Original Article

Brainstem auditory evoked potentials in patients with delayed encephalopathy after acute carbon monoxide poisoning

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Abstract: Objective: This study aimed to evaluate the variation of brainstem auditory evoked potentials (BAEP) in patients with delayed encephalopathy who got acute carbon monoxide poisoning. Methods: Thirty-two controls and forty patients have been performed in BAEPs. Wave I, II, III, IV, V latencies and I-III, III-V, I-V interpeak latencies were measured, respectively. Results: Abnormalities of BAEPs were found in 13 patients (13/40, 32%). Among the 13 abnormal BAEPs, 3 patients displayed prolongation of latency to waves in one side, no potential in another side, 5 patients displayed a similar abnormality which was bilateral prolongation of latency to waves, and 5 patients displayed unilateral latency delay. Comparisons wave I, II, III, IV, V latencies and I-III, III-V, I-V interpeak latencies between the cases and the controls, there was no significant differences (P > 0.05). Conclusions: BAEPs can be used for evaluating delayed encephalopathy after acute carbon monoxide poisoning.

Keywords: Brainstem auditory evoked potentials, delayed encephalopathy, carbon monoxide poisoning

Introduction

Delayed encephalopathy after acute carbon monoxide poisoning is a complication of carbon monoxide (CO) intoxication [1]. It is clinically characterized by a recurrence of neurologic or psychiatric symptoms. This recurrence is preceded by a temporary asymptomatic period (lucid interval) of variable duration (usually 2-3 weeks) after a recovery from the acute stage of CO intoxication [2, 3]. Evoked potentials (EPs) have become standard tools used in the care of certain patients with neurological problems. The techniques have found acceptance because they are relatively objective, reproducible, very sensitive to impairment, and relatively easy to use in many clinical settings [4]. These are now routinely available in most hospitals and many neurological practice settings. BAEPs can provide important diagnostic information regarding the functional integrity of the auditory system. To our knowledge, there are published reports about brainstem auditory evoked potentials (BAEPs) in patients with acute carbon monoxide poisoning [5], but there are few published reports about BAEPs in patients with delayed encephalopathy after acute carbon monoxide poisoning. The purpose of this paper is to observe the diagnostic and prognostic value of BAEPs in patients with delayed encephalopathy after carbon monoxide poisoning. BAEPs were performed in 40 patients with delayed encephalopathy after acute carbon monoxide poisoning. The patients were examined from 2000 to 2004 in the Second Affiliated Hospital of Xinxiang Medical College.

Materials and methods

Patients

40 patients with delayed encephalopathy after acute CO intoxication were admitted to the department of neurology of the Second
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Table 1. Case-Control comparison of BAEPs (mean ± SD) (ms)

| Groups   | n   | I   | II    | III   | IV    | V     | I-III | III-V | I-V  
|----------|-----|-----|-------|-------|-------|-------|-------|-------|------
| Controls | 32  | 1.45±0.11 | 2.51±0.13 | 3.58±0.21 | 4.89±0.18 | 5.70±0.23 | 2.12±0.24 | 2.17±0.29 | 4.25±0.34 |
| Cases    | 40  | 1.46±0.12 | 2.99±0.19 | 3.60±0.23 | 5.02±0.21 | 5.80±0.24 | 2.13±0.28 | 2.20±0.15 | 4.40±0.43 |
| t        |     | 1.50 | 1.55  | 1.60  | 1.66  | 1.78  | 1.00  | 1.60  | 1.68  |

Affiliated Hospital of Xinxiang Medical College and conformed to the diagnostic criteria by Zhao Xiangzhi, et al [6]. There were 27 men and 16 women, their ages ranged from 41 to 83 years old (mean ± SD; 55.5±15.5 years old). All patients were found unconscious, with urinary and fecal incontinence, and the duration of coma ranges from 1 to 23 hours (mean ± SD; 12.65±6.4 hours). All patients completely or partially recovered from the initial symptoms within several days to several weeks. The lucid interval ranged from 4 to 60 days (mean ± SD; 23.77±13.99 days).

All patients were exposed to CO gas, which leaked from coal stove. These patients satisfied the following criteria: (1) evidence of acute CO poisoning, (2) a lucid interval of several days or several weeks, (3) neurologic or psychiatric symptoms, and (4) abnormal EEG. The patients were excluded if they had following evidence: (1) metabolic or neurodegenerative disease, (2) previous history of head trauma, stroke, perinatal hypoxia or encephalitis. Of 32 controls, males were 21; females were 11, their ages ranged from 30 to 67 years (mean ± SD; 53.16±6.97 years).

The electroencephalogram (EEG) was performed in 40 patients. Brain computed tomography (CT) was performed in 39 patients. Brain magnetic resonance image (MRI) was performed in 9 patients.

The main manifestation of patients were dementia and Parkinsonian symptoms. According to the diagnostic criteria of DSM-III-R, 36 patients were conformed to severe dementia, and 4 patients were moderate dementia.

Methods

All patients were examined with Multi-channel evoked potentials instrument from Italian and received no sedation. BAEPs were obtained 25~65 days after their exposure to CO and during a relapse of neuropsychiatric symptoms, which occurred after an initial recovery. Testing was done in a quite room, according to the International 10/20 system, the surface electrode was placed onto the Cz, the reference electrode was placed onto earlobe (A1 or A2), and the ground electrode was placed onto Fpz. The ipsilateral (Cz-Ai) and contralateral (Cz-Ac) BAEPs were recorded between Cz and A1 and between Cz and A2 to obtain after monoaural stimulation.

A Nicolet click generator passed square-wave pulses of 100 msec duration to the subject. Alternating click polarity was used. The ear contralateral to the one stimulated was masked. The click stimulus intensity was 90 dB, sensitivity was 5 μv, frequency was 12 Hz. Electrode impedance was kept below 5,000 ohms, with a band pass of 50 to 1500 Hz, and repeated 2,000 times by average signal of a computed, The usual analysis time of the potential was 10 ms. The records were twice repeated at least.

Results of BAEPs showed an upward deflection. Latency was measured by the cursor from the onset of the stimulus to the positive peak, and interpeak latency (IPL) was measured from the peak to peak. When the result was abnormal, if the repeated tracing failed to confirm any consistent waves, BAEPs was labeled “no potential”.

Statistical analysis

Experimental results were expressed as mean ± SD. The data was dealed with the Statistical Package for Social Sciences (SPSS 12.0 for Windows). Two-independent sample t test was used to assess the differences between the two groups, and P values below 0.05 were considered to be statistically significant.

Results

The abnormal criteria of BAEPs was as follows: (1) no potential (include waves are diffusing, deforming and disappearing). (2) A latency or
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Of 40 cases, 13 patients showed abnormal BAEPs. The abnormal rate was 32.6%. Among the 13 abnormal BAEPs, 3 displayed prolongation of latency of waves at one side, “no potentials” at another side, 5 displayed a similar abnormality which was bilateral prolongation of latency of waves, and 5 displayed unilateral latency delay, normal at another side. The prolongation of latency of BAEPs waves could be divided into two patterns: a peripheral pattern of prolongation of latency of wave I without prolongation of interpeak latency, and a central pattern of prolongation of latencies of all waves and interpeak latencies or no potentials.

EEG of all patients showed diffuse abnormalities, represented by a nearly continuous high voltage 2-2.5 Hz sharp-wave activities. Computed tomograph (CT) scans of brain were obtained in 39 cases. 10 showed low densities in both the basal ganglia and the white matter of the cerebral cortex (Figure 3), 9 showed low densities only in the cerebral cortex, and 20 were normal. There were no correlation between the abnormalities of BAEPs and CT-brain scans. 9 cases were performed with MRI, 7 cases was abnormal. The result showed that multiple and partial confluent T2-hyperintense areas were existed in the white matter of cerebral cortex and both the basal ganglia, or showed focal T2-hyperintense areas in the brainstem (Figure 4).

Figure 1. The peaks seen here are normal BAEPs for one health adult.

Figure 2. BAEPs showed prolongation of latency to wave I in bilateral side without prolongation of interpeak latency.

Figure 3. CT showed low densities in both basal ganglia and the white matter of the cerebral cortex.
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The prognosis were assessed after 2 months, according to the therapeutic effect criteria by Gun Rengjun, et al [7]. Of 40 patients, recovery were 14 (14/40), excellence effectiveness were 20, effectiveness were 5 and 1 was inefficacy. The prognosis of 13 abnormal BAEPs were as follows: recovery were 2 (15.38%, 2/13), excellence effectiveness were 8, effectiveness were 2 and 1 was inefficacy. And of 30 normal BAEPs, recovery were 12 (40%, 12/30), excellence effectiveness were 15, effectiveness were 3. Comparison the rate of recovery and inefficacy, there were significant differences between the normal and abnormal BAEPs groups (P < 0.05).

Discussion

Carbon monoxide (CO) is a common environmental toxin and a leading cause of lethal poisoning around the world [8]. The brain is the most vulnerable organ to the effects of CO. Carboxyhemoglobin (COHb) is produced [9] due to displacement of the hemoglobin oxygen by CO and results in failure of oxygen transportation to brain and causes acute anoxia, and direct cellular toxicity of CO will cause brain damage and neurological deficit. Delayed encephalopathy displays various disorders such as cognitive and motor impairment and may develop within 8 weeks, its recurrence rate is 10% to 30% after acute carbon monoxide poisoning [10, 11]. During the initial anoxic damage, no clinical signs may distinguish patients who will develop delayed neurological sequelae, age and severity of initial anoxia may increase the risk of late encephalopathy [12]. After a variable period of complete recovery from the acute intoxication, new neuropsychological symptoms develop, including: seizures, Parkinsonian features, cognitive deficits, intellectual decline, apathy, apraxia, urinary incontinence, gait abnormalities and agnosia [13]. Short-term outcome of the delayed neurological deterioration after acute CO poisoning is relatively good with 61% to 75% recovery in 1-2 years. The symptoms, especially Parkinsonian symptoms and memory problems, persist in the other patients, [14]. The underlying pathologic lesion is thought to be a diffuse demyelination of the cerebral white matter (leukoencephalopathy) [15], but the pathogenic mechanism remains poorly understood.

BAEPs are now routinely performed in most hospitals. Its advantages are sensitive, reliable and objective. It is enough sensitive to detect abnormalities even when the physical examination is normal. BAEPs are even used in clinical investigations of the pathophysiology on certain neurological diseases [16]. Although it is difficult that the function of auditory pathways is assessed by laboratory tests, brainstem auditory evoked potentials (BAEPs) has been recently used as an electrophysiological means of localizing a lesion of the auditory pathway, localization is possible because five waves in BAEP are generated from different portion of the auditory pathway in the brainstem. Wave I is generated from the portion of the eighth pairs of cranial nerve just near to the brainstem, wave II is generated near or at the cochlear nucleus of the junction of the pons and medulla, wave III is probably generated in the lower pons due to these auditory pathways traversing the region of the superior olive and trapezoidal body, waves IV and V is probably generated in the upper pons and lower midbrain, or in the lateral lemniscus or inferior colliculus [17].

Of 40 cases, 13 showed abnormal BAEPs. The abnormal rate was 32%. The anatomical foundation of evoked potentials is the peripheral and central pathway of medullated sensory
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nerve fibers of I type, which represents the change of the medullated sensory nerve fibers. The results support that the pathologic lesion is a diffuse demyelination of the cerebral white matter (leukoencephalopathy). Studies at present demonstrated that a large number of cases with delayed encephalopathy after acute carbon monoxide poisoning displayed intact BAEPs and some cases displayed abnormal BAEPs, which demonstrated that not only cerebral cortex but also brainstem was impaired, impairment of brainstem only appeared in serious cases. The prognosis have been compared between the patients with normal BAEPs and the other patients with abnormal BAEPs, the former is better than the latter. Therefore, Thus BAEPs can provide prognostic value for the disease.

To our knowledge, BAEPs abnormalities and the various clinical signs usually were considered as evidence of known anatomical level of dysfunction, alteration of wave III to a pontine level and alteration of wave I and II was related to a lower brainstem dysfunction. Among the 13 abnormal BAEPs, 3 displayed prolongation of latency of waves in one side, “no potentials” in another side, 5 displayed a similar abnormality which was bilateral prolongation of latency to waves, and 5 displayed unilateral latency delay and normal latency in another. The prolongation of latency of BAEPs waves could be divided into two patterns: the peripheral pattern and the central pattern. The peripheral pattern was 5 patients and the central pattern was 7 patients. Those results have been suggested that the peripheral pattern of BAEPs abnormality involve the cochlear nerve, and it show that the central nerve can be impaired as well as the peripheral nerve in the cases. The central pattern of BAEPs abnormality was due to the possible involvement of the brainstem. The prognosis of patients with peripheral pattern of BAEPs was better than that of patients with central pattern of BAEPs. The patients with peripheral pattern of BAEPs recovered for a shorter time. The prognosis of 13 abnormal BAEPs were as follows: recovery were 2 (15.38%, 2/13), excellence effectiveness were 8, effectiveness were 2 and 1 was inefficacy. And of 30 normal BAEPs, recovery were 12 (40%, 12/30), excellence effectiveness were 15, effectiveness were 3. Comparison the rate of recovery and inefficacy, there were significant differences between the normal and abnormal BAEPs groups (P < 0.05). The prognosis of the normal BAEPs were better than the abnormal BAEPs. Thus, BAEPs can provide prognostic value for the disease. It can be used to localize the disease region. EEG, BAEPs, CT and MRI could display abnormality in the bilateral hemicerebrum and brainstem, we can speculate that diffuse bilateral hemicerebrum and brainstem be involved in the disease.

In conclusion, BAEPs demonstrated that the disease destroyed the functional integrity of auditory system, and it can help to diagnose and prognosis as well as help to localize impairment position in patients with delayed encephalopathy after acute carbon monoxide poisoning.

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Disclosure of conflict of interest

None.

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