Clinical Application of ICP Monitoring Based on FVEP in Treatment of Patients with Hypertensive Intracerebral Hemorrhage

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Abstract

Objective

To investigate the application value of flash visual evoked potential (FVEP) in the monitoring of the noninvasive intracranial pressure (nICP) in patients with hypertensive intracerebral hemorrhage (HICH).

Methods

One hundred and two patients with HICH were randomly divided into FVEP nICP monitoring group (experimental group) and the non-monitoring group (control group). The experimental group were examined lumbar puncture immediately after intracranial pressure was monitored by FVEP. Mannitol was used to dehydration treatment of intracranial hypertension patients. The serum concentrations of creatinine and urea nitrogen were recorded to assess the renal function. Using the mannitol usage to evaluate the value of FVEP nICP monitoring techniques in guiding the adjustment of dehydrating agent. The Glasgow prognosis scores (GOS) were evaluated for patients' prognosis between two groups.

Results

There was no statistical significance between FVEP nICP measurement and lumbar puncture intracranial pressure measurement (195.76 ± 13.24 mmH₂O vs 197.04 ± 11.98 mmH₂O, $P > 0.05$). The use of mannitol in the experimental group was significantly lower than that in the control group ($P < 0.05$), and the serum creatinine and urea nitrogen concentrations in the two groups were not statistically significant ($P > 0.05$). The cure rate of the experimental group was higher than that of the control group ($\chi^2 = 3.889$, $P = 0.048$).

Conclusion

FVEP nICP monitoring technology could replace invasive intracranial pressure monitoring technology in monitoring intracranial pressure for HICH patients. The application of FVEP nICP technique can reduce the dosage of dehydrating mannitol and improve the prognosis of patients with HICH.

Tables

Table 1. Comparison of kidney function and mannitol usage between two groups

Variables	experimental group	control group
Cr (μmol/L)	120.38 ± 5.93	127.83 ± 6.72
BUN (mmol/L)	7.69 ± 0.97	8.97 ± 1.23
20% mannitol usage (mL)	3509.54 ± 289.18	4569.25 ± 308.74*

Cr, creatinine; BUN, blood urea nitrogen. Compared to the experimental group, * $P \leq 0.05$

Table 2. comparison of GOS scores between the two groups, n (%)

group	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
experimental group (n=52)	2(3.8)	3(5.8)	5(9.6)	7(13.5)	35(67.3)
control group (n=50)	4(8.0)	6(12.0)	8(16.0)	9(18.0)	23(46.0)

Introduction

Hypertension intracerebral hemorrhage (HICH) with the characteristic of high morbidity, mortality and disability is one of the major diseases that endanger the health of the elderly [1]. High intracranial pressure (ICP) caused by HICH is a common critical condition in neurology. The increase of ICP leads to the displacement of local brain tissue or the formation of brain herniation, which is the direct cause of the rapid deterioration of patients' condition and even death [2]. Headache, vomiting, and decreased levels of consciousness are the symptoms of increased ICP, but these clinical symptoms are not specific. At present, most of the ICP monitoring methods are invasive. Some limitations of the invasive methods include short-term monitoring, risk of infection, restricted mobility of the subject, etc [3]. Therefore, it is necessary to find a noninvasive and reliable monitoring method. Noninvasive intracranial pressure (nICP) monitoring technology may replace invasive intracranial pressure (iICP) to help clinical diagnosis and treatment. Flash visual evoked potential (FVEP) has been widely applied in clinical diagnosis due to its noninvasive and easy to operate. Most clinical studies on FVEP nICP monitoring technology focus on patients with craniocerebral trauma, subarachnoid hemorrhage and HICH induced ICP elevation. HICH is the most common disease of increased ICP in neurology department. Mannitol is usually used to dehydration treatment of intracranial hypertension patients, but it can also cause side effects such as renal function damage and electrolyte disorder. In addition, under pathological conditions, mannitol crystals can form a hypertonic state locally through penetrating the damaged blood-brain barrier and aggravate cerebral edema [4]. This study aims to monitor the changes of ICP in HICH patients with FVEP nICP monitoring technology, and help to adjust the dosage of dehydrating agent, shorten the clinical treatment time, improve the prognosis of HICH patients, and reduce the economic burden of patients.

Materials And Methods

Participants

One hundred and two patients HICH were enrolled from the department of neurology and geriatrics from November 2016 to December 2017. All subjects who had a history of hypertension or elevated blood pressure at onset met the diagnostic criteria of the American adult ICH treatment guidelines (2010) [5].

Cranial computed tomography (CT) showed supratentorial hematoma without or only a small amount of intraventricular hemorrhage. The amount of hematoma was less than 30 mL according to the multi-field formula, with midline shift < 1 cm. When admitted to the hospital, their vital signs were relatively stable, and they did not have previous visual impairment. Conservative treatment plan was first adopted after admission with the consent of the family. Exclusion criteria included local infection of the lumbar spine, hypoxemia, severe liver and kidney dysfunction, intracranial tumor, pituitary tumor compression bilateral visual pathway, optic nerve injury, severe cataract, glaucoma, optic nerve atrophy and other visual transmission pathway lesions. Subjects were randomly divided into FVEP nICP monitoring group (experimental group) and the non-monitoring group (control group). There were 52 cases in the experimental group including 28 males and 24 females, mean age 61.15 ± 5.84 years. The volume of bleeding was mean 21.16 ± 4.27 mL calculated by Multi-field formula. There were 50 cases in the control group including 27 males and 23 females, mean age 60.82 ± 4.18 years, and the mean bleeding volume was mean 20.73 ± 5.96 mL. There were no statistically significant differences in the two groups of patients in age, gender and blood loss. The study was approved by the local ethics committees of our institutions, and subjects informed consent.

Therapeutic methods

All HICH patients with increased ICP raised the head of the bed slightly, kept the airway unobstructed, strictly controlled blood pressure, kept the patient calm and the surrounding environment quiet, took antihypertensive drugs and sedatives as appropriate, and maintained the body temperature below 38.0 °C. Clinical symptoms and signs were observed every 30 minutes. 20% mannitol (Sichuan Kelun Pharmaceutical Co.Ltd, Sichun, China, batch no. A17103207-1) was used to dehydration treatment of intracranial hypertension patients. Cranial CT was reviewed after admitting to hospital 24 hours. Patients of the experimental group received the first FVEP noninvasive and lumbar puncture invasive ICP measurement within 1 h after admission. ICP values were monitored by FVEP nICP monitoring device within 24 hours, 3 days, 7 days and 14 days after admission, and mannitol dosage was timely adjusted according to the level of ICP. Patients with ICP less than 180 mmH₂O were no longer treated with dehydrating agent. ICP values of patients in the control group were not monitored. The dosage of mannitol was adjusted according to clinical symptoms, signs, hematoma size shown by CT. Mannitol dosage and renal function were recorded in both groups. In the experimental group, patients with significant changes in ICP should be treated by neurosurgery. Patients in the control group reviewed head CT in time according to the changes of vital signs or clinical symptoms and signs, and actively adopted corresponding internal and surgical treatment measures.

FVEP non-invasive intracranial pressure monitoring

FVEP nICP was determined using the MIP-310 nICP monitor (Chongqing Haiweikang Medical Instrument Co. Ltd, Chongqing, China) before treatment within 1 h after admission. Patients were supine in quiet state, excluding mental factors and environmental interference. The grounding electrode (black line) was placed on the eyebrows, left record electrode (orange line) and the right record electrode (brown line) were

respectively placed on the external occipital protuberance 2 cm, and the reference electrode (red line) was placed at the hairline. After wearing the blindfold, the subject was given flash stimulation (the light source was blue neon light with a frequency of 1.0 Hz and a pulse width of 2ms for 50 times). The incubation period and amplitude of N2 wave were recorded after the stimulation, then calculated the ICP. The testing process should be measured for 3 consecutive times within 15 min for each measurement, and the mean value of 3 times should be taken. The normal ICP range is 80-180 mmH₂O, ≥ 200 mmH₂O means increased ICP.

Lumbar puncture

A physician performed lumbar puncture in routine fashion with patients placed in the lateral recumbent position. Once the appropriate location was palpated, a non-traumatic spinal needle was inserted using aseptic technique between L3-L4, L4-L5 or L5-S1. The opening pressure was measured using a simple column manometer.

Clinical efficacy evaluation

Prognosis was evaluated using GOS standard [6]. level 1: death; Level 2: plant survival state; Level 3: severely disabled, unable to take care of himself; Level 4: mild disability, self-care; Level 5: return to good health and normal life. Level 1 and level 2 were considered invalid, level 3 and level 4 were considered disabled, and level 5 was considered cured. Cure rate = number of patients of level 5 / total number of cases $\times 100\%$.

Statistical analysis

Statistical analysis was performed using SPSS software (Version 22.0, Chicago, IL, USA). Measurement data was given as mean $\pm$ standard deviation (S.D.) of the mean. Enumeration data was expressed as the count and percentage. Differences between study groups were examined with the χ^2 -test for categorical variables, and Student's t-test for continuous variables. $P < 0.05$ was considered statistically significant.

Results

Comparison between monitoring value of nICP and measurement value of lumbar puncture

In the experimental group, the value of FVEP nICP monitoring was 195.76 ± 13.24 mmH₂O and lumbar puncture measurement was 197.04 ± 11.98 mmH₂O. There was no statistically significant difference ($P > 0.05$). FVEP nICP monitoring technique could replace invasive lumbar puncture in evaluating ICP changes in HICH patients.

Comparison of renal function and mannitol usage amount between two groups

There were two cases who suffered kidney dysfunction in the control group, manifested as elevated creatinine and urea nitrogen values, but no statistical significance was found between the experimental

group and the control group ($P > 0.05$). Compared with the control group, the amount of mannitol usage in the experimental group was significantly decreased ($P < 0.05$) (Table 1).

Comparison of GOS scores between two groups

There were 35 patients with GOS grade 5 in the experimental group and 23 patients with GOS grade 5 in the control group. The cure rate in the experimental group was higher than that in the control group (67.3% vs. 46.0%, $\chi^2 = 3.889$, $P = 0.048$) (Table 2).

Discussion

Raised ICP after intracerebral hemorrhage plays an important role in secondary brain injury and is associated with increased mortality [7]. Timely detecting of ICP changes is the key to successful rescue of critically ill patients. Nowadays, most methods of ICP monitoring are invasive, but it's more likely to occur intracranial infection, intracranial hemorrhage and other complications. Mizutani et al. [8] attempted to evaluate the sizes of intracranial hematoma, subdural hematoma, ventricular, and the degrees of subarachnoid hemorrhage and brain trauma injury through CT imaging, and established the relationship equation between CT imaging and increased ICP by applying multiple regression analysis. But the results showed that the error of ICP value was more than 40 mmH₂O. Magnetic resonance imaging (MRI) examination is not convenient to be used in critically ill patients, nor can it be used to monitor ICP in a timely and dynamic manner [9,10]. FVEP nICP monitoring technology had been applied in clinical practice since 1986 [11]. FVEP is the electrical activity generated by the occipital cortex to the visual stimulation induced by the diffuse non-mode light source. The delay time of the second negative wave (N2 wave) of the brain FVEP is directly related to ICP. A microcomputer device can be used to perform visual stimulation and measure the delay time of N2 wave, then we can obtained the ICP value by comparing the relation table of N2 wave delay time and ICP value [12]. York et al. confirmed in the study of pediatric hydrocephalus and non-open craniocerebral trauma that there was a strong linear relationship between increased ICP and prolonged latency of N2 wave of visual evoked potential (the correlation coefficient was 0.8-0.9) [13]. Visual evoked potential is best predicted when cranial hypertension is greater than or equal to 300 mmH₂O [14].

Our research showed that there was an error between the monitoring values of invasive and noninvasive ICP in patients with HICH, but the difference was not statistically significant. Therefore, FVEP nICP monitoring technology can be widely used in the clinical monitoring of HICH patients. The majority of patients with intracerebral hemorrhage experienced further increase in ICP due to hematoma enlargement within 24h after the onset of intracerebral hemorrhage. Some researchers showed that the increase of ICP is significantly earlier than the clinically observed changes in consciousness and vital signs [15,16]. Especially applicable to patients with mild to moderate HICH without invasive ICP monitoring, FVEP nICP monitoring technology can be used as an effective means of early warning of further increase of ICP and further enlargement of hematoma. Moreover, traditional lumbar puncture manometry is forbidden in patients with severe high cranial pressure (intracranial pressure greater than 350 mmH₂O) , because it is

likely to induce cerebral hernia. Therefore, the use of FVEP nICP monitoring is particularly important for HICH patients, especially for monitoring the change of ICP on the hematoma side, for evaluating the degree of cerebral hemorrhage and cerebral edema, and for early understanding of the dynamic changes of hematoma.

In HICH patients, intracranial hematoma and cerebral edema will lead to intracranial hypertension in 70% of patients. If not timely intervention will seriously affect the recovery of neurological function and prognosis of patients. Currently, mannitol is the most commonly dehydrating agents which lower ICP by reducing blood viscosity and increasing plasma osmotic pressure [17]. However, clinical usage amount lacks scientific standards and often relies only on clinical experience, as for mannitol to achieve the expected effect is more difficult to determine. In addition, mannitol can cause kidney function damage and electrolyte disturbance. In order to reduce the possible damage caused by using of high doses of mannitol blindly, the American stroke Association recommends that mannitol should not be used prophylactically and should not be used for more than 5 days during first aid [18,19].

Clinical data showed that mannitol could shorten the incubation period of FVEP N2 wave, and FVEP could observe the changes of ICP after mannitol application [20]. In our experiment, the dynamic changes of ICP in the experimental group were monitored by FVEP nICP monitoring technology, and the using frequency of mannitol was timely adjusted. The amount of mannitol was significantly less than the control group. The complications of kidney function impairment caused by drugs were also rare than those in the control group. The ICP changes monitored by FVEP nICP monitoring technology can accurately guide clinical treatment. Moreover, ICP changes in patients with HICH can be detected timely. It means that FVEP nICP monitoring plays an important early warning role in the treatment of severe craniocerebral injury, and can effectively guide the clinical active use of dehydrating agent and craniotomy.

Our research showed that the recovery rate of the experimental group was significantly higher than that of the control group, and the prognosis of the HICH patients could be improved by closely monitoring the change of ICP value and timely adopting reasonable treatment plan.

In conclusion, FVEP nICP monitoring technology has the advantages of noninvasive, simple operation and reliable results, and can replace the traditional invasive ICP monitoring methods in patients with HICH. The dynamic monitoring of ICP in HICH patients can guide the clinical timely adjustment of the dosage of mannitol and improve the condition and prognosis of HICH patients. However, the limitations and influencing factors of FEVP nICP monitoring technology should also be considered during clinical use, so as to better understand its indications and provide more reliable methods and means for clinical treatment of patients with HICH intracranial hypertension.

Abbreviations

FVEP: flash visual evoked potential; nICP: noninvasive intracranial pressure; HICH: hypertensive intracerebral hemorrhage; GOS: glasgow prognosis scores; ICP: intracranial pressure; nICP: noninvasive

intracranial pressure; iICP: invasive intracranial pressure; CT: computed tomography; MRI: magnetic resonance imaging; Cr: creatinine; BUN: blood urea nitrogen.

Declarations

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Availability of data and materials

The data supporting our findings can be found in our article and its additional files.

Authors' contributions

FP-Y participated in the design of the study, statistical analysis, and drafted the manuscript. YC-Z participated in the design and conduct of the study. Y-Z carried out the operation of the experiment. Y-W provided management and operational assistance to the patients. XH-L helped to modify the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Songjiang Hospital Affiliated to Shanghai Jiaotong University School of Medicine. Written informed consent was obtained from all participants following a detailed explanation of the study. The study was done in accordance with the principles outlined in the Declaration of Helsinki (1964).

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing Interests

The authors have no potential conflicts of interest to disclose.

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