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ORIGINAL ARTICLE

Auditory brain stem responses in the detection of brain death

Beyin ölümü tanısında işitsel beyin sapı yanıtları

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Objectives: We evaluated comatose patients by auditory brain stem responses (ABR) to determine the role of ABR in the diagnosis of impending brain death.

Patients and Methods: Sixty comatose patients in the intensive care unit were evaluated by brain stem evoked response audiometry. Correlations were sought between the absence or presence of ABRs and the presenting pathology, the Glasgow Coma Scale (GCS) scores, and ultimate diagnoses.

Results: The brain stem responses were totally absent in 41 patients. Presence of wave I could be obtained in only 10 patients. All the waveforms were found in nine patients; however, in eight patients the potentials disappeared as the GCS scores decreased to 3. Detection of wave I alone strongly suggested dysfunction of the brain stem. However, loss of wave I particularly in trauma patients aroused doubt as to whether the absence was associated with auditory end organ injury or brain stem dysfunction.

Conclusion: The results suggest that evaluation of ABR may support brain death in a comatose patient *(i)* when wave I is present alone, *(ii)* the absence of wave I is accompanied by a documented auditory end organ injury, or *(iii)* when previously recorded potentials are no longer detectable.

Key Words: Brain death/pathology/diagnosis; brain injuries/etiology; brain stem/pathology/injuries; coma/etiology; evoked potentials, auditory, brain stem.

Amaç: Komadaki hastalarda beyin ölümü tanısını desteklemede işitsel beyin sapı yanıtlarının (ABR) değeri araştırıldı.

Hastalar ve Yöntemler: Komadaki 60 hastanın yoğun bakım ortamında işitsel uyarılmış beyin sapı yanıtları kaydedildi. Beyin sapı yanıtlarının varlığı ya da yokluğu ile var olan patoloji, Glasgow Koma Skalası (GCS) skorları ve nihai tanılar arasında ilişki araştırıldı.

Bulgular: Kırk bir hastada beyin sapı yanıtları alınamadı. Birinci dalga yalnızca 10 hastada kaydedilebildi. Dokuz hastada tüm dalgalar vardı; bunların sekizinde GCS skoru 3'e düştüğünde yanıtlar alınamadı. Yalnızca birinci dalganın varlığı kuvvetle beyin sapı disfonksiyonuna işaret etmekteydi. Ancak, özellikle travma geçirmiş olgularda birinci dalganın kaybı kokleanın veya sekizinci sinirin travmadan etkilenmesine bağlı olabileceğinden, beyin ölümü kararını destekleyici bulunmadı.

Sonuç: Çalışmamız, *(i)* birinci dalganın tek başına bulunması durumunda, *(ii)* işitme organı hasarının saptandığı olgularda birinci dalganın alınamaması durumunda; ya da *(iii)* daha önce kaydedilebilmiş dalgaların izlem süresi içinde kaybolması durumunda ABR'nin beyin ölümü tanısını destekleyebileceğini gösterdi.

Anahtar Sözcükler: Beyin ölümü/patoloji/tanı; beyin yaralanmaları/etyoloji; beyin sapı/patoloji/yaralanma; koma/etyoloji; uyarılmış potansiyeller, işitsel, beyin sapı.

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Diagnosis of brain death requires evidence of irreversible destruction or dysfunction of neurons in the brain stem and the cerebrum.

Patients sustaining intracranial pathologies are evaluated by several methods in intensive care units (ICU). Monitoring the vital signs such as blood pressure, heart rate, oxygen levels, and body temperature is always essential. Evaluation of the neurological status is extremely important. The Glasgow Coma Scale (GCS), papillary reactions to light, corneal reflex, and eye movements are highly significant indicators of prognosis.

However, findings from all these methods should be incorporated into a definitive diagnosis of brain death with the use of several complementary diagnostic tools. One way to assess the cessation of brain stem function may be through measuring auditory brain stem responses (ABR) in comatose patients, in whom the brain stem is the primarily affected organ.

The elicitation of ABRs is simple and easy in ICU settings. It is a non-invasive procedure and imposes no risks on the patient. Moreover, ABRs can be reliably interpreted at the bedside with high precision and validity. Its findings are not confounded by central nervous system (CNS) depressants[1] and highly correlated with those of other complementary tests including clinical neurological examination and cerebral electrophysiologic tests such as EEG and sensory-evoked responses.

This study was designed to evaluate brain death with the use of ABRs among comatose patients with various GCS scores.

MATERIALS AND METHODS

Sixty comatose patients (38 males, 22 females; mean age 47 years; range 15-67 years) in the intensive care unit were evaluated by brain stem audiometry. The clinical findings and GCS were recorded. The patients were not diagnosed as having brain death at the time of ABR recordings.

Patients with a GCS score less than 10 were supported by mechanical ventilation to keep the P_aCO_2 values between 25 and 30 mmHg. Those presenting with no cardiac disease underwent computed axial tomography scan of the brain at regular intervals.

The recording system was adapted for use in accordance with the ICU settings, with the electrode impedances being below 5 Kohms and all interferences by electrical equipment being eliminated. Stimuli were delivered through ear-phones at a rate of 11 stimulus per second for 0.1 msec duration with non-filtered alternating clicks at 110-120 dB sound pressure level. Exposure to 60 dB white noise was used to mask the other ear. The responses were analog filtered with a band pass between 200 Hz and 2000 Hz. Two sets of 2000 clicks were applied to each side to ensure that consistent wave forms were recorded. Analyses were conducted on the data recorded from the electrodes placed on the vertex (Cz) and bilaterally on the posterior side of the lobule of the pinna (A1 and A2) and on the midline of the forehead (Ground). The recordings were made by the use of the Amplaid MK 15 system.

RESULTS

The main etiologic factor was traffic accidents causing injury to the brain tissue and hematoma. The main pathology was subarachnoid hematoma resulting from aneurysm of the brain vessels and intracranial injury. None of the patients in the study group had drug intoxication (Table I).

Auditory evoked potentials were absent in 41 patients. Wave I could be obtained in only 10 cases (Fig. 1). All the waveforms were found in nine cases; however, in eight patients the potentials disappeared as the GCS scores decreased to 3. Five patients were transferred to another hospital for organ donation.

The GCS scores ranged from 3 to 6 in cases in which evoked potentials could not be obtained. On

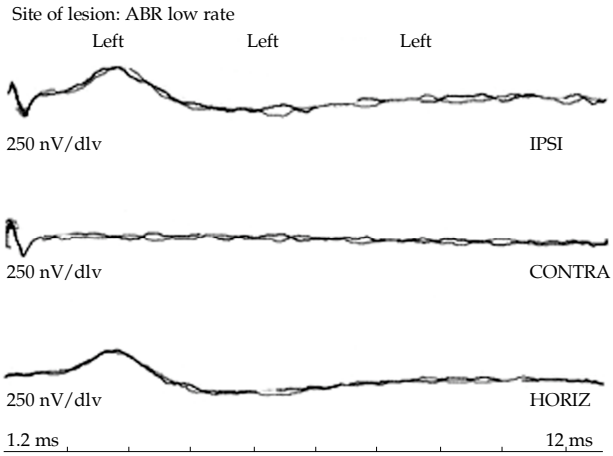

Fig. 1– Brain stem auditory evoked response audiometry of a patient having wave I.

TABLE I

ETIOLOGIC FACTORS, GCS SCORES, AND ABR FINDINGS IN COMATOSE PATIENTS

Etiologic factor	Pathology	GCS on admission	ABR	Outcome
Subarachnoid hemorrage (37 patients)	Aneurysm (n=13)	GCS 3 (n=6)	No potentials	All died
		GCS 4-6 (n=4)	Wave I in 2 patients (GCS 6) No potentials in the others	All died
		GCS 7-14 (n=3)	Wave I in 2 patients (GCS 13, 14) No potentials in the others	All died
	Traffic accident (n=15)	GCS 3 (n=11)	No potentials in 9 patients	8 died, 1 transferred
			Wave I in 2 patients	1 died, 1 transferred
		GCS 4-6 (n=4)	No potentials	All died
	Tumor (n=1)	GCS 3	No potentials	Died
	Hypertension (n=3)	GCS 3, 5 and 7	Wave I in one patient with GCS 5, no potentials in the others	All died
	Gun shot (n=1)	GCS 3	Wave I	Died
	Falling from height (n=4)	GCS 3	No potentials	3 died, 1 transferred
Infarct of the cerebral tissue (4 patients)	Cerebrovascular pathology	GCS 3 - 7	No potentials	All died
Injury to the cerebral tissue (10 patients)	Traffic accident (n=9)	GCS 3 (n=7)	Wave I in 2 patients No potentials in the others	All died
		GCS 5 and 8	Normal wave pattern disappeared afterwards	All died
	Lance-Adams syndrome (n=1)	GCS 7; later 3	Normal wave pattern disappeared afterwards	Transferred
Cardiac arrest (5 patients)	Cardiac arrest	GCS 3 (n=3)	No potentials	All died
		GCS 8 and 10	Normal wave pattern disappeared afterwards	1 discharged, 1 died
Other causes (4 patients)	Traffic accident: spleen rupture (n=1)	GCS 15; later 3	Normal wave pattern disappeared afterwards	Died
	Bronchial asthma: acute respiratory insufficiency (n=2)	GCS 15; later 3	Normal wave pattern disappeared afterwards	Died
	Post laparoscopic disseminated intravascular coagulation (n=1)	GCS 6; later 3	Normal wave pattern disappeared afterwards	Transferred

the other hand, all potentials were detectable in all patients with a GCS score above 8. The GCS score seemed to be in correlation with the presence of ABRs during admission; however, disappearance of ABRs was observed as the GCS scores dropped to very low values.

DISCUSSION

The diagnosis of brain death has to be established on evidence of irreversible destruction of the neurons within the brain and the brain stem. The initial response of the brain tissue to trauma is edema, which results in serious injury and increased

intracranial pressure compressing the vascular network.

Until recently, the diagnosis of brain death was based on neurological examination and EEG findings. However, these methods have proven to be of little value especially in drug intoxication and barbiturate-induced comas. In contrast, auditory brain stem responses are not seriously influenced by central nervous system depressants, including therapeutic high doses of barbiturates and the quality of recordings is often enhanced by elimination of the muscle artifact in chemical paralysis. They are mostly affected by hypothermia.[1]

An ideal evaluation method in an ICU environment should not be invasive, should do no detriment to the patient, and should be repeatable. It has to allow the use of portable instruments nearby the patient's bed without interrupting or interfering with the main treatment given to the patient. Moreover, it should yield objective and reliable findings and give information on the different levels of the CNS. Finally, implementation of the test should be independent from the consciousness level of the patient and its findings should not be influenced by medications such as sedatives and barbiturates. Recording ABRs in an ICU patient conveniently satisfies all the above mentioned prerequisites.

In a comatose patient with an intact peripheral auditory system, the evidence of a change in, or loss of, an ABR wave pattern indicates a poor prognosis.

Auditory brain stem responses are inevitably absent whenever function of either the cochlea or the brain stem is lost. Since wave I is generated by the cochlear nerve itself, the presence of wave I in the absence of other waves may indicate abnormal brain stem function and possible brain stem death. If wave I is also absent then it is not possible to draw a conclusion regarding the state of the brain stem. Whether loss of wave I is due to auditory end organ dysfunction or to irreversible changes in the brain stem remains unresolved.[2]

Otoacoustic emissions (OAE) are emitted by the hair cells in the cochlea. It is possible to detect click-evoked otoacoustic emissions in cases with normal cochlear function even if the cochlear nerve and the brain stem are affected. Thus, the presence of click-evoked OAEs verifies normal cochlear function and supports brain death in cases in which the auditory evoked brain stem responses are absent.

Dear and Godfrey[3] reported two newborn infants who showed noticeable signs of brain stem dysfunction in the presence of detectable wave I, indicating the activation of the cochlea and the eighth nerve. When the auditory brain stem components are not detected, the possibility of a lesion of the peripheral auditory apparatus cannot be excluded; therefore, no inference can be drawn about brain stem function. This is especially important in very immature infants in whom detectable auditory brain stem responses may not have yet developed. Although the transient disappearance of the auditory brain stem response waveforms remains a matter of speculation in the newborn, it seems clear that this is associated with neuronal damage due to swelling-induced compression in the brain tissue.[3]

The presence of wave I in the absence of other waves is generally believed to be a significant prognostic indicator for brain death, suggesting that the auditory end organ is intact while the higher structures are not functional. The absence of wave I, however, do not invariably support the diagnosis of brain death. Especially in cases with temporal bone trauma, the possibility of auditory end organ injury should be eliminated. In these cases, computed axial tomography may not be specific enough to determine whether the end organ is functional or not.[4]

As death following a traumatic or vascular coma mainly occurs in the first week and especially within the first 48 hours after the accident, normal ABR recordings obtained within the first days of coma may predict a favorable prognosis.[5]

Transient ABR changes lasting from minutes to hours are frequently encountered in comatose patients. Many of these may not necessarily signify a pathologic event and may be associated with alterations in temperature. However, when these changes correspond to clinically relevant episodes, they may be regarded as an early sign of brain stem dysfunction, especially in the presence of associated critical alterations in other parameters such as the intracranial pressure. It happens that more than 90% of patients show progression to brain death in the following hours or days. This association, even though ABR changes are transient and totally reversible, may be a reliable sign of a fatal progno-

sis.[6] Hence, the presence of ABR stability is the only desirable finding during coma monitoring; the detection of a wave I component, without wave III or V, is the most clear-cut ABR predictor compatible with brain death.

Mjoen et al.[7] pointed out that integrity of wave I and loss of other waves indicated activity in the intracranial structures and, therefore, was inconsistent with a diagnosis of brain death.

Garcia-Larrea et al.[6] revised the criteria to distinguish changes associated with CNS dysfunction from those of non-pathologic causes. In non-pathologic conditions ABRs did not manifest statistically significant changes and the latencies essentially remained within normal limits. In contrast, termination of the wave pattern was prominent in patients exhibiting progressive irreversible changes before brain death.

Kaga et al.[8] demonstrated that irreversible changes in the brain stem and the temporal bone had occurred hours before death.

The era of organ transplantation has not only offered considerable hope for cure to many chronically ill patients and their families, but also imposed a matter of time factor on the determination of brain death, for which a complex host of moral, ethical, medical and medico-legal issues should be considered. Some erroneous declarations on potential donors in organ transplant centers have appreciably aroused significant concern about the real incidence of brain death.

For serious brain injuries, a GCS score of 8 is accepted as a threshold value. In patients who do not have brain stem injuries, auditory brain stem responses are not influenced by the severity of coma, suggesting that it is possible to detect ABRs regardless of a GCS score lower than 8. A very low GCS score does not necessarily indicate the absolute brain death and may be reversible. On the other hand, in the presence of a GCS score above 8, muscular artifacts may considerably affect ABRs. Although environmental conditions of ICUs are generally suitable to obtain ABRs properly, electromagnetic interference and electricity-induced noise at 60 Hz may cause problems in recording potentials. Fluorescent lamps, mechanical ventilators, monitors, and thermal blankets may give rise to artifacts. Skin impedance should be as low as possible to reduce these interfering effects.

Wave I was detected in 10 patients. Detection of wave I in the absence of other wave patterns indicates dysfunction of the upper brain stem levels, which is accepted to be specific to brain death. Auditory brain stem responses were absent in 41 cases. The loss of end organ function may also be related to the etiologic cause, especially in trauma patients. Of 24 traumatized patients, wave I was present in four patients, all of whom died within a week. Thirteen patients had temporal bone fractures (one patient with wave I). The end organ injury is more likely in cases exposed to direct temporal bone traumas. Even the absence of a fracture sign on CAT scans does not rule out the possibility of a traumatic end organ injury.

Among patients with intracranial hematoma due to aneurysm rupture, wave I could not be detected in any case. Since the hearing end organ is rarely involved in comatose patients without trauma, it is more likely that loss of all waves may indicate an ominous diagnosis of brain death in these patients.

Of cardiac arrest patients, the normal waveform was lost in two patients within a few days. This is also a very specific sign for the diagnosis of brain death.

Soustiel et al.[9] proposed that ABR recording had a reliability of 50% to 70%, and significance of 78% in the diagnosis of brain death. Guerit[10] favored ABRs as a reliable diagnostic tool in determining brain death. Serafini et al.[11] found in 21 traumatized comatose patients that ABRs were more reliable than other evaluation methods including GCS, EEG, and auditory middle latency potentials. Facco et al.[12] indicated that central latencies as shown by ABRs were in correlation with the prognosis in post-traumatic comatose patients with severe head injuries. They found with high prognostic accuracy that an interpeak latency of waves V-I greater than 4.48 msec represented irreversible damage to the brain-stem after severe head injuries.

The presence of wave I corresponds to the persistence of residual activity of the cochlear nerve. Desbordes et al.[13] found that wave I was present in 3.42% of brain-dead patients. The mean latency of wave I was longer (2.25±0.24 msec) in this group when compared with normal values (1.65±0.10 msec). The variation in wave I latencies was prominent in these cases.

It is arguable that cerebral ischemia due to cardiocirculatory arrest affects cortical structures more than subcortical ones. In particular, the auditory pathway integrity indicates partial preservation of the brain stem function, and thus, possible maintenance of residual neuronal activity. The long-lasting detection of all waveforms, at least mono-aurally, in post-ischemic anoxic encephalopathy may indicate that *(i)* the essential clinical symptoms, such as a positive apnea test and brain stem areflexia can only partially explain brain stem anatomo-functional damage, thus these usual signs do not always justify a diagnosis of brain death after a hypoxic cerebral insult; *(ii)* reliance should be placed on neurophysiologic assessment, namely auditory evoked potential responses, in confirming a brain death diagnosis. Hence, all post-anoxic encephalopathy patients should undergo neurophysiologic assessment before they are declared brain dead.[14]

It has been stated that loss of ABRs is equivalent to an isoelectric EEG in patients with supratentorial lesions, whereas in infratentorial lesions, the loss of ABRs does not confirm brain death. Demonstration of preserved wave I or ABRs followed by a subsequent evaluation showing disappearance of ABRs is mandatory for a confirmatory decision on brain death. In infratentorial lesions, a negative or pathologic result on ABRs represents dysfunction of the brain stem, but no conclusion can be drawn concerning the function of the supratentorial brain areas. Nevertheless, no patient has even been reported to survive when waves III-V were not detectable, making ABRs a highly prognostic indicator in patients showing deterioration.[15]

Facco et al.[16,17] emphasized that an essential tool will be spared in the diagnosis of brain death if ABR assessment is lacking, even though it is less reliable than somatosensory evoked potentials (SEP). They addressed the necessity of including ABR and SEP in the criteria of brain death.

In conclusion, ABR results may support brain death in conditions in which the presence of wave I is not accompanied by other wave forms. Loss of all waves in the presence of a functioning auditory end organ and then the termination of remaining wave patterns in the course of treatment may also be regarded as a reliable indicator for brain death. For a definite diagnosis, it may be necessary to support ABR findings with other diagnostic assessments such as intracranial pressure measurements or somatosensorial evoked potentials.

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