Brainstem Auditory Evoked Potentials (BAEPs) Study in Chronic Arsenic Poisoning Patients

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Objectives: *To explore the possible neurotoxicity of arsenic to auditory sensory pathways and evaluate roles of BAEPs in the detection of early brain damage resulting from arsenic exposure.*
Design: *Cross-sectional analytic study.*
Material and Method: *Twenty nine females with skin lesions consistent with arsenical dermatoses and 27 controls who met the inclusion criteria were investigatetd by Auditory Evoked Potentials (AEPs). Case findings resulted from a house-to-house survey in village 12, Ronphibun subdistrict and village 5, Saothong subdistrict, Nakhon Si Thammarat Province, southern Thailand in 1995.*
Results: *Differences between the arsenic-exposed population and the referent group regarding BAEP parameters, BAEP latencies and interpeak latencies were not found.*
Conclusion: *Evidence of the abnormalities of the auditory sensory pathways was not found among female patients with arsenical dermtoses in Ronphibun. The role of BAEPs in the detection of brain damage resulting from arsenic exposure could not be demonstrated.*

Keywords: *Arsenic, Arsenical dermatoses, Brainstem evoked potentials, BAEPs, Auditory evoked potentials, AEPs, CNS*

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The involvement of the CNS among arsenic poisoning patients is not common. It can be found in acute and subacute arsenic poisoning and rarely in chronic arsenic poisoning [1]. Several authors reported cases of arsenic poisoning presented with encephalopathy [2-7].

Auditory evoked potentials (AEPs) are the averaged electrical responses of the central nervous system following the repetitive auditory stimulation. The short latency AEPs comprise peaks of up to 10 milliseconds (msec) after the stimulus and are presumably generated from the brainstem structures. Brainstem auditory evoked potentials (BAEPs) are called for this part of AEPs. BAEPs have been applied widely to the examination of the integrity of brainstem nuclei and peripheral auditory pathways. They provide objective and reproducible data and are used extensively in patients with suspected multiple sclerosis, acoustic neuroma or pontine gliomas.

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They are also applied to detect the abnormalities resulting from neurotoxicant exposure, lead, n-hexane, toluene [8-10]. A few reports have been published on BAEP results in patients with arsenic poisoning [5, 11].

The aim of this study was to explore the possible neurotoxicity of arsenic to auditory sensory pathways and evaluate roles of BAEPs in the detection of early brain damage resulting from arsenic exposure.

Material and Method

In the present study, BAEPs were applied on the female patients with skin lesions consistent with arsenical dermatoses and the BAEP results were compared to those obtained from the controls.

The arsenic-exposed group

The group consisted of 29 females aged between 20-59 years who had arsenic exposure via drinking arsenic-contaminated shallow-well water in the past (arsenic level in shallow-well water was >0.01 mg/l) and who had skin lesions consistent with the diag-

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nosis of arsenical dermatoses. Case findings resulted from a house-to-house survey in village 12, Ronphibun subdistrict, Nakhon si Thammarat Province, southern Thailand in 1995. Shallow wells in this community were contaminated with arsenic which resulted from the past tin mining activities. The patients were admitted for the BAEP study if they met the selection criteria mentioned in elsewhere [12].

The referent group

The group consisted of 27 females aged between 20-59 years who drank water from shallow wells which had a low level of arsenic (WHO recommended level < 0.01 mg/l). These referent subjects were selected from the results of a house to house survey in village 5, Saothong subdistrict, Nakhon Si Thammarat Province, southern Thailand in 1995. They were admitted to the study if they met the criteria mentioned in elsewhere [12].

Audiological examination

The author explained the details of BAEP investigation and the objective of the study to every subject before the study was initiated. Informed consent was obtained from these subjects. Every subject had been examined in their external auditory canals with an auroscope and removal of foreign objects and excessive earwax was performed on each subject if needed.

The brainstem evoked potentials (BAEPs)

The BAEP recordings were performed in a quiet room. Electrode application followed the International 10/20 System of Electrode Placement. Figure 7-2 shows the 10-20 system of electrode placement. Silver-silver chlorided cup electrodes were attached on each earlobe (A1, A2), at the vertex (Cz, as the positive electrode) and on the forehead (as a ground electrode). Before any electrodes were applied, the area of application was cleaned with an abrasive cleanser. A contact cream was then applied to the electrode and placed over the prepared area. A cotton ball was placed over the electrode to prevent drying and subsequent loss or shifting of the electrode. The electrode impedances were checked and were kept lower than 3,000 ohms. The subjects lay on a bed and their neck muscles were relaxed by placing pillows under their heads and adjusting the position of the bodies.

The subjects wore earphones and were advised to sleep during the investigation. The hardware and the software used were the Bio-logic^{a} Version 5.10 Model: 752. Condensation clicks were presented monaurally through earphones at a repetition rate of 13 per second. The intensity of the click stimulus was 65 dB above the individual ear's threshold, while a white masking noise at a level of -40 decibels was applied on the contralateral non-stimulating ear. A total of 1,024 responses were averaged for each record. Each ear was tested separately and at least two trials were performed on each subject in order to ensure reproducibility. The low-frequency filter was set at 100 Hz, while the high filter was set at 3,000 Hz. The analysis time was 10.24 millisecond. The duration of the trial was about 30 minutes.

Absolute latencies were measured from the stimulus to the positive peaks. The absolute latencies of wave I, III and V were measured. The interpeak latencies (IPLs) between wave I-III, III-V and I-V were also measured. In order to reduce inter-observer variation, only one neurologist operated the EP equipment and marked the EP components. The neurologist who operated the EP equipment had trained in the United States for one year and had more than five years' experience operating the EP equipment. He did not know the arsenic exposure history and the medical history of subjects.

Results

The subjects in the exposed group and referent group were females aged between 20-59 years. The average ages between the subjects of these two groups were comparable. Regarding the average arsenic concentrations in hair, nails and shallow well water, they were higher in the exposed group compared with the referent group.

Table 1 shows the absolute latencies of wave I, III, V and interpeak latencies of I-III, III-V, and I-V from right ears. It was found that the means of those latencies in the exposed group were not significantly different from those in the referent group ($p>0.05$). According to table 2, most of the minimum and maximum BAEP parameters (wave I, III, V absolute latencies and I-III, III-V and I-V interpeak latencies) in the exposed group were similar to the referent group except for the I-V interpeak latency. The maximum value of the I-V interpeak latency in the exposed group was obviously longer than that of the referent group (4.21 and 3.98 msec, respectively). However, the mean of this latency in the exposed group was not significantly different from that in the referent group ($p>0.05$).

Discussion

The controls lived in an area in which arsenic

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Table 1. Comparison of BAEP latencies obtained from the subjects in the exposed group and the referent group

Latency (msec)	Exposed group (n=29)	Referent group (n=27)	Statistical values
Wave I	1.59±0.157	1.58±0.189	t=0.24, p=0.81
Wave III	3.58±0.229	3.48±0.195	t=1.73, p=0.09
Wave V	5.37±0.242	5.28±0.205	t=1.60, p=0.12
IPL I-III	1.99±0.174	1.90±0.172	t=1.93, p=0.06
IPL III-V	1.79±0.124	1.80±0.132	t=0.10, p=0.92
IPL I-V	3.79±0.200	3.70±0.201	t=1.59, p=0.12

Remark: BAEP presented as mean ± standard deviation IPL = Interpeak latency

Table 2. Ranges of wave I, III, V absolute latencies and I-III, III-V, I-V interpeak latencies obtained from the subjects in the exposed group and the referent group

	Exposed group (n=29)	Referent group (n=27)
Wave I	1.33-1.79	1.33-1.95
Wave III	3.08-4.02	3.16-3.95
Wave V	4.91-5.73	4.95-5.81
IPL I-III	1.56-2.38	1.60-2.30
IPL III-V	1.48-1.99	1.37-1.97
IPL I-V	3.43-4.21	3.20-3.98

Remark: IPL = Interpeak latency

in the environment was low. The low concentrations of arsenic in hair, nails and shallow-well water provided the evidence [12]. The subjects in the exposed group lived in the arsenic contaminated area. Past arsenic exposure of the subjects in the exposed group was confirmed by the presence of skin manifestations characteristic of chronic arsenic poisoning.

It was recognised that age and gender could affect the BAEP results [13,14]. The older persons had longer I-V interpeak latency than the young subjects [15]. The females had shorter absolute and interpeak latencies than males [16]. In the present study, the subject variables including age and gender were comparable between the exposed and the referent group. Only females aged between 20-59 years were included in the present study. All subjects had no appreciable hearing loss and had no history of alcoholism which might affect the BAEP results.

BAEP components also were affected by stimulus parameters such as stimulus repetition rate, intensity and polarity [13, 14, 16]. In the present study, the same stimulus parameters were applied to all subjects. In order to reduce inter-observer variation, only one neurologist operated the EP equipment and measured the BAEP parameters.

BAEPs were applied to detect the abnormalities resulting from neurotoxicant exposure. Otto et al studied children at risk of lead poisoning and found increases of wave III and wave V latencies [8]. Chang reported prolongation of the wave I-V interpeak latencies among patients with n-hexane poisoning [9]. Abnormal BAEP results were also documented in chronic toluene sniffers [10, 17]. Regarding the BAEPs results obtained from the toluene abuser, Rosenberg et al reported on the prolongation of the wave V latency, the III-V interpeak latency and the I-V interpeak latency when compared with the controls [10].

CNS involvement resulting from arsenic exposures is not common. BAEPs have rarely been applied to patients with arsenic poisoning who ingested a massive dose of arsenic. Goebel reported normal BAEPs in a patient with arsenic neuropathy [6]. Fincher and Koerker reported low amplitude of AEPs in a patient with arsenic encephalopathy [5].

In the present study, the means of the absolute latencies of Wave I, III, V and the interpeak latencies of I-III, III-V and I-V showed no significant differences between those obtained from the subjects in the exposed group and those in the referent group. This may be explained by two reasons. Firstly, the subjects in the present study were not exposed to arsenic in high doses or long enough to cause the conduction defect in the brain stem auditory pathway between the eighth nerve and the inferior colliculus. Secondly, the BAEPs were not affected by arsenic exposures. Unfortunately, BAEP studies in human and animal populations exposed to arsenic have rarely been conducted. Comparison of the BAEP results among the different studies were limited.

In summary, the present study failed to identify the role of BAEP in the detection of early brain damage resulting from chronic arsenic exposure via drinking water.

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การศึกษาการชักนำของระบบประสาทการได้ยินในคนไข้พิษสารหนูเรื้อรัง

สุนทร ศุภพงษ์, จิรุตม์ ศรีรัตนบัลล์

วัตถุประสงค์: *เพื่อค้นหาความผิดปกติของการชักนำของระบบประสาทการได้ยินในคนไข้เพศหญิงที่มีอาการแสดงทางผิวหนังจากพิษสารหนูเรื้อรังโดยเปรียบเทียบกับกลุ่มควบคุม และประเมินบทบาทของการศึกษาการชักนำของระบบประสาทการได้ยินในการตรวจหาความผิดปกติของระบบประสาทการได้ยินในคนไข้พิษสารหนูเรื้อรัง*

รูปแบบการวิจัย: *การศึกษาเชิงวิเคราะห์แบบตัดขวาง*

วัสดุและวิธีการ: *คนไข้เพศหญิงที่มีอาการแสดงทางผิวหนังจากพิษสารหนูเรื้อรัง จำนวน 29 คน และกลุ่มควบคุมจำนวน 27 คน ที่ตรงกับเกณฑ์การคัดเลือกเข้าศึกษา ได้รับการตรวจการชักนำของระบบประสาทการได้ยินโดยประชากรในกลุ่มศึกษาและกลุ่มควบคุมได้จากการสำรวจชาวบ้านในหมู่ที่ 12 ตำบลร่อนพิบูลย์ และหมู่ที่ 5 ตำบลเสาธง อำเภอร่อนพิบูลย์ จังหวัดนครศรีธรรมราช ในปีพุทธศักราช 2538*

ผลการศึกษา: *ไม่พบความแตกต่างของค่าเฉลี่ยเวลาชักนำประสาทของคลื่นที่ I, III และ V และเวลาชักนำประสาทระหว่างคลื่นที่ I และ III, III และ V และ I และ V ของกลุ่มที่ศึกษาและกลุ่มควบคุม*

สรุป: *การศึกษานี้ไม่พบหลักฐานความผิดปกติของการชักนำของระบบประสาทการได้ยินในคนไข้เพศหญิงที่อยู่ในตำบลร่อนพิบูลย์ที่มีอาการแสดงทางผิวหนังจากพิษสารหนูเรื้อรัง และไม่พบบทบาทของการศึกษาการชักนำของระบบประสาทการได้ยินในการตรวจหาความผิดปกติของระบบประสาทการได้ยินในคนไข้พิษสารหนูเรื้อรัง*

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