the HS group.*

Conclusion*: On the basis of non-invasion and ability to continuously monitor intracerebral haemorrhage, detection of non-invasive intracranial pressure can be used to predict the hematoma enlargement after non-invasive intracranial pressure.*

Key words**:** *hypertensive intracerebral haemorrhage, non-invasive intracranial pressure, cerebral perfusion pressure, hematoma enlargement; early prediction.*

Received *March 05, 2013;* ***Accepted*** *April 25, 2013*

Introduction

Hypertensive intracerebral haemorrhage (HICH) has high disability and high mortality[1,2], and has been a major disease threatening the health of the middle-aged and the elderly. In addition, it has been demonstrated that hematoma enlargement (HE) following cerebral haemorrhage is an important independent factor increasing the mortality and disability[3,4]. Thus, to early detect and treat the HE is crucial for the improvement of HICH prognosis. Monitoring of noninvasive intracranial pressure (NICP) based on the detection of flash visual evoked potentials (FVEP) had been used in the continuous detection of ICP in 158 HICH patients who received conservative treatment in our department from October 2009 to February 2012. At the same time, HE was observed in some of them, and timely treatment was performed achieving favourable outcome. Herein, the role of monitoring of NICP in predicting the HE following HICH was evaluated in these patients.

Subjects and Methods

Inclusion criteria

1) The ICH was diagnosed according to the Criteria for Diagnosis of ICH in Adults (USA)[5], patients had a history of hypertension or the blood pressure increased on the disease onset; 2) Cranial CT showed supratentorial hematoma, the hematoma volume was estimated to be ≤30 ml with coniglobus formula, the midline slightly shifted (<1 cm), and the intraventricular blood was absent or very small; 3) On admission, the vital signs were stable, patients

had no prior eye diseases or other diseases affecting the visual conduction; 4) Patients received conservative therapy after the informed consent was obtained.

General information

A total of 158 patients were recruited; of these 87 were males and 71 females with a mean age of 53.89±7.61 years (range: 42-83 years). The mean time from disease onset to admission was 3.08±1.82 h (range: 1-6 h). The first symptom was headache in 73 patients of whom 8 developed concomitant vomiting, unilateral limb dysfunction in other 8, and slurred speech/aphasia in the last 51. The score in Glasgow Coma Scale (GCS)[6] was 13-15 in 102 patients, 9-12 in 52 and 3-8 in 4, and the mean score in GCS was 11.07±3.12. The cranial CT or MRI revealed haemorrhage in the putamen in 55 patients, lenticular nucleus in 58, subcortex in 29, and thalamus in 16. In addition, 3 patients also developed mild intraventricular hemorrhage. The mean hematoma volume was 21.10±5.07 ml (range: 8-30 ml).

Monitoring of NICP

The MICP-1A FVEP-NICP monitor (Mingxi Medical Device Company, China) was used to monitor the NICP according to the manufacturer's instructions (the difference in NICP detected by our monitor and invasive ICP monitor [Camino, USA] was less than 10%). After admission, NICP was detected once every 1 h. The latencies following binocular flash stimulation were summed, and the average was obtained as the latency. On the basis of principle of superposition of flash visual evoked potential (FVEP), the FVEPs were superposed to calculate the ICP of both sides. Then, the mean NICP and D ($D=ICP_{affected\ side} - ICP_{unaffected\ side}$) were calculated. At the same time, the multifunctional ECG monitor was used to detect the blood pressure followed by calculation of mean arterial pressure. The cerebral perfusion pressure (CPP) was also calculated. Monitoring was done for 1-5 days (mean: 2.81±1.59) until the NICP and CPP were stable for 48 h or surgery was performed.

Treatment

Step therapy of intracranial pressure was performed as previously described 7: the head of the bed was elevated 30 degrees, smooth respiratory tract was maintained, the blood pressure was controlled ≤160mmHg, the environment was kept quiet, pressure-lowering drugs and sedatives were used if necessary, the body temperature was maintained at <38°C, and the daily liquid volume was controlled at 1500-2000 ml. Within 72 h after admission, the clinical symptoms, state of consciousness (GCS), pupil, limb activity and vital signs were observed once every 30 min, and the NICP was detected once every 1 h. Cranial CT was performed once the NICP was significantly increased or the disease aggravated, and treatment was promptly done. For all patients, at 24 h after admission, routine cranial CT was performed.

Determination of HE

The hematoma volume on re-examination was compared with that on admission. The hematoma volume increase of >33% or 12.5 ml was defined as HE. In the present study, 158 patients were divided into 2 groups: HE group (patients with HE) and HS group (patients with stable hematoma). The NICP, CPP and D were recorded in both groups, and the outcome was determined with the Glasgow Outcome Scale (GOS).

Statistical analysis

Statistical analysis was done with SPSS version 16.0, and quantitative data were expressed as mean ± standard deviation (SD) (±s). Comparisons between two independent samples were done with t test and those between two groups or intragroup were performed with repeated measures analysis of variance. The score in GOS was compared with Mann-Whitney test and chi square test / Fisher's exact test. A value of $P<0.05$ was considered statistically significant.

Results

HE incidence

On the basis of criteria for HE, HE was diagnosed in 59 patients (37.34%) who were then included in the HE group. The remaining 99 patients were included in the HS group. HE occurred within 6 h after disease onset in 37 patients (62.71%), 6-12 h in 17 (28.81%), 12-24 h in 4 (6.78%) and at 24 h after disease in 1 (1.69%). At 48 h after disease onset, HE was not observed. In the HE group, the hematoma volume was 44.49±6.03 ml, which was markedly larger than that on admission (20.68±5.18 ml; $t=22.417$, $P=0.000$). In the HS group, the hematoma volume on re-examination was 22.78±5.52 ml, which was comparable to that on admission (21.35±5.02 ml; $t=1.901$, $P=0.059$). Moreover, the hematoma volume was comparable between two groups on admission ($t=0.809$, $P=0.420$).

NICP monitoring results

The NICP, CPP and D are shown in Table 1. On admission, there were no significant differences in the NICP, CPP and D between two groups (P=0.464). In the HE group, the NICP and D were significantly increased when compared with those on admission (P<0.05), but the CPP remained unchanged (P=0.804). In the HS group, the NICP, CPP and D at 24 h after admission were comparable to those on admission (P>0.05). In addition, patients with D of ≥1.3 mmHg were further analyzed.

Group		HE# (n=59)			HS$ (n=99)			F/P
		NICP	*CPP*	*D*	*NICP*	*CPP*	*D*	
On admission	$\bar{x}$	14.78	71.92	0.78	14.53	72.65	0.76	F=0.537
	s	1.53	4.97	0.29	13.04	5.25	0.38	P=0.464
Re-examination or 24 h after admission	$\bar{x}$	15.90	72.17	1.91	14.78	73.41	0.79	F=14.801
	s	1.91	6.06	0.41	15.01	4.66	0.36	P=0.000
t/F		3.525	0.249	17.341	1.279	1.088	0.715	F=391.800
P		0.001	0.804	0.000	0.202	0.278	0.476	P=0.000

Table 1: NICP, CPP and D in two groups on admission and 24 h after admission (mmHg).

 # F=14.206, P=0.000: NICP, CPP and D in HE group between two examinations; $ F=2.514, P=0.113: NICP, CPP and D in HS group between two examinations

Results showed, among these patients, 2 patients development HE (3.39%) and 4 had stable hematoma (4.04%) on admission, showing no marked difference ($\chi2$=0.260, P=0.873). However, at 24 h after admission or in re-examination, D of ≥1.3 mmHg was found in 51 patients in the HE (86.44%) and 7 patients in the HS group (7.07%), showing marked difference ($\chi2$=108.500, P=0.000).

Prognosis

In the HE group, 17 patients continued to receive conservative therapy and 42 patients underwent emergency surgery. The outcome was determined with GOS (Table 2).

Group	Good recovery	Moderate disability	Severe disability	Vegetative state	Death
HE (n=59)	13(22.03)	31(52.54)	5(8.47)	6(10.17)	4(6.78)
HS (n=99)	59(59.60)	37(37.37)	3(3.03)	0(0.00)	0(0.00)
$\chi2$	21.029	0.269	1.288	7.867	4.413
P	0.000	0.604	0.256	0.005	0.036

Table 2: Score in GOS in two groups (%)

Z=10.243; P=0.000

In the HE group, the proportion of patients with good recovery was markedly lower than that in the HS group (P=0.000), but the proportion of patients with vegetative state or death significantly higher than that in the HS group (P=0.005 and 0.036, respectively). Moreover, there were no pronounced differences in the proportions of patients with severe disability and moderate disability between two groups (P=0.604 and 0.256, respectively).

Discussion

HICH is a major disease threatening the health of the elderly. Previously, it was proposed that the intracranial bleeding might stop within 30 min. However, hematoma enlargement following HICH is a common phenomenon in clinical practice. Davis et al[3] reported that 72.9% of 218 patients with cerebral haemorrhage developed hematoma enlargement. In addition, Ji et al[8] indicated that the hematoma enlargement reached a maximal level within 6 h and was less found 24 h after HICH. A more recent study also reveals patients with HICH still have risk for hematoma enlargement even at 24 h after disease onset[9]. However, there are no criteria for determining the hematoma enlargement. Fuji et al proposed that the increase in hematoma volume of ≥ 50% or ≥ 20 ml could be used to determine the hematoma enlargement[10]. Kazui et al proposed that the increase in hematoma volume of ≥1.4 folds or ≥12.5 ml could be used to determine the hematoma enlargement[11]. In most studies, the increase in hematoma volume of >33% or ≥12.5 ml could serve as the criteria for hematoma enlargement. In the present study, HE was found in 59 patients (37.34%) following HICH. Of note, the HE was found within 12 h in 54 patients (91.52%) and 12-24 h in 1 (1.69%). Thus, we speculate that the post-HICH HE mainly occurs within 12 h after HICH, and the incidence of post-HICH HE significantly reduces at 12 h after HICH. However, HE occurring at 24 h after HICH is also possible. Thus, in clinical practice, clinicians should pay attention to the diagnosis and treatment of delayed HE at 24 h after HICH. We propose that the early monitoring of NICP can be performed until 72 h after HICH even the hematoma is stable within 24 h.

Anderson and Cucchiara et al[12,13] proposed that the HE was attributed to the increase in blood pressure, abnormal coagulation, hematoma shape, baseline hematoma volume and other factors. The HE aggravates the damage to the brain leading to the deterioration of HICH, which is also harmful for the survival and prognosis of HICH patients. Davis et al[3] found the increase in hematoma volume of 10% led to a 18% reduction in neurofunction and 5% increase in mortality, and the HE was one of independent factors leading to the deterioration of HICH or even the post-HICH death.

In the present study, although there were no marked differences in the proportion of patients with severe or moderate disability, the proportion of patients with good recovery demonstrated by the score in GOS in HE group was markedly lower than that in the HS group, but the incidence of severe events (vegetative survival and mortality) significantly increased when compared with the HS group. These findings suggest that the HE is an important factor leading to the reduction in quality of life and increase in severe events in HICH patients. Thus, early diagnosis and timely intervention of HE may be beneficial for the improvement of HICH prognosis.

Currently, Chinese Neurotrauma Expert Committee proposes a consensus on the changes in ICP following brain trauma[14]: the increase in ICP occurs earlier than the changes in consciousness and vital signs. Thus, to monitor the ICP, especially the ICP of affected hemisphere, in HICH patients is important to evaluate the severity of brain injury and to early recognize the dynamic change in hematoma.

However, in clinical practice, invasive technique is currently employed to detect the ICP[10]. Thus, for HICH patients with mild symptoms and/or small hematoma volume at early stage (≤30ml) who received conservative therapy, effective strategies have not developed to early detect and predict the HE.

The latency of FVEP peak was delayed, which was positively related to the extent of ICP increase[15,16]. In addition, the difference in ICP detected by invasive technique and non-invasive technique was 9.8%in our previous study[17], which provides evidence for the accurate monitoring of NICP. Our results revealed the NICP and D in re-examination were markedly higher than those on admission in the HE group, but the CPP remained unchanged. In addition, the NICP, CPP and D remained unchanged in the HS group. We postulate that the stable CPP in the HE group may be attributed to the compensatory increase in blood pressure following change in ICP.

The alteration of NICP and D further demonstrates that the increase in ICP following HE occurs earlier than the changes in consciousness and vital signs. Theoretically, the D is more susceptible to change than the NICP. In the present study, when the D was ≥1.3 mmHg, the detection rate of HE was 86.44%, and the misdiagnosis rate was 7.07%.

In our study, D of 1.3 mmHg was used as a cut-off value. For patients with D of ≥1.3 mmHg, timely cranial CT is necessary to early detect the change in intracranial hematoma and to predict the HE, which may provide evidence for the application of interventions. In our study, with the help of these measures, the effective rate (good recovery + moderate disability) in HE group was as high as 74.57% and the mortality was only 6.78%, suggesting favorable outcome. However, the cut-off value of D was determined on the basis of the sensitivity of instrument and the experience of clinicians, and the effectiveness of D in detecting HE should be confirmed in more studies.

Although the delayed latency is highly consistent with the change in ICP11, this can not directly reflect the ICP, and is also influenced by the integrity of visual pathway. Any change in the visual pathway may eventually affect the NICP. Thus, NICP is not applicable in patients with eye disease or diseases influencing the visual conduction.

Taken together, monitoring of NICP is non-invasive, simple and can be performed continuously and objectively and accurately reflect the change in ICP. Thus, monitoring of NICP has favourable promise in clinical practice, especially for patients with mild HICH and without invasive monitoring of ICP. In addition, monitoring of NICP can be used to effectively early predict the HE following HICH. Moreover, we postulate that the difference in bilateral NICP is more sensitive and can be applied to predict the HE earlier. However, the monitoring of NICP is still in its infant stage in the studies and trials[14], and more studies are required to confirm the importance of monitoring of NICP in the prediction of HE following HICH.

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