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RESEARCH ARTICLE

EFFICIENCY OF OPTIC NERVE SHEATH DIAMETER IN INDICATION OF CEREBRAL EDEMA IN UNCONSCIOUS PATIENTS.

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Abstract

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Aim: The objective of this study was to investigate the efficiency of optic nerve sheath diameter expansion in detection of brain edema.
Material and Method: One hundred seventy nine patients were examined in the study. Before any diagnostic methods were used, both eyes were scanned with ultrasonography device and optic nerve sheath diameter were measured in unconscıous patients. Computed Brain Tomography scan was performed the optic nerve sheath diameter were measured bilaterally on the Computed Brain Tomography images by the same researcher. These patients were classified as group 1. Healty volunteers measured optic nerve sheath diameter by ultrasonography were classified as group 2. The patients with brain edema on Computed Brain Tomography scan were classified as group 3 and the patients with non-traumatic Computed Brain Tomography scan and whose images are normally evaluated were classified as group 4. After that the difference between ultrasonography and Computed Brain Tomography measurements of optic nerve sheath diameter was examined by comparing the group 2 and group 4 patients. Group 3 and group 4 patients were compared and the difference of optic nerve sheath diameter measurement averages was examined. After that patients with and without cerebral edema in group 1 were compared.
Results: There was no significant difference optic nerve sheath diameter measured between ultrasonography and Computed Brain Tomography with brain edema patients ($p > 0,05$). Patients with brain edema and without brain edema were compared and there was a significant difference ($p = 0,0001$). As the cut-off value of optic nerve sheath diameter 5 mm, 5,5 mm and 6 mm was taken there was no difference between averages optic nerve sheath diameter in patients with brain edema. When the cut-off value increased, the sensitivity decreased and the specificity increased. There was a significant diffence between the healthy participants' optic nerve sheath diameter with ultrasound and, patients with Computed Brain Tomography scans which were reported as normal ($p = 0,000105$).
Conclusion: Optic nerve sheath diameter is expanding in patients with cerebral edema and can be measured by imaging methods. There is a

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significant difference between the measurement of optic nerve sheath diameter with ultrasound and Computed Brain Tomography.

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Introduction:-

There is always the possibility of increased intracranial pressure (ICP) during intracranial events in unconscious patients. Cerebral edema is a result of pathological fluid accumulation in intracellular and extracellular areas of the brain. Cerebral edema is a common symptom in ischemic stroke, traumatic brain injury, brain aneurysm rupture, and neoplasia, depending on the range of neurological conditions (1).

ICP monitoring is standard in the vast majority of brain surgery centers for severe traumatic brain injury (TBI) in North America and Europe (2). Today, non-invasive techniques have been developed and used to replace the invasive techniques with high complication risks to minimize the harm and maximize the benefits for the patients during diagnosis. The studies on the topic aim to use ultrasonography (USG) and the thickness of the optic nerve sheath diameter (ONSD) measurement, which are non-invasive techniques that can monitor ICP and diagnose Increased Intracranial Pressure (IIP).

The measurement of ONSD with USG was first described in 1987 as the noninvasive measurement method of ICP (3). Optical USG is an easy to learn technique and the results of a study conducted by Foster et al. confirmed that emergency physicians were good observers in ONSD measurement (4).

Similarly, the present study aimed to assess the efficiency of the ONSD enlargement measurement as a diagnostic tool for early recognition and rapid treatment of IIP due to its anatomy and physiology.

Material and Method:-

In the present prospective and observational study, 179 patients, who were over 18 years old, unconscious, with an elevated traumatic and non-traumatic intracranial pressure and applied to Abant Izzet Baysal University, Faculty of Medicine Hospital Emergency Department between September 2014 and September 2015, were included in the study. Patients younger than 18 years of age, patients with bilateral eye trauma, penetrating eye injuries, and patients with a known optic nerve disease were excluded from the study.

Without using any diagnostic imaging method, patient ONSDs were measured bilaterally with a 7.5 mHz linear probe using Hitachi ALOKA F 37 ultrasonography (USG) device. The optic nerve was scanned over the closed eyelids of both eyes of the patients. ONSDs for both eyes were measured with USG and recorded. ONSD was measured 3 mm behind the retina. The measurement was conducted by one researcher on B-scan mode, oriented vertically at an angle of 30 degrees on both eyes with closed eyelids, when the patient was lying in supine position. To obtain clear images USG gel was applied on the eyelids. Subsequently, the patients were scanned with Computed Brain Tomography (CBT) and the same researcher used the CBT images to measure the ONSD in both eyes and recorded the findings. These patients were classified as Group 1. Healthy volunteers scanned with USG for ONSD were classified as Group 2, Group 3 included patients who were diagnosed with cerebral edema with CBT images and the patients scanned for non-traumatic CBT and whose images were considered normal were classified in Group 4. Then the difference between USG and CBT measurements of ONSD was examined by comparing Group 2 and Group 4 patients. Group 3 and Group 4 patients were compared and the difference between mean ONSD measurements were examined in patients whose CBT images exhibited edema and patients with normal CBT images. Later, the patients in Group 1with and without brain edema were compared.

Measurements were evaluated with Statistical Package for Social Sciences for Windows (SPSS, Inc., Chicago, IL), version 22.0. Analysis of normal distributed data was conducted with t-test was and the significance level was accepted as $p < 0.05$. The t-test was individually applied to each group based on age and gender properties. Subsequently, t-test was applied to assess the difference between the groups. Mann Whitney U-test was applied to the group data that did not exhibit normal distribution and to investigate the differences between group averages. ONSD cut-off values were taken as 5 mm, 5.5 mm and 6 mm.

Results:-

A total of 179 patients were included in the study and patient demographics are presented in Table 1.

Table 1:- Study group demographics

		Group 1 Unconscious Patients (n:46)	**Group 2** Healthy Volunteers (n:67)	**Group 3** With Brain edema Patients (n:41)	**Group 4** Normal CBT Patients (n:66)
n	Male	27	42	25	36
	Female	19	25	16	30
Age	Male	56	33	54	35
	Female	75	31	62	43

The mean ONSD measurements for the study group patients are presented in Table 2.

Table 2:- Mean ONSD measurements for the study groups

		Group 1 Unconscious Patients (n:46)		**Group 2** Healthy Volunteers (n:67)		**Group 3** With Brain edema Patients (n:41)		**Group 4** Normal CBT Patients (n:66)	
		USG	CBT	USG	CBT	USG	CBT	USG	CBT
ONSD (mm)	M	6,1 ± 1,1	6,3 ± 1	6,3 ± 0,8	----	----	6,1 ± 0,8	----	5,5 ± 0,8
	F	5,8 ± 1,1	5,7 ± 0,7	6,3 ± 0,8	-----	-----	5,7 ± 1	----	5,2 ± 0,6

Group 4 was formed by conducting ONSD measurements using CBT images that were assessed as normal. This group aimed to investigate the difference between USG and CBT measurements by determining the mean ONSD value with CBT and comparing it with the measurements of healthy volunteers (Group 2). This comparison was not conducted with the same patients since imaging the healthy volunteers with radiation tomography would not be ethical.

To compare the CBT and USG measurements of ONSD, the ONSD measurements of healthy participants (Group 2) with USG were compared with the CBT ONSD mesurements of the patients with normal USG and CBT ONSDs (Group 4). There was a significant difference between the measurement of bilateral ONSD averages with USG and CBT (bilateral p = 0.000105). Since the patient group with normal CBT was created with archived images, it was not possible to measure the ONSD with USG (Table 3).

Table 3:- Comparison of ONSD measurements of patients with normal USG-CBT in healthy subjects (Groups 2 and 4)

	Female		**Male**		**p**
	USG (n: 25)	CBT (n:36)	USG(n: 42)	CBT (n: 30)	
Mean Bilateral ONSD	5,4 ± 0,8 mm	5,2 ± 0,6 mm	5,2 ± 0,6 mm	5,5 ± 0,8 mm	0,000105

ONSD averages of patients with normal archived CBT images (Group 4) and that of the patients diagnosed with cerebral edema with CBT (Group 3) were compared to investigate the relationship between edema and ONSD (Table 4). There was a significant difference between OCD measurements of patients with and without brain edema. For the mean bilateral ONSD, it was found that p = 0.0001.

Table 4:- Comparison of ONSD averages of patients diagnosed with edema with CBT and with normal CBT images

	Female		Male		p
	Normal CBT (n: 36)	Brain Edema CBT (n:16)	Normal CBT (n: 30)	Brain Edema CBT (n: 25)	
Mean Bilateral ONSD	5,2 ± 0,6 mm	5,7 ± 1 mm	5,5 ± 0,8 mm	6,1 ± 0,8 mm	0,0001

ONSD averages of the 46 unconscious patients in Group 1 that were measured with USG were compared with those measured with CBT. Examination of this group for edema demonstrated that there was no significant difference between the mean ONSD measurements with CBT (p = 0,163) and USG (p = 0,459) (Table 5).

Table 5:- The ONSD values measured by USG and CBT of patients who were in an unconscious state (Group 1)

	Female(n: 19)		Male (n: 27)		p
	USG	CBT	USG	CBT	
Mean ONSD	5,8 ± 1,1 mm	5,7 ± 0,7 mm	6,1 ± 1,1 mm	6,3 ± 1 mm	0,459

Brain edema was identified in 9 male and 4 female patients out of 46. Four patients were diagnosed with subarachnoid hemorrhage, 4 patients were diagnosed with midline shift, 2 patients were diagnosed with subdural hemorrhage, mass was observed in 3 patients, 9 patients were diagnosed with brain edema, 19 patients were diagnosed with acute infarction, 2 patients were diagnosed with parenchymal hemorrhage and 1 patient was diagnosed with encephalitis.

Group 1 was studied separately for males and females. Edema was present in 9 of 27 male patients. There was no significant difference between the mean ONSD measurements conducted with USG in patients with and without edema (p = 0.322). No significant difference was found in the measurements with CBT based on the presence of edema (p = 0,253). Measurement averages are presented in Table 6.

Table 6:- Comparison of mean ONSD measurements conducted with USG and CBT in unconscious male patients

	With Edema (n:9)	No Edema (n:18)	p
USG	6,4 ± 0,8 mm	5,9 ± 1,1 mm	0,322
CBT	6,7 ± 1,1 mm	6,1 ± 0,9 mm	0,253

Similarly, edema was determined in 4 of 19 female unconscious patients. There was no significant difference between the mean ONSD measurements conducted with USG based on the presence of edema (p = 0.596). There was no significant difference between the mean ONSD measurements conducted with BBT based on the presence of edema (p = 0.411). Measurement averages are presented in Table 7.

Table 7:- Comparison of mean ONSD measurements conducted with USG and CBT in unconscious female patients.

	With Edema (n:4)	No Edema (n:15)	p
USG	5,5± 0,6 mm	5,9 ± 1,2 mm	0,596
CBT	5,8 ± 0,4 mm	5,7 ± 0,8 mm	0,411

Sensitivity and specificity values were investigated for 5 mm, 5.5 mm and 6 mm cut-off values to evaluate the significant difference between groups of patients with and without cerebral edema with ONSD averages using CBT images. Sensitivity was 88% and specificity was 33% with 5 mm cut-off value, sensitivity was 68%, specificity was 59% with 5.5 mm cut-off value of, and Sensitivity was 53%, specificity was 77% with 6 mm cut-off value (Table 8).

Table 8:- The comparison of the cut-off value measurements of patients with edema in CBT and normal CBT

Mean Bilateral ONSD	With Edema (N: 41)	No Edema (N:66)	sensitivity (%)	specificity (%)
ONSD >5 mm	36 (33,6%)	44 (41,1%)	88%	33%
ONSD <5 mm	5 (4,7%)	22 (20,6%)		
ONSD >5.5 mm	28 (26,2%)	27 (25,2 %)	68%	59%
ONSD <5,5 mm	13 (12,1%)	39 (36,4%)		
ONSD >6 mm	22 (20,6%)	19 (17,8%)	53%	77%
ONSD <6 mm	15 (14,2%)	51 (47,7%)		

Comparison of the averages when the cut-off value is taken as 5,5 mm, sensitivity was high in brain edema diagnosis, while sensitivity decreased and specificity increased when cut-off value is taken as 6 mm.

Discussion:-

Brain edema induces post-ischemic edema in middle cerebral artery infarction, cerebral herniation and progressive brain stem dysfunction and IICP (5). Patients with post-resuscitation GCS of 3-8 or abnormal CBT findings are indicated for ICB follow-up (6). Brain edema is a common symptom in ischemic stroke and lesions that occupy space such as tumors. Early diagnosis of IICP is critical for the timely and adequate treatment (7). Various diagnostic methods are available for the detection of intracranial pathology in an unconscious patient. Although CBT and MR are used for diagnostic purposes, these diagnostic tools have various challenges.

ONSD enlargement can be used as an indirect indicator in the determination of IICP as a non-invasive method (8). In an empirical study conducted with Yorkshire pigs, a linear correlation was determined between ONSD and increased ICP (9).

The most important of these is the urgent need to provide adequate treatment for unstable severe patient in critical condition as early as possible in the emergency clinic. It is both risky and time consuming for an unstable patient to be taken to the CT or MR room for imaging where there is no facility for intervention. Furthermore, imaging facilities are not available at all centers and the patient may need to be referred to the external center. In the present study, the possibility of detecting brain edema in unconscious patients with ONSD measurements.

Previous studies reported that there is a linear correlation between ICP and ONSD enlargement (38). In the present study, it was found that there was a significant difference between the patients with and without brain edema in ONSD measurements conducted with CBT. The present study findings demonstrated that the effect of the cerebral edema to enlarge ONSD was significant between the groups 3 and 4 in CBT measurements. There was a significant difference between the measurements of ONSD conducted with USG and CBT when the Group 2 and Group 4 measurements were compared. Based on the findings of the present study, there was a scientifically significant difference between the measurement of ONSD with CBT and USG. Thus, if the ONSD measurement would assist the diagnosis of IICP, conducting measurements with only the bedside USG would not be sufficient and CBT imaging would be inevitable despite its negative aspects such as the limited intervention facilities during imaging.

In a study involving 53 adult patients with known or suspected intracranial hypertension, IICP (> 20 mm Hg) was determined in 19 patients, and ONSD was measured scientifically significantly higher in patients with IICP when compared topatients with low ICP (6,2 ± 0.6 mm). In the control group, it was found that the ONSD was 4.9 ± 0.4 mm [10]. According to the findings of the study, there was a significant correlation between IICP and ONSD. In the current study, for the comparison between different patient groups (Groups 2 and 4), ONSDs were measured with USG and CBT images and a significant difference was determined between these groups. Although other studies reported a correlation between USG and MR, there was a significant difference between the ONSD averages measured with USG and CBT in the present study. The fact that it was not possible to give radiation to the healthy volunteers in Group 2 without indication and the resulting lack of the comparison based on post-USG CBT images differentiates the present study from others.

In a study conducted with 131 patients, 38 (29.0%) patients were confirmed to have IICP and 102 (77.9%) patients were identified as IICP based on ONSD USG measurements when the upper value was accepted as 5 mm. Based on the study results, it was found that the sensitivity of ONSD measurement with USG in identification of IICP was similar to ophthalmoscopy (sensitivity: 100, specificity: 35,5), although its sensitivity was 100%, however its specificity was low (23.7%). Measurements between 5 and 6 mm require clinical correlation. Kimberly et al. determined the pathological ONSD threshold as > 5mm (sensitivity: 88%, specificity: 93%) [12] and Blaivas et al. determined the pathological ONSD threshold as 5 mm (sensitivity: 100%, specificity: 95%) [13].

In the present study, the Group 3 and 4 ONSD averages were compared via BBT images. When the cut-off value as taken as 5 mm, ONSD identified the cerebral edema in 36 of 41 patients with cerebral edema (sensitivity 87%) and identified 22 of 66 patients without cerebral edema (specificity 33%). In studies where the cut-off value was taken as 5 mm, it was observed that the sensitivity of the ONSD measurement in determining the IICP varied between 88% and 100% [13, 14, 15]. Similarly, it was determined that the sensitivity was 87% in the current study.

Blaivas et al. evaluated ONSD with CBT, Kimberly et al. used invasive intracranial methods to determine ICP and compared the enlargement in ONSD with USG measurement [13]. We did not use invasive methods in the present study and compared the USG measurements with noninvasive CBT. Lack of comparison of CBT and USG measurements with invasive methods is one of the limitations in the present study. Contrary to the abovementioned studies, specificity was 33% in the present study, while Kimberly et al. determined the specificity as 93% and Blavias et al. determined the specificity as 95%. As shown in Table 8, the sensitivity was generally high in similar studies, however there were certain differences in specificity figures. In the present study, when the cut-off value was taken as 5 mm, our findings were consistent with other studies in the literature and it was considered adequate to use ONSD to determine IICP.

In the present study, when the cut-off value was taken as 5.5 mm, ONSD identified brain edema (sensitivity 68%) in 28 of 41 patients with brain edema (sensitivity 68%) and identified 39 of 66 patients without brain edema (specificity 59%). In another study, when the ONSD was greater than 5.5 mm, ICP was estimated as > 20 cm H_2O values were estimated with 100% sensitivity (95% CI, 100-100) and 100% specificity (95% CI, 100-100) [16]. Geeraerts et al. [17] reported a cut-off of 5.86 mm (sensitivity: 95%, specificity: 79%), Soldatos et al. [18] reported a cut-off of > 5.7 mm (sensitivity: 74%, specificity: 100%). There are discrepancies between the findings of the present study and the results of the abovementioned studies. However, there are differences among these studies as well. Sensitivity was 74% after the comparison of USG measurements with intracranial catheter in the study by Soldatos et al., while Geeraerts et al. compared USG and MR measurements and reported sensitivity as 95%. On the contrary, specificity was 100% in the study by Soldatos et al., while Geeraerts et al. reported the same figure as 79% in their study.

When the cut-off value was taken as 6 mm, ONSD measurement with USG identified 22 out of 41 participants with cerebral edema (sensitivity, 53%). Forty-six of 66 patients without brain edema were correctly identified with the same method (specificity 77%). When the cut-off value is taken as 5 mm, the sensitivity increased and when it is taken as 6 mm, the specificity increased. In literature, different studies determined different cut-off values up to 6 mm, however the commonly accepted value was 5 mm (16). Our findings and our analyzes were similar to those of the previous studies.

In the present study, CBT measurements were analyzed separately for three cut-off values (5 mm, 5.5 mm, and 6 mm). Significant differences were found when cut-off was taken as 5.5 mm and 6 mm for ONSD between those with and without cerebral edema. A definite cut-off value is yet to be determined for the determination of IICP with ONSD measurement, and clinical evaluation is still significant between 5 mm and 6 mm.

There was no difference between the edema and ONSD enlargement when the ONSDs measured with USG and averages based on 5 mm, 5.5 mm and 6 mm cut-off values of 46 patients who were accepted in the emergency service in unconscious state were compared. Similarly, there was no difference between the measurements conducted using CBT images. Since the present study demonstrated differences between ONSD based on gender, unconscious subjects (Group 1) were divided into male and female groups. There was no significant difference between ONSD averages of male patients with both USG and CBT measurements based on edema. Similarly, There was no significant difference between ONSD averages of unconscious female patients with both USG and CBT measurements based on edema.

In the current study, consistent with other papers in the literature, it was found that ONSD in IICP demonstrated a linear increase with the increasing pressure in patients with cerebral edema and midline shift. This enlargement was also demonstrated in animal model studies and it was demonstrated that in patients with increased ICP, a reduction in ONSD was observed due to the BOS drained after LP. Determination of cerebral edema by ONSD measurement with USG could be beneficial for the patient to receive effective treatment.

Conclusion:-

The determination of the enlargement in the ONSD with USG, which is a fast, non-invasive, easy and effective method due to the linear relationship between IICP and ONSD, can be considered as a promising diagnostic method that can be beneficial for the patient.

Ethics Approval:-

This retrospective single center case study was approved by the local ethics committee of the Abant Izzet Baysal University Hospital Bolu, Turkey, and followed the ethical guidelines of Declaration of Helsinki from 1975.

References:-

1. Walcott, B.P., K.T. Kahle, and J.M. Simard (2012). *Novel treatment targets for cerebral edema.* Neurotherapeutics, 9(1): p. 65-72.
2. Mattei, T.A. (2013). *Intracranial pressure monitoring in severe traumatic brain injury: who is still bold enough to keep sinning against the level I evidence?* World neurosurgery, 79(5): p. 602-604.
3. Gangemi, M., et al. (1987). *Echographic measurement of the optic nerve in patients with intracranial hypertension.* Neurochirurgia, 30(2): p. 53-55.
4. Foster, T., et al. (2003). *Al pressure in head injury patients: preliminary study of interobserver variability in normal human subjects.* Ultrasound in Medicine & Biology, 29(5): p. S154.
5. Simard, J.M., et al. (2011). *Managing malignant cerebral infarction.* Current treatment options in neurology, 13(2): p. 217-229.
6. Bratton, S., et al. (2006). *Guidelines for the management of severe traumatic brain injury. I. Blood pressure and oxygenation.* Journal of neurotrauma, 24: p. S7-13.
7. Hightower, S., E. Chin, and J. Heiner (2011). *Detection of increased intracranial pressure by ultrasound.* Journal of special operations medicine: a peer reviewed journal for SOF medical professionals, 12(3): p. 19-22.
8. Newman, W., et al. (2002). *Measurement of optic nerve sheath diameter by ultrasound: a means of detecting acute raised intracranial pressure in hydrocephalus.* British journal of ophthalmology, 86(10): p. 1109-1113.
9. Hamilton, D.R., et al. (2011). *Sonography for determining the optic nerve sheath diameter with increasing intracranial pressure in a porcine model.* Journal of Ultrasound in Medicine, 30(5): p. 651-659.
10. Riccardo Moretti, M.a.B.P., MD. (2009). *Optic Nerve Ultrasound for Detection of Intracranial Hypertension in Intracranial Hemorrhage Patients Confirmation of Previous Findings in a Different Patient Population.* Journal of Neurosurgical Anesthesiology. 21(1): p. 16-20.
11. Golshani, K. (2015). *Diagnostic Accuracy of Optic Nerve Ultrasonography and Ophthalmoscopy in Prediction of Elevated Intracranial Pressure.* Emergency, 3(2): p. 54.
12. Kimberly, H.H., et al. (2008). *Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure.* Academic Emergency Medicine,. 15(2): p. 201-204.
13. Blaivas, M., D. Theodoro, and P.R. Sierzenski (2003). *Elevated intracranial pressure detected by bedside emergency ultrasonography of the optic nerve sheath.* Academic emergency medicine, 10(4): p. 376-381.
14. Le, A., et al. (2009). *Bedside sonographic measurement of optic nerve sheath diameter as a predictor of increased intracranial pressure in children.* Annals of emergency medicine, 53(6): p. 785-791.
15. Kimberly, H.H., et al. (2008). *Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure.* Academic Emergency Medicine, 15(2): p. 201-204.
16. Amini, A., et al. (2013) *Use of the sonographic diameter of optic nerve sheath to estimate intracranial pressure.* The American journal of emergency medicine,. 31(1): p. 236-239.
17. Geeraerts, T., et al. (2008). *Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients.* Intensive care medicine, 34(11): p. 2062-2067.
18. Soldatos, T., et al. (2008). *Optic nerve sonography in the diagnostic evaluation of adult brain injury.* Critical care, 12(3): p. 1.