Brainstem Auditory Evoked Potentials in Acute Carbon Monoxide Poisoning

Il Saing Choi, M.D.

Of 32 cases suffering from acute carbon monoxide (CO) poisoning, brainstem auditory evoked potential (BAEP) abnormalities were exhibited in 8 cases. The abnormalities of BAEPs could be divided into two patterns: a peripheral pattern (6 cases) of prolongation of latency to wave I without prolongation of interpeak latency, and a central pattern (2 cases) of prolongation of latencies to all waves and interpeak latencies. The incidence of BAEP abnormality tended to increase in accordance with an unconscious duration of more than 24 hours during acute CO poisoning. A BAEP abnormality exhibiting a peripheral pattern usually returned to normal within one month after anoxia, but cases showing central patterns of BAEP abnormality died during acute anoxic insult due to the possible involvement of the brainstem. Thus, BAEPs can be used for evaluating the functional integrity of the auditory pathways and for providing prognostic values in acute CO poisoning.

Key Words: Acute carbon monoxide poisoning, Brainstem auditory evoked potential.

Carbon monoxide (CO) has the toxic effects of tissue hypoxia and produces various neurologic deficits (Haldane, 1895; Shillito and Drinker, 1936; Finck, 1966; Garland and Pearce, 1967; Choi, 1983b). Among them, it is a well-known fact that the brainstem and cochlear nerve may be involved, but this occurrence is rare (Walton, 1977; Choi, 1983b). Although assessing the function of auditory pathways using laboratory tests is difficult, brainstem auditory evoked potential (BAEP) recently has been used as an electrophysiological means of localizing a lesion of the auditory pathway (Starr and Achor, 1975; Starr and Hamilton, 1976; Stockard and Rossiter, 1977; Hashimoto et al., 1979). Localization is possible because the first five waves in BAEP are generated from serial parts of the auditory pathway in the brainstem (Jewett, 1970; Buchwald and Hwang, 1975). However, to the author's knowledge, the ability to assess an auditory pathway lesion in acute CO poisoning by means of BAEP has not yet been demonstrated.

MATERIALS AND METHODS

A total of 32 patients with acute carbon monoxide (CO) poisoning were studied. There were 15 men and 17 women, and their ages ranged from 17 to 82 years (mean, 41.8). All patients except 5 received hyperbaric oxygen therapy and there was no clinical evidence of auditory pathway lesions except in cases of prolonged coma. Of 32 cases, 3 delayed neurologic sequelae occurred 14 to 30 days after acute insult. They were divided into 5 groups according to the duration of unconsciousness during acute anoxia: group 1 (13 cases) was unconscious less than 12 hours; group 2 (8 cases), 12-24 hours; group 3 (3 cases), 24-48 hours; group 4 (3 cases), 48 hours; and group 5 (5 cases), more than 72 hours (prolonged coma).

All patients except cases of prolonged coma underwent BAEP recording at a conscious state 1 to 5 days after acute CO poisoning. They received no sedation. Testing was done in a quiet room. Subjects were studied in a supine or sitting position.

The electroencephalogram (EEG) disk electrodes were placed on the vertex (C2) and mastoids (A1 &
A ground electrode was placed on the forehead. Electrode impedance was kept below 5,000 ohms.

Potentials were recorded between Cz and Al and between Cz and A2 to obtain the ipsilateral (Cz-Al) and contralateral (Cz-Ac) BAEPs after monaural stimulation: i.e., with stimulation of the left ear, the Cz-A1 response was the ipsilateral BAEP (Cz-Al) and the Cz-A2 response was the contralateral BAEP (Cz-Ac). In 2 cases, only the ipsilateral response was obtained.

The potentials were amplified to a gain of 10³, filtered with a band pass of 150 to 1,500Hz, sampled at a rate of 10 per second, and averaged to 2,000 times by a computed signal average (the Nicolet CA 1,000). The averaged potentials were recorded with an X-Y plotter. The usual analysis time of the potential was 10 msec. However, a 15 msec analysis was sometimes used to improve delineation.

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 75 dB, although in some cases an intensity of 85 dB was used to obtain better wave forms.

Positivity of BAEP was shown by an upward deflection. The waves were labeled according to the method of Jewett and Williston (1970). Latency was measured from the onset of the stimulus to the positive peak; amplitude was measured from peak to peak. When wave 1 showed prolonged latency, all interpeak latencies (IPL) were measured. A latency or an interpeak latency was judged "prolonged" when the value was more than two standard deviations (SD) from normal mean values (Table 1). When BAEP was abnormal, the recordings were repeated at least twice to confirm a consistent abnormality. If the repeated tracing failed to confirm any consistent waves, BAEP was labeled "no potential".

Follow-up BAEPs were obtained in 11 cases 2 weeks to 2 months after acute anoxic insult. There were 6 initial BAEP abnormalities, 2 prolonged coma and 3 delayed neurologic sequelae which developed later.

**RESULTS**

Of 32 cases, eight exhibited abnormal BAEPs (Table 2). Among the eight abnormal BAEPs, six (cases 3 to

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**Table 1. Normal values of BAEPs**

<table>
<thead>
<tr>
<th>Waves (PL)</th>
<th>Latency</th>
<th>S.D.</th>
<th>+2 S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>Mean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1.50-2.22</td>
<td>1.80</td>
<td>0.16</td>
</tr>
<tr>
<td>II</td>
<td>2.68-3.20</td>
<td>2.91</td>
<td>0.14</td>
</tr>
<tr>
<td>III</td>
<td>3.54-4.50</td>
<td>3.96</td>
<td>0.22</td>
</tr>
<tr>
<td>IV</td>
<td>4.52-5.60</td>
<td>5.05</td>
<td>0.26</td>
</tr>
<tr>
<td>V</td>
<td>5.36-6.42</td>
<td>5.87</td>
<td>0.22</td>
</tr>
<tr>
<td>(I-II)</td>
<td>0.94-1.34</td>
<td>1.13</td>
<td>0.10</td>
</tr>
<tr>
<td>(II-III)</td>
<td>0.60-1.16</td>
<td>0.95</td>
<td>0.13</td>
</tr>
<tr>
<td>(III-V)</td>
<td>1.50-2.34</td>
<td>1.92</td>
<td>0.17</td>
</tr>
</tbody>
</table>

(35 subjects, 70 ears; age range: 19-58; 75 dB)
Table 2. Clinical data and summary of brainstem auditory evoked potential abnormalities

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Duration of Unconsciousness (days)</th>
<th>Right BAEP</th>
<th>Left BAEP</th>
<th>C-T findings</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>F</td>
<td>3½</td>
<td>Prolongation of latency to waves I-V and II-III and III-V IIIs (Fig. 2)</td>
<td>No potentials</td>
<td>Low densities in both B.G. and white matter of cerebral cortex</td>
<td>Decerebrate rigidity</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>M</td>
<td>31</td>
<td>Prolongation of latency to waves II-V and II-III IPL</td>
<td>No potentials</td>
<td>Same as the above (Fig. 4)</td>
<td>Decerebrate rigidity</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>M</td>
<td>98</td>
<td>Prolongation of latency to wave 1 (2.52 msec)</td>
<td>Prolongation of latency to wave 1 (2.64 msec)</td>
<td>Normal</td>
<td>Prolonged coma</td>
</tr>
<tr>
<td>4</td>
<td>24</td>
<td>M</td>
<td>3</td>
<td>Prolongation of latency to wave 1 (2.65 msec) (Fig. 1)</td>
<td>Normal</td>
<td>Low densities with contrast enhancement in both B.C. (Fig. 5)</td>
<td>Normal audiogram</td>
</tr>
<tr>
<td>5</td>
<td>28</td>
<td>M</td>
<td>3</td>
<td>Prolongation of latency to wave 1 (2.64 msec) (Fig. 3)</td>
<td>Prolongation of latency to wave 1 (2.22 msec)</td>
<td>Normal</td>
<td>Normal audiogram</td>
</tr>
<tr>
<td>6</td>
<td>45</td>
<td>M</td>
<td>2</td>
<td>Normal</td>
<td>Prolongation of latency to wave 1 (2.22 msec)</td>
<td>Normal</td>
<td>Normal audiogram</td>
</tr>
<tr>
<td>7</td>
<td>17</td>
<td>F</td>
<td>2</td>
<td>Prolongation of latency to wave 1 (2.14 msec)</td>
<td>Prolongation of latency to wave 1 (2.16 msec)</td>
<td>Normal</td>
<td>Normal audiogram</td>
</tr>
<tr>
<td>8</td>
<td>73</td>
<td>F</td>
<td>1</td>
<td>Normal</td>
<td>Prolongation of latency to wave 1 (2.24 msec)</td>
<td>Normal</td>
<td>Normal audiogram</td>
</tr>
</tbody>
</table>

IPL: interpeak latency  B.C.: basal ganglia

8) displayed a similar abnormality which was prolongation of latency to wave 1 without prolongation of interpeak latency (Fig. 1).

Cases 1 and 2 also had a similar abnormality showing prolongation of latencies to waves and interpeak latencies (Fig. 2). In case 1, latencies to waves 1-V (2.94, 3.60, 5.46, 9.60, and 9.84 msec) and II-III and III-V interpeak latencies (1.86 and 4.38 msec) were markedly prolonged, and in case 2, latencies to waves II-V (3.20, 4.76, 6.36, and 6.96 msec) and II-III interpeak latency (1.56 msec) were prolonged.

All cases but one (case 8) showing BAEP abnormality had an unconscious duration of more than 24 hours during acute anoxia insult (Table 3). Thus the incidence of BAEP abnormality tended to increase in accordance with the duration of unconsciousness during acute CO poisoning.

Table 3. The incidence of BAEP abnormality in accordance with the duration of unconsciousness during acute CO poisoning

<table>
<thead>
<tr>
<th>Duration (hours)</th>
<th>No. Tested</th>
<th>No. of Abnormal BAEPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>12 – 24</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>24 – 48</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>48 – 72</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>72</td>
<td>5*</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>8</td>
</tr>
</tbody>
</table>

* Four died-two of anoxia, and two of infection

Number 1
Fig. 3. (A) BAEPs from case 5 on the third day after CO poisoning showed bilateral prolongation of latency to wave I. (B) Follow-up BAEPs 14 days later showed normal.

Fig. 4. CT scan showed low densities in both basal ganglia and the white matter of the cerebral cortex (case 2).

Fig. 5. CT scan from case 4 showed low densities (A) with contrast enhancement (B) in both basal ganglia.

Of 8 cases with abnormal BAEPs, audiograms could be obtained in five cases and all were normal. Ten out of 11 cases of follow-up BAEPs were revealed as normal. Among 6 initial abnormal BAEPs (cases 3 to 8), five returned to normal from 2 weeks to 1 month after acute anoxia (Fig. 3), but one (case 3) had no interval change even 2 months later, and the auditory function could not be evaluated clinically due
to prolonged coma. Follow-up BAEPs were revealed as normal in 2 cases of prolonged coma showing initial normal BAEPs and in 3 cases which later developed delayed neurologic sequelae.

Computed tomographic (CT) brain scans were obtained in 13 cases. Four showed low densities in both the basal ganglia and the white matter of the cerebral cortex (Fig. 4), two showed low densities in only the basal ganglia (Fig. 5), one showed decreased density in only the cerebral cortex, and six were normal. There was no correlation between the abnormalities of BAEPs and CT-brain scans.

Out of the 32 cases, four patients died-two (cases 1 & 2) of hypoxia at the acute stage of anoxia, and two of infection 2 months after anoxia.

**COMMENT**

Carbon monoxide reversibly interacts with hemoglobin and causes tissue anoxia (Haldane, 1895; Finck, 1966). There are at least two topographical patterns of anoxic-ischemic alterations in the central nervous system – a rostrocaudal pattern of decreasing vulnerability and a pattern of brainstem and thalamic damage (Leech and Alvord, 1977).

In human adults, there is the well-recognized rostrocaudal pattern of decreasing vulnerability with the cerebral cortex. The hippocampus and cerebellar cortex are the most sensitive and the brainstem is the least sensitive. The brainstem involvement in the adult is rarely seen and is usually restricted to the substantia nigra, inferior colliculi and inferior olives (Brierley et al., 1973; Leech and Alvord, 1977).

Statement has been made that a patient has a poor prognosis if acute CO poisoning is accompanied by of prolonged coma (more than 72 hours), severe hypoxemia, hyperthermia, and other complications (Choi, 1983a); but in fact, it is difficult to decide the prognostic values during acute anoxic insult. When the patient exhibited decerebrate rigidity during a comatose state, the brainstem involvement was suspected clinically (Plum and Posner, 1980), but assessing the brainstem function using laboratory tests was difficult. Changes in the brain after acute CO poisoning have mainly been investigated at necropsy. Although a CT brain scan can establish a lesion of the cerebral cortex and basal ganglia in CO poisoning (Swada et al., 1980), the brainstem lesion is usually missed.

BAEP is thought to be the far-field recording of sequential electrophysiologic events at successively higher levels of the brainstem auditory pathway (Jewett, 1970). In animals, the primary generators of waves 1-V are the cochlear nerve, the cochlear nuclei, the superior olivary complex, and the lateral lemniscus and inferior colliculi, respectively (Jewett, 1970; Buchwald and Hwang, 1975).

In humans, similar location of BAEPs were reported (Starr and Achor, 1975; Starr and Hamilton, 1976; Stockard and Rossiter, 1977; Hashimoto et al., 1979).

The present study demonstrated that a large number of cases of CO poisoning exhibited intact BAEPs and some CO poisoning cases exhibited abnormal BAEPs. There are at least two patterns of BAEP abnormalities in this study: a peripheral pattern of prolongation of latency to wave I without prolongation of interpeak latency, and a central pattern of prolongation of latencies to all waves and interpeak latencies.

It has been suggested that the peripheral pattern of BAEP abnormality involves the cochlear nerve. An interpretation of BAEPs in comatose patients usually requires caution, because non-neurologic factors may affect the responses and produce false localizing signs. For example, some comatose patients (15%) exhibited increased absolute latencies of major peaks suggesting a conductive-type hearing loss, but interpeak latency is not affected by conductive-type hearing loss (Uziel et al., 1982). Prolonged BAEP latencies may also represent a temporary conductive hearing deficit brought about by the inability of comatose patients to equilibrate middle ear pressure (Starr, 1977). A conductive hearing deficit may also be brought about by hyperbaric oxygen therapy in acute CO poisoning (Yun and Cho, 1977). In this study, the above affecting factors could be excluded; all patients except cases of prolonged coma performed BAEPs at a conscious state, and some of the cases displaying abnormal BAEPs didn't receive hyperbaric oxygen therapy. The peripheral pattern of BAEP abnormality usually returned to normal within one month.

The central pattern of BAEP abnormality (cases 1 and 2) was due to the possible involvement of the brainstem. Uziel and Benezech (1978) observed a clinical significant relationship between BAEP abnormality and the various clinical signs usually considered as evidence of known anatomical level of dysfunction, alteration of wave III to a pontine level, and alteration of wave 1 and 2 and subsequent waves was related to a lower brainstem dysfunction. Thus, BAEPs also have a prognostic value in comatose patients. Uziel and Benezech et al., (1982) observed that the major alterations which concerned waves III-V seemed to provide a particularly poor prognosis. Findings in cases 1 and 2 in this study agree with this assumption.
In conclusion, the results of the present study suggest that BAEPs can be used for evaluating the functional integrity of the auditory pathways, and for providing prognostic values in cases of acute CO poisoning.

REFERENCES


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