



Original Contribution

Association of optic nerve sheath diameter measurement with hyponatremia in emergency department ☆



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ABSTRACT

Objective: Investigation of association of ONSD with hyponatremia in symptomatic patients.

Methods: 89 patients who were diagnosed to have hyponatremia (Na + <135 mmol/L) were prospectively analyzed and compared with 72 patients who have normal serum sodium levels presented to ED at the same time interval. Subjects' demographic properties including age and sex were recorded, as were admission symptoms, serum Na + level, and pre-treatment and post-treatment optic nerve sheath diameter (ONSD).

Results: The mean age of the study population was 62.3 ± 17.6 years, and the control group 55.1 ± 20.0 years (p < 0.05). There was a significant difference between the patient group's pre-treatment and post-treatment OSNDs compared to the controls (p < 0.05). There was a significant negative correlation between the admission sodium level and ONSD in the patient group (p < 0.05). In the pre-treatment period, patients with symptoms had a significantly greater mean ONSD than those without symptoms (0.546 ± 0.068 mm vs 0.448 ± 0.081 mm; p < 0.05). The area under the curve was 0.870; the cut-off level calculated for hyponatremia was 0.49 mm, which had a sensitivity of 81% and a specificity of 81.9%.

Conclusion: Ultrasonic imaging of ONSD measurement in the emergency department appears to reflect changes consistent with ICP changes in hyponatremia and change in serum sodium.

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1. Introduction

Sodium is the most important cation in the body, and the amount of water determines the serum sodium (Na) concentration; serum Na determines changes in serum osmolality [1]. The related association is a feedback cycle; when anterior hypothalamic osmoreceptive neurons perceive serum osmolality changes, body water is regulated by neurohumoral mechanisms, and water flow into the intravascular space begins [2]. The movement of water between compartments is provided by the osmotic pressure

gradient as a result of solute load; relative hyponatremia and difference of effective osmolality between brain and plasma induces water movement from the extracellular to the intracellular compartment; brain cells begin to swell and consequently intracranial pressure increases [1].

The optic nerve is a central nervous system structure that is wrapped by a dural sheath. The optic nerve has a direct anatomic relationship with the intracranial subarachnoid space. ONSD increased in parallel with ICP elevation has been shown to correlate well with other indicators of ICP elevation [3].

ONSD measurement is an increasingly investigated tool in many conditions related with ICP increases; there are many studies evaluating this relationship in the literature; however, to the best of our knowledge, this study is the first to assess the connection of ONSD and hyponatremia. Therefore, the aim of the present study, where the relationship between hyponatremia and ONSD

☆ ONSD in bottomless pit of Emergency Department

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is studied, was to investigate the prognostic and predictive value of ONSD measurement in the diagnosis and treatment of hyponatremia in the emergency department.

2. Materials and methods

2.1. Study design

This study was approved by Antalya Training and Research Hospital local ethics committee and was prospectively conducted on 151 patients who presented to the emergency department of our hospital between 16.02.2017 and 16.06.2017; all patients provided informed consent for study participation.

The inclusion criteria were patients with hyponatremia ($\text{Na}^+ < 135 \text{ mmol/L}$) aged over 18 years. The exclusion criteria were age below 18 years, referrals from other institutions, facial trauma affecting the orbits and/or eyeballs, pre-existing ocular disease affecting the optic nerve and/or orbital cavity, and clinical causes of ICP increases (e.g., endocrinopathies, metabolic disorders, infectious and immunological disorders and malignancies).

2.2. Data collection

Seventy-nine patients admitted to our emergency department who were diagnosed to have hyponatremia ($\text{Na}^+ < 135 \text{ mmol/L}$) and 72 control subjects with normal serum sodium levels were included. Demographic characteristics including age and gender were recorded, as were admission symptoms, serum Na^+ level, and pretreatment and posttreatment optic nerve sheath diameter (ONSD).

2.3. Measurement of the optic nerve sheath diameter

Optic nerve sheath diameter (ONSD) measurements were carried out with a Toshiba Aplio 500 platinum device using 11 and 14 MHz linear transducers. During the examination, the subjects

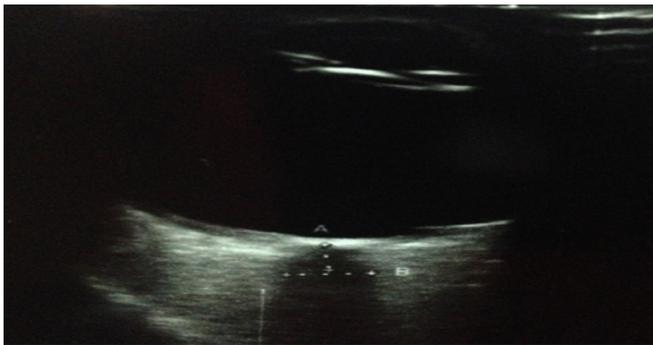


Fig. 1. The ONSD measurement technique; Measurement of optic nerve disc diameter at a distance of 3 mm from the optic disc on the transverse plane, with the eyelids closed.

were kept in the supine position with their eyes closed. The optic disc was visualized over the eyelid, with ONSD measurement being performed 3 mm proximal to the optic disc on the transverse plane by referencing hypoechoic lines (Fig. 1). Two measurements were separately performed for both eyes and the arithmetic mean of both ONSDs was considered for statistical analyses.

2.4. Statistical analysis

Statistical analyses were performed using the SPSS for Windows v. 22 software package. The normality of the distribution of continuous and discrete variables was tested using the Kolmogorov-Smirnov test. Descriptive statistics included mean \pm standard deviation for continuous and discrete variables and number and percentage (%) for categorical variables. Categorical variables were compared using the Chi-square test; parametric variables were compared with the Student's *t*-test; and numeric variables were compared with the Pearson's correlation test. ROC analysis was used to determine the cut-off value with best sensitivity and specificity values. A *p*-value of <0.05 was considered to be statistically significant for all statistical analyses.

3. Results

The mean age of the study population was 62.3 ± 17.6 years, and the control group 55.1 ± 20.0 years ($p < 0.05$). The number of males in the patient and control groups were 38 (48.1%) and 41 (56.9%), respectively ($p > 0.05$) (Table 1).

The patients had an admission right-eye mean ONSD of $0.543 \pm 0.075 \text{ mm}$, a left-eye mean ONSD of $0.544 \pm 0.073 \text{ mm}$, and a mean over all ONSD of $0.544 \pm 0.070 \text{ mm}$. Posttreatment right eye mean ONSD was $0.505 \pm 0.069 \text{ mm}$, left eye mean ONSD was $0.509 \pm 0.07 \text{ mm}$, and mean overall ONSD was $0.507 \pm 0.066 \text{ mm}$. The difference between pretreatment and posttreatment right eye mean ONSDs was $0.038 \pm 0.003 \text{ mm}$; the difference between pretreatment and posttreatment left eye mean ONSDs was $0.035 \pm 0.03 \text{ mm}$; and the difference between pretreatment and posttreatment mean overall ONSDs was $0.037 \pm 0.028 \text{ mm}$. There was a significant posttreatment drop in the mean ONSD levels of both eyes and overall ONSD levels ($p < 0.05$). In the control group, on the other hand, right eye mean ONSD was $0.434 \pm 0.075 \text{ mm}$, mean left eye ONSD was $0.431 \pm 0.081 \text{ mm}$, and mean overall ONSD was $0.432 \pm 0.076 \text{ mm}$. There was a significant difference between the patient group's pretreatment and posttreatment mean ONSDs compared to the controls ($p < 0.05$) (Table 1).

The patients had a minimum serum sodium level of 105 mmol/l , a maximum serum sodium level of 134 mmol/l , and a mean serum sodium level of $125.9 \pm 6.7 \text{ mmol/l}$; the control group had a minimum serum sodium level of 135 mmol/l , a maximum serum sodium level of 143 mmol/l , and a mean serum sodium level of $137.4 \pm 2.1 \text{ mmol/l}$. There was a significant negative correlation between the admission sodium level and ONSD in the patient group ($p < 0.05$) (Table 2).

Table 1

Comparison of pretreatment and posttreatment ONSDs of the study groups

		Patients (n:79) mean \pm SD	Controls (n:72) mean \pm SD	<i>p</i>
Admission ONSD (mean \pm SD)	Right eye ONSD	0.543 ± 0.075	0.434 ± 0.075	<0.001
	Left eye ONSD	0.544 ± 0.073	0.431 ± 0.081	<0.001
	Mean ONSD	0.544 ± 0.07	0.432 ± 0.076	<0.001
Posttreatment ONSD (mean \pm SD)	Right eye ONSD	0.505 ± 0.069	0.434 ± 0.075	<0.001
	Left eye ONSD	0.509 ± 0.07	0.431 ± 0.081	<0.001
	Mean ONSD	0.507 ± 0.066	0.432 ± 0.076	<0.001

Table 2
Correlation between sodium level and ONSD of the patient group

		Pretreatment ONSD	Posttreatment ONSD
Admission Na level	r	−0.239	−0.098
	p	0.034	0.390

Twenty-eight (35.4%) patients were treated with 0.9% saline solution and 51 (64.6%) were treated with 3% saline solution. Patients who were administered 0.9% saline solution had a pretreatment ONSD of 0.511 ± 0.052 mm and a posttreatment ONSD of 0.487 ± 0.052 mm; those who were administered 3% saline solution had a pretreatment ONSD of 0.562 ± 0.073 mm and a posttreatment ONSD of 0.518 ± 0.07 mm. The difference between the pretreatment and posttreatment ONSDs in the 0.9% saline administered and 3% saline administered groups were 0.024 ± 0.024 mm and 0.043 ± 0.028 mm, respectively, with reductions in ONSD being statistically significant in both groups ($p < 0.05$) (Table 3).

In the pretreatment period, patients with symptoms had a significantly greater mean ONSD than did those without symptoms (0.546 ± 0.068 mm vs 0.448 ± 0.081 mm; $p < 0.05$). No significant relationship could be found between symptom type and ONSD ($p > 0.05$). In the posttreatment period, patients with symptoms had a mean ONSD of 0.508 ± 0.066 mm and those without had a mean ONSD of 0.448 ± 0.091 mm; there was no significant difference between symptom presence and ONSD values ($p > 0.05$).

The area under the curve was 0.870; the cut-off level calculated for hyponatremia was 0.49 mm that had a sensitivity of 81% and a specificity of 81.9% (Fig. 2).

Fourteen (17.7%) patients were admitted to hospital. Among those admitted, the median Na level was 115.5 mg/dl (range, 19 mg/dl; minimum, 105 mg/dl; maximum, 124 mg/dl). The median duration of hospital stay was 6 days (range, 10 days; minimum 3 days; maximum 13 days). The mean admission ONSD of the admitted patients was 0.556 ± 0.074 mm; those who were discharged from the emergency department had a mean admission ONSD of 0.541 ± 0.069 mm. The mean posttreatment ONSD of the patients treated in the emergency department was 0.507 ± 0.066 mm; those who were admitted to hospital had a mean posttreatment ONSD of 0.509 ± 0.068 mm. No significant difference was noted between the admission and discharge ONSDs of the admitted patients and patients discharged from the emergency department ($p > 0.05$).

4. Discussion

Although several studies reported that hyponatremia causes ICP elevation, no study to date has investigated the relationship between hyponatremia-induced intracranial pressure increase and ONSD [4–8]. Nevertheless, it is already known that ONSD reflects ICP in many pathological conditions (intracranial bleeding, stroke, pseudotumor cerebri) [9–16].

We detected a significantly greater ONSD in patients with hyponatremia. These patients' posttreatment ONSD was also greater. We believe that the main reason for this finding was hyponatremia-induced brain edema. It should also be noted that

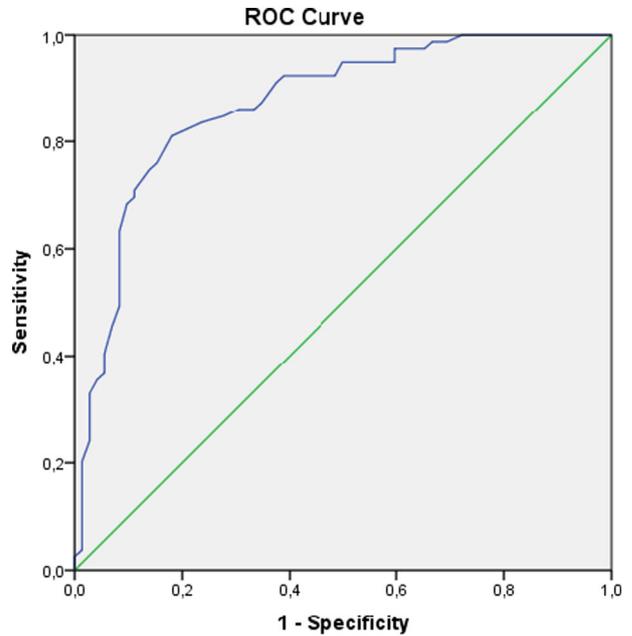


Fig. 2. ROC analysis for the hyponatremia for prediction of ONSD.

other conditions with potential to cause hyponatremia may have increased ONSD. As it may take time for brain edema to resolve and ICP to decrease in order to reduce ONSD, this value may even be greater compared to the control group. Moreover, in patients with comorbidities, even if hyponatremia-induced ICP drops, ONSD partly remains higher due to the underlying pathology.

Prior studies have shown a correlation between ONSD and ICP elevation [13,17–20]. Amini et al. made ICP measurements and compared them with ONSD in patients undergoing lumbar puncture for various reasons. These researchers found significantly greater ONSD in patients with elevated ICP [4]. Deepening hyponatremia parallels worsening brain edema, which may cause varying degrees of neural injury [8,21]. Vilapurathu et al. found a correlation between hyponatremia severity and severity of clinical condition and symptoms [5]. We revealed a negative correlation between ONSD and admission sodium but not between posttreatment ONSD and admission sodium level. The main reason for this finding may be dropping sodium levels causing worsening brain edema and thus ICP elevation. The correlation between ICP elevation and ONSD agrees with literature findings. Although it may not be appropriate to make a comment on a possible correlation since posttreatment sodium levels are unknown, impaired correlation may be attributed to sodium level increase. The lack of any study in the literature examining the relationship between hyponatremia and ONSD naturally makes it impossible to find any study comparing pre- and posttreatment levels.

Measurement of ONSD has been reported as a candidate tool to diagnose and monitor patients with ICP elevation [22,23]. Ertl et al., in a study of patients with hydrocephalus, reported that ONSD increased in parallel with an increase in CSF volume and that

Table 3
Relationship between saline concentrations and the resulting ONSD difference.

	n	Pretreatment ONSD mean ± SD	Posttreatment ONSD mean ± SD	ONSD difference mean ± SD	p
0.9% NaCl	28	0.511 ± 0.052	0.487 ± 0.052	0.024 ± 0.024	<0.001
3% NaCl	51	0.562 ± 0.073	0.518 ± 0.07	0.043 ± 0.028	<0.001

ONSD significantly dropped upon CSF drainage [24]. We showed a significant reduction in posttreatment ONSD level. We believe that depending on the administered therapy, as serum sodium level elevates, edema regresses, ICP decreases, and as a result, ONSD decreases. No study in the literature has yet examined how ICP varies upon treatment with 3% or 0.9% saline solution and how this is related to ONSD. However, restrictions with the use of 3% saline, which was the case until recently, was overcome by recent studies. Studies have recommended the use of 100 ml 3% saline solution through a peripheral venous access to treat patients with hyponatremia and neurological symptoms [25]. When brain injury and/or hypochloremic metabolic alkalosis is detected, it is advised that hyponatremia be slowly corrected using 0.9% saline [26].

While ONSD was greater in patients who had symptoms prior to treatment, no significant relationship was noted between pretreatment symptom type, posttreatment ONSD and symptoms. We believe that some symptoms regressed as a result of reduction of ICP by the administered therapy. We also suggest that ONSD was greater in the presence of symptoms due to ICP increase caused by hyponatremia leading to symptoms.

Hyponatremia is a non-neurological disease resulting in intracranial hypertension that is a critical life-threatening condition and a sign of poor prognosis [27]. This disease requires rapid recognition to allow for timely effective treatment. Therefore, simple, noninvasive, point-of-care predictive tools in ED as measurement of ONSD (which is one of the parameters used for indirect prediction of ICP) make the management of critically ill patients more practical. Although we did not identify any study that provides sensitivity and specificity values for ONSD in hyponatremia, studies examining the relationship between ICP increase and ONSD revealed a sensitivity of 88% and a specificity of 93% at a cut-off value of 5 mm; another found a sensitivity of 74% and a specificity of 100% at a cut-off value of 5.7 mm [18, 20]. In other studies on this subject, sensitivity was reported to be 74–98.6%, and specificity was 65–92.8% [28–30]. We detected a sensitivity of 81% and a specificity of 81.9% for a cut-off value of 0.49 mm. The sensitivity and specificity values found in our study agreed with those reported by other studies where ICP increase and ONSD measurement were performed.

5. Conclusions

Ultrasonic imaging of ONSD measurement in the emergency department appears to reflect changes consistent with ICP changes in hyponatremia and changes in serum sodium.

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