Assessment of Ultrasonic Pulse Waves in Patients with Diagnosed Brain Death

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Objective. To evaluate changes in ultrasonic pulse waves using the trans-intracranial volume-metric device (Vittamed Ltd., USA–Lithuania U.S. patent No. 5388583, European patent 0717606) in patients with diagnosed brain death.
Material and methods. Eight patients (6M, 2F, age range 37–59 years, mean age 47.4 ± 10.5 years) with the clinically and radioisotopically confirmed brain death were assessed with the trans-intracranial ultrasound and pulse waves acquired. The analysis of ultrasound pulses amplitude and waveforms was performed and then compared to the data of 34 healthy volunteers (21M, 13F, age range 8–75 years, mean age 31.3 ± 18.4 years).
Results. The non-invasively measured pulse wave amplitude in the brain death group was 1.55 ± 0.6 ns, compared to 4.04 ± 2.48 ns in the control group ($p = 0.00001$). The pulse sub-waves from brain death patients demonstrated a P1 value of 79.7 ± 16.3%, P2 value of 84.0 ± ± 14.8%, and P3 value of 85.9 ± 14.1%. The same values calculated in the control group were 97.2 ± 4.3%, 68.3 ± 22.5% and 39.6 ± 26.5%, respectively. The differences between the groups were statistically significant ($p < 0.05$).
Conclusion. The association of abnormal pulse waves and low amplitude may strongly suggest brain death, providing the diagnostic information for future manipulations.

Key words: brain death, trans-intracranial ultrasound, pulse wave analysis

Abbrevations: CBF – cerebral blood flow; CBV – cerebral blood volume; CSF – cerebrospinal fluid; CVA – cerebrovascular accident; ICP – intracranial pressure

INTRODUCTION

Evaluation of patient with suspected brain death is always followed by important medical (1, 2], ethical (3, 4), religious (5) and economic consequences. The need for further immediate management or further examination confirming the brain death must be determined as soon as possible. Trans-intracranial ultrasound device might be useful for this purpose, because it is a quick, bedside and cheep examination.

Trans-intracranial ultrasound device measures the time of ultrasound flight inside the trans-intracranial acoustic trajectory, which is a path from one internal surface of the skull to another. The ultrasound speed inside this path depends on media density, which changes during each cardiac cycle. Under the normal conditions, the changing components are cerebral blood volume (CBV) and cerebrospinal fluid (CSF) volume. Each of these changes, depending of the flow of arterial blood into intracranial cavity and corresponding venous outflow (6), as well as CSF inflow and outflow (7, 8), can be reflected in pulse wave changes and detected by trans-intracranial ultrasound.

The ultrasound time-of-flight along the trans-intracranial trajectory reflects the shape of intracranial blood volume and CSF volume pulse wave, because ultrasound speed is highest in blood, lower in CSF and lowest in parenchyma (9, 10).

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Trans-intracranial ultrasound device has a real-time external tissue blood flow compensation (9), what gives the ability to examine only the intracranial pulsations.

A pilot examination still revealed the pulses in patients with diagnosed brain death, what provides the opportunity to study the possible pulse wave changes in this disastrous condition.

The objective of the study was to evaluate changes in ultrasonic pulse waves using the trans-intracranial ultrasound device in patients with diagnosed brain death.

MATERIAL AND METHODS

Device

The non-invasive trans-intracranial ultrasound device (Vittamed Ltd., USA–Lithuania (11)) has been used for intracranial pulse wave data acquisition (1.5 MHz ultasound transducers). All the data were collected into the personal computer (Intel Pentium III processor) using special Vittamed software.

Control group

Control group included 34 neurologically healthy volunteers (21M (61.8%), 13F (38.2%); mean age 31.3 ± 18.4 years, age range 8–75 years). Averaged pulse wave values were extracted of every volunteer; average of the entire group was calculated for comparison. Single or several sets of examinations were performed on every volunteer.

Patient group

Eight patients (6M (75.0%), 2F (25.0%); mean age 47.4 ± 10.5 years, age range 37–59 years) were examined in the patient group. The majority of them (7 persons, 87.5%) sustained a closed head trauma. One patient (12.5%) was declared dead after the CVA. Brain death diagnosis was made after all the brain death criteria of President's Commission on the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research Guidelines (12) were met and no cerebral blood flow was demonstrated by nuclear scan. All of the patients were artificially ventilated; hemodynamics was stabilized with adrenergic agents (MAP 100.2 ± 29.4 mmHg). Single set of examination was performed after the patient was declared as brain-dead.

Data collection. The measurement was performed at patient's bedside. The total time of the procedure rarely lasted longer than 20 minutes. The time of data collection was set to 100 seconds. This time is sufficient for the recording of pulse wave with the assurance in data reproducibility and for getting enough data for the analysis. Usually, a few data files were recorded during a single data collection set.

Pulse wave analysis

Pulse wave shape analysis was based on normalized intracranial volume-metric pulse waves. The highest point of the pulse was equated to the relative value 1.0, the lowest (diastolic) point was equated to the zero value. Normalization of the pulse wave in time was based on synchronic recordings of ECG and in this way establishing the start of a single pulse wave. The duration of the pulse wave was also normalized from 0 to 1.0. This allowed comparison of the different pulse waves under standard conditions, avoiding variations caused by the pulse wave difference in amplitude or heart rate. (Fig. 1.) The normalized pulse wave, which represents an averaged pulse wave of every consequent 20 pulses, was recorded and displayed in software window.

The sub-wave analysis carried out on normalized pulse wave, was based on documented typical sub-wave peaks in ICP pulse (13, 14, 34). The sub-wave values were extracted as percentage values from the highest point of the normalized pulse.

Ultrasound pulse wave amplitude analysis was performed on non-normalized data.

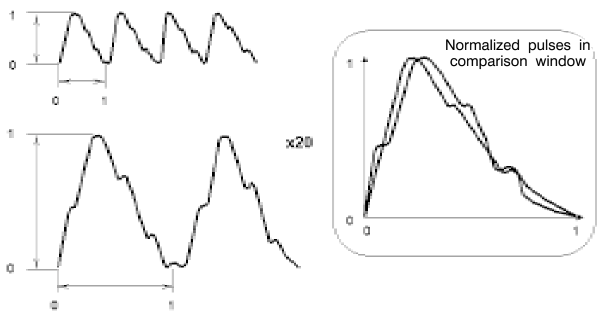

Fig. 1. Normalization of intracranial volume-metric pulse wawes. Note that pulses differing in amplitude and time are adapted to standard conditions available for pulse wave comparison

Statistical analysis

Data were analyzed using a standard Microsoft Excel worksheet and Statistica for Windows (Ver. 5.0, StatSoft Inc., USA) statistical package. Descriptive data are reported as mean ± standard deviation. The two-tailed unpaired t test was used to define the difference in means. A difference was considered significant if a p value 0.05 or less was calculated.

RESULTS

Control group

The pulse wave shape in the control group carried out a typical pattern. No marked differences depending on age or gender were observed. Although the trans-intracranial ultrasound pulse wave represents a volumetric pulse wave, not ICP wave, it meets the normal pulse wave criteria – the initial pulse part is highest, followed by a gradual decrease in the slope of the curve (13, 14) (Fig. 2).

The averaged sub-wave values calculated in control group were 97.2 ± 4.3% (P1), 68.3 ± 22.5% (P2), and 39.6 ± 26.5% (P3). Despite the relatively variant sub-waves, the P1, P2 and P3 ratio was always consistent with the expected normal pulse waveform. The averaged amplitude was 4.04 ± 2.48 ns (varied from 0.9 to 12.5 ns).

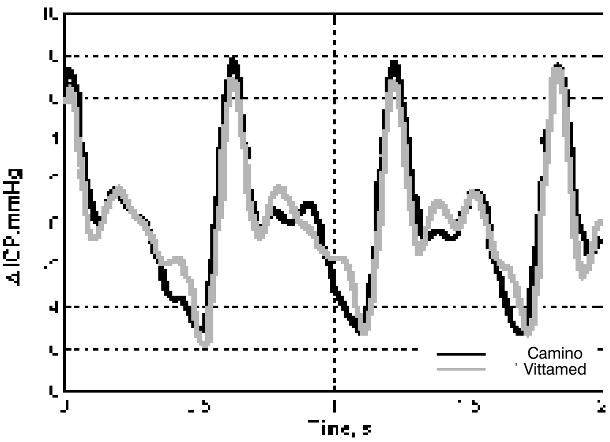

Fig. 2. Comparison of invasively (Camino) and non-invasively (Vittamed) acguired pulse wawes (patient With traumatic brain injury, ICP 60 mmHg)

Patient group

The intracranial volume-metric pulse waves in brain-dead patients were obtained in all cases of examination. As can be expected, the quality of the pulses obtained in brain-dead patients was markedly lower than in volunteers. Despite the lower quality of them, the pulse waveform was distinguishable and typical, although not specific enough to use it as a criterion for brain death. The calculated sub-wave values were (Fig. 3): P1 79.2 ± 16.4% (p = 0.03 *vs*. controls), P2 84.0 ± 14.8% (p = 0.04 *vs*. controls), and P3 85.9 ± 14.1% (p = 0.00001 *vs*. controls). The intracranial pulses amplitude was (Fig. 4) 1.55 ± ± 0.62 ns (varied from 0.51 to 2.39 ns), what was statistically significantly lower as compared to control group (p = 0.00001).

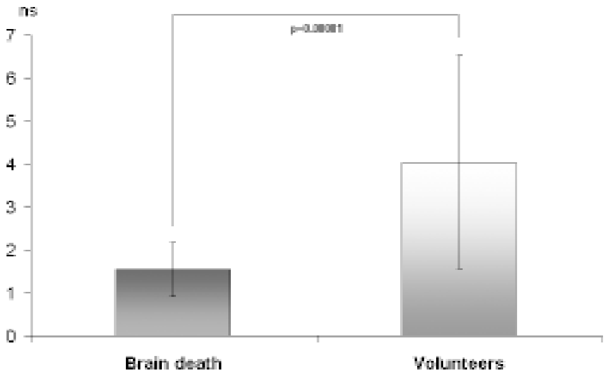

Fig. 3. Difference in ultrasonic pulse wave amplitude in the group of brain-dead patients and volunteers (1.55 ± ± 0.6 ns *vs*. 4.04 ± 2.48 ns control group; p = 0.00001)

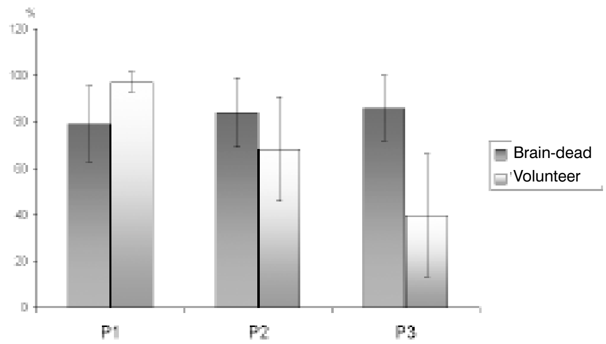

Fig. 4. Comparison of sub-waves in brain-dead patients and controls (P1 79.2 ± 16.4% *vs*. 97.2 ± 4.3%, p = 0.03; P2 84.0 ± 14.8% *vs*. 68.3 ± 22.5%; p = 0.04 and P3 85.9 ± 14.1%, 39.6 ± 26.5%, p = 0.00001)

DISCUSSION

Brain death is an irreversible loss of function of the brain, including the brainstem (15, 16). Brain death diagnosis is based on the clinical signs of brain stem function absence and confirmed by various studies demonstrating terminal reduction or complete loss of cerebral blood flow (12, 17).

The evolution of ICP showed that it reached a maximum 5 to 12 h before a decrease in wave amplitude occurred. The tracing became linear approximately 30 hours before irreversible cardiac failure appeared (18). Another case report of two brain death patient cases in barbiturate coma reports a persistent 3–5 mmHg ICP with a recognizable pulse after all brain death criteria were met (19).

A confirmation of brain death with portable technetium – 99 m isotope angiography performed in 204 patients revealed some flow on initial scan in 115 (56.4%) of all the cases (20), what was considered not important as there was no influence on bad outcome. The theoretical possibility of radionuclide cerebral angiography of not detecting minimal flow within the brain, particularly in the brain stem, because of a combination of low counts and attenuation due to interposed tissue is also included in the description of this methodology (17). This is also considered not a significant factor, because there are no patients who recovered after the confirmation of the brain death.

The orbital Doppler sonographic examination in 8 brain-dead patients revealed the absence or reversal end-diastolic blood flow in ophthalmic arteries (21), although the peak-systolic velocity was present in all 8 patients.

The pulsatile M-echo examination performed on 28 brain-dead patients nearly 30 years ago revealed a normal pulsatile midline echo in 2 patients (22). The A-mode ultrasound without the compensation of external tissue pulsation was used.

A review of these articles suggests a speculation that minimal CBF is still present in brain-dead patients, and only the sensitivity of the technique employed limits the visualization of it. On the other hand, visualization of the minimal cerebral blood flow is not clinically important, because it does not correlate with clinical findings and the outcome of the patient. The accurate sensitivity of the trans-intracranial device enrolled in the current study is not yet established precisely, because it is a very new technique.

The ultrasound speed measured with trans-intracranial ultrasound depends on CSF volume changes as well. The CSF volume changes might not have a marked influence on ICP change, but it is not visualized by cerebral blood flow studies. The search of literature did not reveal any direct CSF volume change studies in brain death. However, the indirect sign of this may be a preservation of spinal cord reflexes and other spontaneous movements, known as Lazarus sign in brain-dead patients (23–25). It is hard to believe, that CSF pulsations are possible in a traumatic brain stem herniated patients, but they may play a role if brain death is caused by hypoxia or other conditions in which the craniospinal anatomy is not changed.

Changes of pulse wave in the case of increased ICP are well documented in medical literature (26–29). The changes are often associated with a decrease of cerebral compliance (13, 29, 30, 34). The change of pulse waveform demonstrated by trans-intracranial ultrasound is consistent with the critical decrease of cerebral compliance, provided there is still a minimal cerebral blood flow present. There is no rapid increase in CBV or consequent rapid decrease in CSF volume, so the P1 sub-wave peak is low. There is no rapid venous outflow or it is negative, as demonstrated in on orbital Doppler study (21), so the P2 and P3 sub-wave peaks stay high.

However, this change in pulse wave is not specific to brain death. It was also observed in several cases of critically decompensated hydrocephalic patients (unpublished data).

It has been suggested that ICP pulse wave amplitude positively correlates with the SAP pulse wave amplitude (31–33). However, the significantly lower CBV amplitude demonstrated in the current study may represent also a reduction in CBF. All the patients in our group had a MAP of 100.2 ± 29.4 mmHg with the use of adrenergic agents. We have no SAP data from control group, although it can be thought not to be lower than normal.

It should be emphasized that trans-intracranial examination was performed on the bedside of patients, and the duration of the measurement rarely exceeded 20 minutes. Consequently, the trans-intracranial ultrasound methodology can be used as a quick adjunct for clinical decision-making in suspected brain death cases, what makes it supreme against other, more time consuming technologies.

CONCLUSIONS

The association of abnormal pulse waves and low amplitude acquired with this innovative technique may strongly suggest the brain death. Trans-intracranial ultrasound methodology provides the diagnostic information and can be used as an adjunct for clinical decision-making when dealing with comatose patients.

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PACIENTŲ SU PATVIRTINTA SMEGENŲ MIRTIMI ULTRAGARSO PULSINIŲ BANGŲ ĮVERTINIMAS

S a n t r a u k a

Tyrimo tikslas. Įvertinti pacientų su patvirtinta smegenų mirtimi ultragarso pulsinių bangų pokyčius panaudojant transintrakranijinį ultragarso aparatą (Vittamed Ltd. JAV–Lietuva).

Tyrimo metodai ir tiriamoji populiacija. Aštuoni pacientai (6V, 2M, amžiaus ribos 37–59 metai, vidutinis amžius 47,4 ± 10,5 metai), kuriems smegenų mirtis patvirtinta kliniškai bei radioizotopiniu būdu, buvo ištirti naudojantis transintrakranijiniu ultragarso aparatu. Gautos smegenų pulsacijos ultragarso bangos, kurių amplitudė bei bangų forma buvo palyginta su 34 sveikų savanorių (21V, 13M, amžiaus ribos 8–75 metai, vidutinis amžius 31,3 ± 18,4 metai) duomenimis.

Rezultatai. Ultragarso pulsinių bangų amplitudė tiriamojoje grupėje buvo 1,55 ± 0,6 ns, o savanorių – 4,04 ± 2,48 ns ($p = 0,00001$). Vertinant pacientų, kurių smegenys mirusios, pulsinių bangų formą, išskirti trys pobangiai: P1 79,7 ± 16,3%, P2 84,0 ± 14,8% ir P3 85,9 ± 14,1%). Ta pačia metodika išskirti savanorių pobangiai buvo atitinkamai 97,2 ± 4,3%, 68,3 ± 22,5% ir 39,6 ± 26,5%. Skirtumai tarp grupių statistiškai patikimi ($p < 0,05$).

Išvada: Esant pakitusiai pulsinių bangų formai bei mažai jų amplitudei galima įtarti smegenų mirtį. Tai suteikia diagnostinę informaciją tolimesniems gydytojo veiksmams šioje sudėtingoje situacijoje.

Raktažodžiai: smegenų mirtis, ultragarso pulsinės bangos, transintrakranijinis ultragarso aparatas