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Clinical experience with the noninvasive ICP monitoring system

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Summary

The Noninvasive ICP (Intracranial Pressure) Monitoring System NIP-200/210 has been used in several hospitals with more than 2000 patients since March 2002. It is based on the N2 wave response to flash visual evoked potentials (FVEP). According to our data, the mean latency period for the FVEP-induced N2 wave in healthy controls was 126.61 ± 14.64 ms, in which that of females was shorter than that of males (123.95 ± 10.345 ms vs. 130.75 ± 14.632 ms; $p < 0.05$). There was no significant difference between the left or right side response (126.71 ± 14.91 ms vs. 124.468 ± 15.043 ms, $p > 0.05$). No significant difference in latency was found across age groups in our patient pool. In general, the N2 wave was stable and easily identified in most of the patients or healthy controls. When the data obtained with the NIP-200/210 Noninvasive ICP Monitoring System was compared with that from invasive techniques, the results were quite consistent (correlation index 0.651–0.97, standard error 8–15%). From our clinical trial results, we conclude that the latency periods for the FVEP-induced N2 wave reflected ICP values. However this technique is not suitable in patients with bifrontal hematoma, retinal concussion, or contusion of the optical nerve, because an FVEP value cannot be measured accurately in these cases. In our clinical trials, we used the FVEP technique to determine the effectiveness of mannitol in decreasing the ICP. The data revealed that ICP values decreased significantly within 20 minutes after a mannitol injection, and reached a minimum level at 40 minutes. For a single bolus of mannitol, the duration of the ICP decrease ranged from 30–210 minutes. Elevated ICP is one of the most important clinical issues in neurosurgery and neurology. The present noninvasive technique is safe and easy to perform, with a minimal risk of complications.

Keywords: Intracranial pressure; monitoring; visual evoked potential.

Introduction

Intracranial hypertension is an acute, severe symptom in nervous diseases and is one of the most common direct causes for a patient's death. Thus, a key step for rescuing such patients is to monitor their intracranial pressure promptly and accurately, and to deliver effective treatment.

Currently, there are various ICP monitoring methods used in clinical practice, but most of them are invasive. Although the invasive methods can measure ICP with relative accuracy, these methods require sophisticated technology and complicated procedures, and often induce additional complications such as intracranial infection, leakage of cerebrospinal fluid and intracranial hemorrhage. Their application is thus limited, and currently in most of the hospitals in China, doctors assess ICP levels through by clinical observation, which can result in the inappropriate usage of dehydrating agents. It is imperative to find a noninvasive technique for monitoring ICP in order to incorporate this factor into the clinical diagnosis.

Flash visual evoked potential (FVEP) can accurately reflect injuries of the visual pathway. Because the latency period for FVEP is prolonged in parallel with increases in ICP, a study was designed to apply both FVEP and invasive methods to the monitoring of ICP in patients, and to analyze the correlation and consistency between these methods. The feasibility of FVEP as a noninvasive means for monitoring ICP is discussed.

Clinical data and methods

Clinical data

Subjects: 152 participants in this study (89 males and 63 females) were enrolled from patients in the Department of Neurosurgery between March and April 2002 who had signed informed consent forms. Blood pressure, respiration rate, heart rate and body temperature were recorded for each patient, and tests of consciousness, pupil size and response to light were carried out before determining blood pressure. For patients under treatment with diuretics or anesthetics, the dosage and the schedule (day, hour) of these medications were recorded.

The following criteria were used to exclude patients from this study: (1) bilateral visual pathways under pressure from a hypophyseal tumor; (2) hypoxia (O2 saturation less than 95%); (3) obvious liver dysfunction (abdominal dropsy, severe hypoproteinemia, jaundice); (4) uremia; (5) severe acidosis; (6) diseases obviously affecting the visual acuity, such as severe cataracts, glaucoma or optic atrophy.

Methods

Instruments: the NIP-200 noninvasive ICP monitoring system (produced by Chongqing HaiWeiKang Medical Instrument Co., Ltd) was used to induce the flash visual stimulation.

Method: According to the operating instructions for the monitor, the sunflower-shaped galactic disk electrodes (8 mm in diameter) were placed 3 cm above the occipital tuberosity separately on the left and right sides, the reference electrode was located on the midline of forehead hairline, and the ground electrode was located on the glabella. The impedance between the electrodes was lower than 50 kΩ. The FVEP stimulation was produced by a light emitting diode array that was arranged in a pair of LED light glasses; dispersed yellow light was emitted in a pulsed-wave mode that was triggered by computer. The brightness of light glasses was 20000 cd/m^2.

Invasive examination: either the lumbar puncture method or the cerebral epidural manometric method (LCY-3.10 intelligent intracranial pressure monitor) were carried out to measure the pressure, depending on the diagnosis and condition of the individual patients. All invasive examinations were performed after carrying out the FVEP.

Statistical analysis

All data were expressed as means $\pm$ standard deviation, and were analyzed with a paired t-test and linear correlation analysis using SAS 6.12 software.

Results

A total of 152 patients were examined, including 89 males and 63 females, with an average age of 45 years (13–82 years). The indications included: 32 cases with cerebral hemorrhage, 27 cases with subarachnoid hemorrhage, 24 cases with meningitis, 16 cases with brain trauma (subdural hematoma, contusion and laceration of brain, etc.), 9 cases with brain tumor, 8 cases with hydrocephalus, and 36 cases with various other indications (cerebral infarction, benign intracranial hypertension, encephalitis, headache, etc.).

Recognition of the FVEP waveform

Figure 1a shows the FVEP waveform of a normal person, where the waves that appear below the baseline are negative waves (Negative, N). N126 is the large peak that occurs early on: it is stable and easy to distinguish, so the latency period of the N126 wave in NIP-200 noninvasive ICP monitoring system was adopted as a baseline reflecting the indices of ICP changes. Figures 1b–d show the FVEP waveforms for intracranial hypertension patients.

Comparisons between the results from FVEP and those of the invasive ICP methods

(1) Figure 2 displays the results for a correlation analysis of the ICP values showing a linear correlation between FVEP and the invasive methods, with a correlation coefficient (r) of 0.97. This indicates that the ICP values from the FVEP examination are remarkably well correlated with those from the invasive methods.
(2) A paired t-test gives a t-value of 0.37, which demonstrates there is no significant difference between the results from noninvasive and invasive ICP examinations ($p > 0.05$).
(3) The average relative error (δ) for the FVEP ICP values from the non-invasive ICP technique is 13.2%. 95% confidence limit for prediction is around 8 mm Hg.

There were no patterns in the alterations of the N126 wave amplitude, and there are no correlations of the amplitude with the ICP.

Discussion

The FVEP reflects the integrity of the visual pathway from the retina to the occipital lobe cortex [1, 2]. When the ICP increases, ischemia and anoxia are induced in the neurons and nerve fibers and the level of lactic acid increases, which results in a decrease in cerebrospinal fluid pH and elicits a nerve conduction blockade. The conduction velocity of the electrical signal decreases so as to prolong the latency period of FVEP peak, which is positively correlated with the ICP level. Based on this mechanism, it should be valid to employ FVEP as an indicator of changes in the ICP. Furthermore, FVEP is less affected by visual acuity and can easily be performed for patient monitoring without their active cooperation, for example, including patients with severe diseases and especially in comatose patients.

Changes in the FVEP waveform accompanying ICP increases

We have adopted the general international conventions for naming the waveform, and the portion above

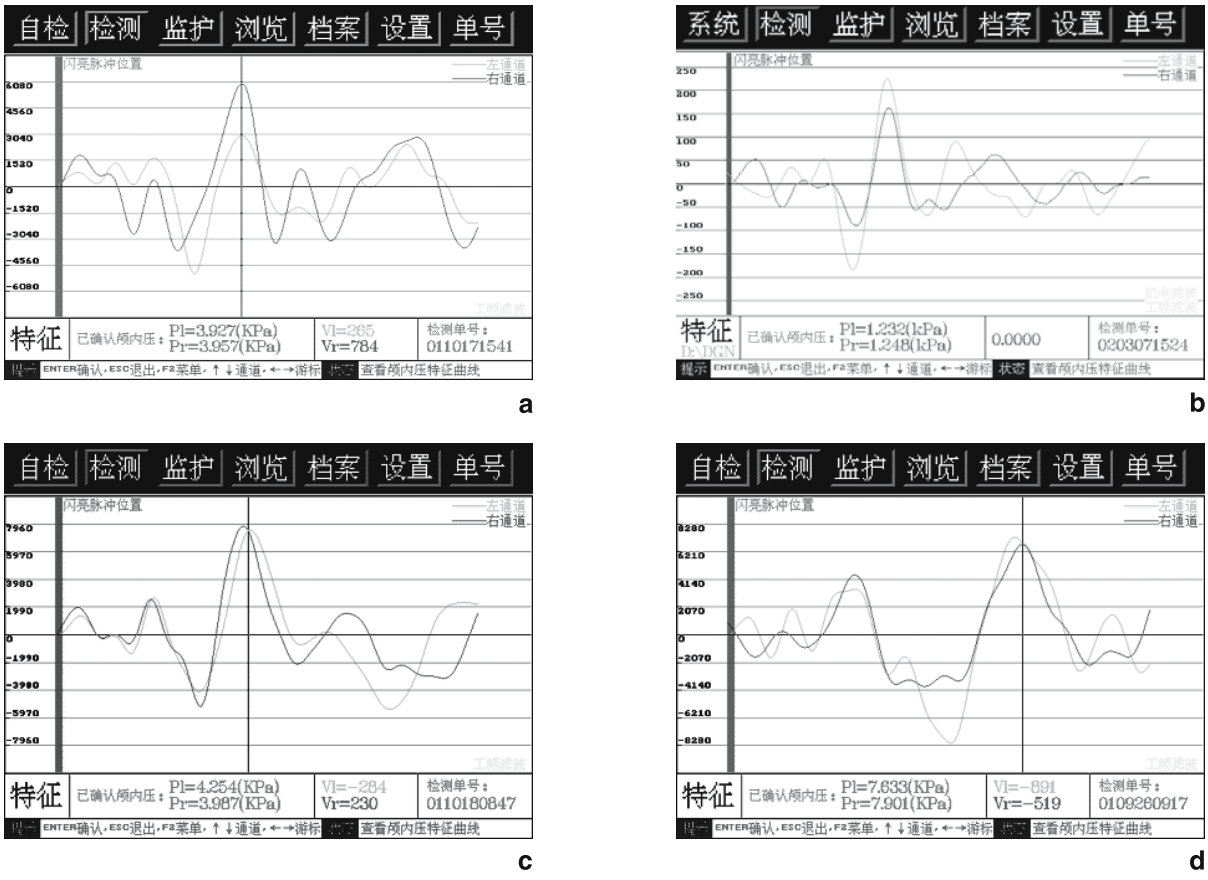

Fig. 1. (a) FVEP of a normal person. The marker is the N126 wave, showing that the average ICP is 126.5 mmH_2O. (b) FVEP of a patient with cerebral hemorrhage. The latency period of N126 is prolonged (147.25 ms). The FVEP indicates an ICP of 363 mmH_2O, while the cerebral epidural pressure is 380 mmH_2O. (c) FVEP of a patient with a subarachnoid hemorrhage. The latency period of the N126 peak is 155.91 ms. The average ICP from FVEP is 400 mmH_2O, while the pressure from lumbar puncture is 375 mmH_2O. (d) FVEP of a patient with a cerebral hemorrhage (hemorrhage volume is about 80 mL, patient is deceased). The FVEP displays double peaks; the marker indicates the N126 wave, and the average ICP of noninvasive methods is 741.5 mmH_2O

the baseline is referred to as a negative wave N. A review of the literature (2–9) shows that various researchers use different names to refer to the waveforms that reflect ICP changes, such as N2, N3, P1, P2, P100 wave, etc. The reasons for these differences may be related to the instruments, the use of different conventions for positive vs. negative waves, delays in the instrument's response time, different times to commence sampling, etc. For example, the N2 and N3 waves could refer to the same signal on different FVEP instruments. In order to facilitate comparisons of these findings, we propose that a typical graphic output for the instrument used should be included in publications in this field, and also the adoption of a standard peak to establish a benchmark for latency times, such as the N125 peak. In our preliminary experiments (manuscript in preparation), we have adopted the N125 wave latency period for the NIP-200 noninvasive ICP monitoring system as an index for changes in the ICP.

As seen from Figures 1b–d, the latency period for the N126 peak is prolonged with increases the ICP, and there is a linear correlation with these ICP values, but there were no patterns in the wave amplitude changes. The results of this study also showed that when the ICP exceeded 900 mmH_2O, the FVEP displayed 2 large waves (double peaks), as shown in Figure 1d, of which the N126 should be the latter peak. A dying patient's FVEP wave shows a similar change.

The correlation analysis of FVEP and ICP

Correlations between the FVEP and ICP have already been reported by researchers from different parts of the world. Donald *et al.* [3] used FVEP and

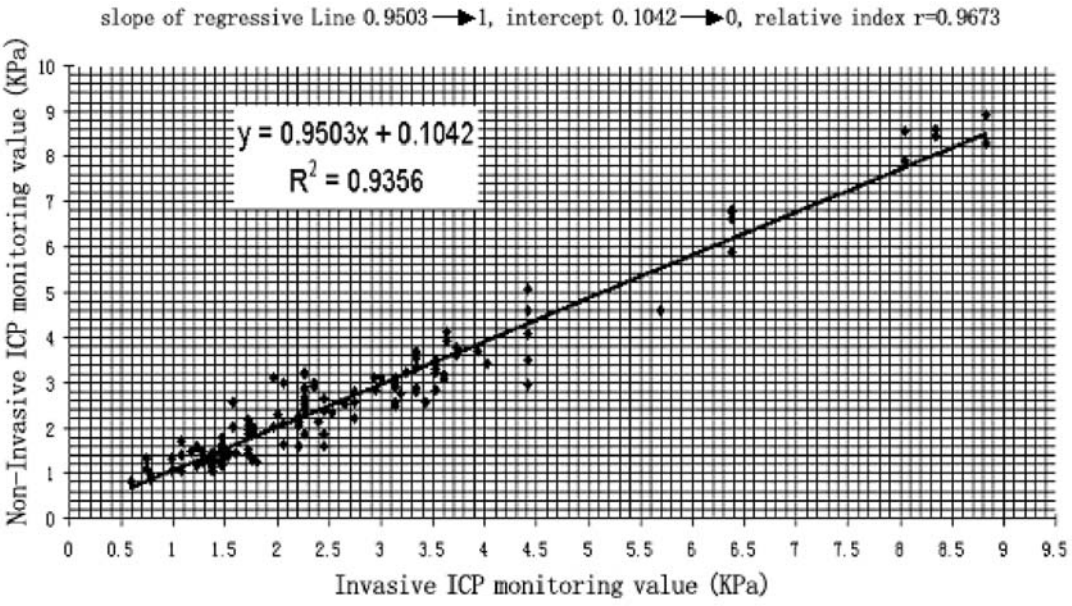

Fig. 2. Correlation analysis of ICP values from FVEP and from invasive examinations

the subdural ICP monitoring technique to conduct a comparative study of the patients with hydrocephalus and brain trauma. They discovered that the N2 latency period increased continuously in tandem with ICP increases, and the N2 latency period showed a positive correlation with ICP and a negative correlation with cerebral perfusion pressure. York *et al.* [4] obtained the same results, and suggested that FVEP could be used to examine the ICP in patients with hydrocephalus and brain trauma. They proposed that the prolongation of the latency period was related to a drop in the blood flow and oxygen pressure in the brain.

Burrows *et al.* [5] also confirmed this relationship in extracorporeal circulatory support in infants. Liu Jianjun *et al.* [6] studied the correlation between FVEP and brainstem auditory evoked potentials (BAEP) with ICP using the acute ICP rabbit model, and discovered that the latency periods for the N2 and P1 waves in the FVEP were positively correlated with increases in ICP, but there was no obvious correlation between BAEP and ICP. Our findings also indicated that the ICP values obtained from FVEP were remarkably well correlated with those from invasive methods, with a correlation coefficient (r) of 0.9. The paired t-test across both methods proved that the difference has no statistical significance ($p > 0.05$), and the average relative error is only 13.22%.

At present, there are many studies of noninvasive ICP monitoring methods, including the relatively mature methods such as FVEP, TCD, etc., and anterior fontanelle can be used in infants [1, 2, 10]. Compared with other methods, FVEP itself is an effective means for monitoring brain function and doing follow-up with seriously injured patients.

Both our findings and other literature reports indicate a good linear correlation between the prolongation of the FVEP peak with changes in ICP, and FVEP has the advantages of being simple, rapid, and convenient for bedside use. Thus, it is strongly recommended for clinical practice as a noninvasive ICP monitoring method to inform the design of treatment strategies. We have used the NIP-200 noninvasive ICP system to monitor dynamically a number of patients with intracranial hypertension, and subsequently obtained significant results (manuscript in preparation). However, there remain several important issues to be resolved before FVEP-based ICP noninvasive monitoring is ready for wider application, including enhancements in the accuracy, analysis of potential variations in the FVEP wave with different clinical indications, and recognizing and controlling any other factors that may influence the FVEP-based ICP system as a noninvasive monitoring method.

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