

Optic Nerve Sheath Diameter Used as Ultrasonographic Assessment of the Incidence of Raised Intracranial Pressure in Preeclampsia

A Pilot Study

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ABSTRACT

Background: In some cases of severe preeclampsia/eclampsia, brain imaging displays signs compatible with raised intracranial pressure. We aimed to estimate the incidence of raised intracranial pressure in preeclampsia using ocular ultrasonography.

Methods: Optic nerve sheath diameter (ONSD) measurements were compared in 26 preeclamptic and 25 healthy pregnant women. For each optic nerve, two measurements were made (transverse plane and sagittal plane) using a 7.5 MHz ultrasound linear probe. Preeclamptic patients were followed-up until postpartum day 7.

Results: Median ONSD values were significantly greater in preeclamptic patients compared with healthy pregnant women at delivery (5.4 mm [95% CI: 5.2, 5.7] vs. 4.5 mm

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What We Already Know about This Topic

- Severe preeclampsia/eclampsia may be associated with raised intracranial pressure

What This Article Tells Us That Is New

- Optic nerve sheath diameter (ONSD) measurements may offer a practical means of monitoring intracranial pressure trends
- In about 20% of preeclamptic patients, ONSD reaches values compatible with intracranial pressure above 20 mmHg

(95% CI: 4.3, 4.8), $P < 0.0001$). At delivery, 5/26 (19%) of preeclamptic patients had ONSD values above 5.8 mm (value associated in the literature with 95% risk of raised intracranial pressure) whereas none of the healthy pregnant group had such high ONSD values. In the preeclamptic group, ONSD decreased after the third postpartum day. ONSD values at day 7 were not significantly different from those obtained in the normal pregnancy group ($P = 0.10$).

Conclusion: In about 20% of preeclamptic patients, ONSD reaches values compatible with intracranial pressure above 20 mmHg. Further work is needed to confirm this incidence and to better understand the diagnostic and therapeutic usefulness of this easy-to-do monitoring technique.

◇ This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 9A.

◆ This article is accompanied by an Editorial View. Please see: Rollins M, Flood P: Imaging intracranial pressure: An introduction to ultrasonography of the optic nerve sheath. ANESTHESIOLOGY 2012; 116:983–4.

PREECLAMPSIA occurs in 7% to 8% of pregnancies and eclampsia in up to 0.9%.^{1,2} Preeclampsia/eclampsia is a potentially severe disease associated with maternal complications such as pulmonary edema, abruptio placenta, cardiac or renal complications, hemolysis, increased liver enzyme, low platelet count syndrome, and neurologic complications. Neurologic complications are now believed to be associated with the reversible cerebral vasoconstriction syndrome^{3,4} and/or the posterior leukoencephalopathy syndrome,⁴⁻⁶ which apparently overlap in a significant proportion of cases. These lesions share similar symptoms (headache, reversible blindness, confusion, seizures)³ but reversible cerebral vasoconstriction syndrome is predominantly associated with subarachnoid and intracerebral hemorrhage,⁴ whereas posterior leukoencephalopathy syndrome is typically associated with diffuse brain edema.⁷ The coexistence of posterior leukoencephalopathy syndrome with reversible cerebral vasoconstriction syndrome is noted in several reports,⁴ suggesting a common pathophysiology. Cerebral edema is predominantly vasogenic and may be related to failure of cerebral autoregulation with subsequent hyperperfusion, blood brain barrier disruption, and endothelial cell dysfunction.⁸ In some cases of eclampsia, computed tomography and magnetic resonance imaging show signs compatible with significant raised intracranial pressure (ICP).^{8,9} Clinical signs of raised ICP are not specific and often difficult to interpret, especially during pregnancy and preeclampsia. The actual incidence of raised ICP in preeclampsia is unknown, however.

The gold-standard method for ICP measurement is based on the use of invasive devices.¹⁰ Recently, clinical studies have suggested that ultrasonographic measurements of the optic nerve sheath diameter (ONSD) correlate with signs of raised ICP. The optic nerve, as part of the central nervous system, is surrounded by a dural sheath and a subarachnoid space containing cerebrospinal fluid. Three millimeters behind the ocular globe, the optic nerve is only surrounded by fat and the dural sheath is distensible within its fatty environment, particularly in case of raised pressure in the cerebrospinal fluid. In 1997, Hansen and Helmke showed that intrathecal infusion of lactated Ringer's solution leads to an increase in ONSD measured by ultrasonography.¹¹ Since then, numerous clinical studies have confirmed the accuracy of ONSD measurement at detecting raised ICP in several clinical situations: traumatic brain injury,^{12,13} hydrocephalus,¹⁴ and intracranial hemorrhage.¹⁵ Two recent meta-analyses suggest that ONSD may be a reliable noninvasive surrogate marker of raised ICP.^{16,17}

The aim of this descriptive study was to evaluate the incidence of raised ICP in preeclampsia using ocular ultrasonography with ONSD measurement. We hypothesized that preeclamptic patients had higher intracranial pressure than healthy pregnant patients at delivery. The study also aimed at describing the relationship between preeclampsia severity and the magnitude of raised ICP, along with the

effect of preeclampsia treatment and delivery on ONSD values.

Materials and Methods

Between January and September 2009, an observational study was conducted in preeclamptic patients and in healthy pregnant women. Exclusion criteria were: patient's refusal, ocular wound, and prior ocular surgery.

Preeclamptic patients were included at hospital admission. Preeclampsia was defined using the National High Blood Pressure Education Program criteria¹⁸: association of a blood pressure elevation (systolic pressure more than 140 mmHg or diastolic pressure more than 90 mmHg) and a proteinuria more than 0.3 g per day in a pregnant woman after 20 weeks of gestation. Severe preeclampsia was determined by the presence of one or more of the following signs and symptoms: blood pressure more than 160/110 mmHg; proteinuria more than 2 g per day; increased serum creatinine level more than 1.2 mg/dL; platelet count less than 100,000 cells/mm³; increased liver enzyme activities; epigastric pain; persistent headache; or other cerebral or visual disturbances. Patients suffering from preeclampsia without any of the above severe parameters were classified as mild preeclamptic women. Patient care was in line with existing protocols and was not modified during the study.

Healthy pregnant women from the same hospital were included at the time of the anesthesia antenatal visit, which is mandatory in France and generally performed around 35 weeks of gestation. These control subjects were consecutively included. To assess the stability of ONSD over time, ocular sonography was also performed in a second group of healthy pregnant women before (1 to 7 days) and after delivery (4 or fewer days after delivery).

We planned to include 25 preeclamptic patients compared with healthy pregnant women in a 1:1 process. As we conducted a pilot study, we did not perform any *a priori* power analysis.

All patients gave informed consent. The study protocol was approved by the institutional review board of Begin military hospital, Saint-Mandé, France.

Ultrasound measurement of ONSD was performed by two investigators trained in ocular ultrasonography (CD or VJ) as previously described.^{12,19,20} Patients were placed in supine position with the upper part of the body and the head at 30° above the horizontal position. A thick layer of gel was applied over the closed upper eyelid. A 7.5-MHz linear probe (Micromaxx®, Sonosite, Bothell, WA) was placed on the temporal area of the eyelid, the hand holding the probe placed on the forehead of the patient, to prevent excessive pressure being exerted on the eye. The placement of the probe was adjusted to give a suitable angle for displaying the entry of the optic nerve into the globe.¹¹ The field was reduced to a depth of 4 cm. The two-dimensional mode was used and ONSD was measured 3 mm behind the globe using an electronic caliper and an axis perpendicular to the optic



Fig. 1. Example of optic nerve sheath diameter (ONSD) measurement using ocular ultrasonography.

nerve (fig. 1). For each optic nerve two measurements were made, one in the transverse plane and the other in the sagittal plane. The reported ONSD corresponds to the mean of the four values obtained for each patient (transverse and sagittal plane for both eyes).

Statistical Analysis

Data were considered to have a nonnormal distribution and non parametric tests were used. Two-tailed comparisons were used. A Mann–Whitney U test was used to compare continuous data between groups and a chi-square test was used for proportion comparisons. Data from the participants of the second control group were analyzed using the Wilcoxon signed-rank test. Continuous data are expressed as median with 95% CI. $P < 0.05$ were considered significant. Statistical analyses were performed using Prism[®] 4.00 for Mac (Inc GraphPad Software, San Diego, CA).

Results

Twenty-six preeclamptic patients were included. Among them, 13 were classified as having severe and 13 as having mild preeclampsia. Twenty-five healthy pregnant women were included during the preanesthesia visit as a control group. Demographic data are presented in table 1. The two groups were similar in terms of age, weeks of gestation at the time of ocular sonography examination, number of gestations, and parity.

At admission, systolic, mean, and diastolic arterial pressures were significantly higher in the preeclamptic group compared with healthy pregnant women: respectively 143 mmHg (138,153) *vs.* 111 mmHg, (102,119) $P < 0.0001$; 105 mmHg (98,109) *versus* 84 mmHg, (80,92) $P < 0.0001$;

Table 1. Epidemiologic and Clinical Features of the Two Groups at the Time of First Ocular Sonography Examination

	Preeclamptic Patients (n = 26)	Healthy Pregnant (n = 25)	P Value
Age (years)	34 (31–36)	31 (28–34)	0.09
Gestation weeks	36.8 (33.5–37.2)	34.7 (33.5–35.0)	0.06
Gestivity	2 (1–4)	2 (1–3)	0.22
Parity	0 (0 to 1)	0 (0 to 1)	0.69
Primipara	58%	60%	0.88
Weight (kg)	80 (70–90)	69 (63–79)	0.04
Previous medical history of preeclampsia	31%	0%	0.24

Values are medians (95% CIs) unless specified.

and 84 mmHg (79,88) *versus* 70 mmHg, (66,75) $P < 0.0001$.

Ocular ultrasonography for both eyes was feasible in all patients. Five preeclamptic patients out of 26 (19%) had ONSD values above 5.8 mm (value associated in the literature with 95% risk of raised ICP¹³), whereas none of the healthy pregnant group had ONSD value 5.8 mm or greater. The median baseline ONSD in preeclamptic patients was 5.4 mm (5.2, 5.7) *versus* 4.5 mm (4.3, 4.8) in healthy pregnant women ($P < 0.0001$) (table 2).

After delivery, in the preeclamptic group, a decrease in ONSD was observed after the third postpartum day with values on day 7 not significantly different from those obtained in healthy pregnant women ($P = 0.10$) (fig. 2). At day 7 all preeclamptic patients had improved their clinical and biologic profile.

In the second control group, composed by healthy pregnant patients studied in the period surrounding delivery, ONSD measurement did not show any significant changes within this period: 4.9 mm (4.4, 5.4) before delivery *vs.* 4.8 mm (4.6, 5.4) after delivery, $P = 0.86$, $n = 9$ (figure 3).

Table 2. Optic Nerve Sheath Diameter Measurements and Hemodynamic Data at the Day of Delivery in Preeclamptic and Healthy Pregnant Women at the Time of Anesthesia Antenatal Visit

	Preeclamptic Patients (n = 26)	Healthy Pregnant (n = 25)	P Value
ONSD (mm)	5.4 (5.2–5.8)	4.5 (4.3–4.8)	<0.0001
Systolic BP (mmHg)	143 (138–153)	111 (102–119)	<0.0001
Diastolic BP (mmHg)	84 (79–88)	70 (66–75)	<0.0001
Mean BP (mmHg)	105 (98–109)	84 (80–92)	<0.0001

Values are medians and 95% CI.

BP = blood pressure; ONSD = optic nerve sheath diameter.

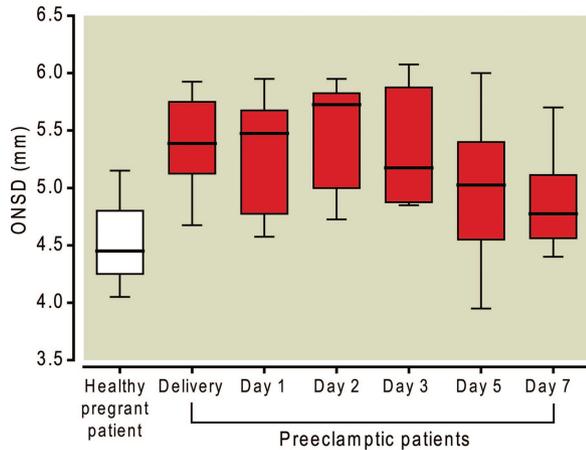


Fig. 2. Optic nerve sheath diameter (ONSD) in healthy pregnant women at the anesthesia antenatal visit and in pre-eclamptic patients on the day of delivery. Evolution over time in the 7 days after delivery. Tenth, 25th, 75th, and 90th percentiles, as well as median values, are represented.

Thirteen pre-eclamptic patients presented at least one criterion of severity. ONSD was not different in patients with mild and severe pre-eclampsia (table 3). Four patients presented criteria for hemolysis, increased liver enzyme, low platelet count, but ONSD values were not significantly different in this subgroup ($P = 0.83$). None of our patients presented with eclampsia.

Discussion

In this pilot study, we found a significantly higher ONSD in pre-eclamptic patients on the day of delivery when compared with values obtained in healthy pregnant women. Nineteen percent of pre-eclamptic patients had ONSD values compatible with raised ICP (above 5.8 mm). To our knowledge, this is the first description of the incidence of raised ICP in a cohort of pre-eclamptic patients. However, we were not able

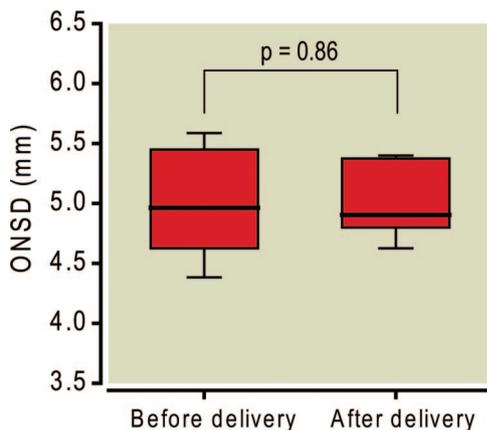


Fig. 3. Optic nerve sheath diameter (ONSD) in nine healthy pregnant women. Evolution before and after delivery. Tenth, 25th, 75th, and 90th percentiles, as well as median values, are represented.

Table 3. Comparison between Severe and Mild Preeclampsia: Optic Nerve Sheath Diameter, Hemodynamic Data, and Preeclampsia Severity Criteria on the Day of Delivery

	Severe Preeclampsia (n = 13)	Mild Preeclampsia (n = 13)	P Value
ONSD (mm)	5.4 (4.7–5.9)	5.4 (5.2–5.8)	0.70
Systolic BP (mmHg)	143 (137–160)	145 (135–153)	0.43
Diastolic BP (mmHg)	84 (77–93)	84 (74–92)	0.85
Mean BP (mmHg)	106 (98–114)	105 (95–113)	0.72
Proteinuria (g/l)	4.8 (0.3–10)	0.5 (0.4–1.5)	0.04
Serum creatinine (mg/dl)	0.75 (0.66–1.0)	0.73 (0.58–0.82)	0.18
Platelet count (/mm ³)	193 (99–233)	189 (174–222)	0.62
AST (U/l)	50 (27–261)	24 (22–34)	0.01
ALT (U/l)	45 (15–285)	15 (12–29)	0.01
Epigastric pain	4/13	0/13	0.10
Headache	7/13	1/13	0.03

Values are median and 95% CI.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BP = blood pressure; ONSD = optic nerve sheath diameter.

to show any relationship between pre-eclampsia severity and the magnitude of ONSD enlargement.

Loureiro *et al.* found criteria for vasogenic edema in 100% of their 17 patients by diffusion weighted imaging.²¹ Schwartz *et al.* showed evidence of brain edema in 20 out of 28 patients using the same imaging methods.²² Zeeman also assessed 27 patients with eclampsia and found cerebral edema in 25 of them (92%) on T2-weighted imaging.²³ This edema primarily involved the parieto-occipital gray-white junctions and the deep white matter. Using apparent diffusion coefficient mapping, they were able to show that although most patients had only vasogenic edema, one-fourth of them also had cerebral infarction with cytotoxic edema.²³ Whatever the mechanism, cerebral edema may lead to raised intracranial pressure. In a case report of severe pre-eclampsia with coma, Keswani and Wityk highlighted the magnitude of vasogenic edema in parieto-occipital lobes using magnetic resonance imaging.²⁴ In this case, a subarachnoid bolt showed raised intracranial pressure of 32 cm H₂O. In all these studies, however, the vast majority of patients had eclampsia. The incidence of cerebral edema and raised intracranial pressure in pre-eclampsia (but without eclampsia) is unknown.

Optic nerve sheath ultrasound is a noninvasive method for the assessment of the risk of raised ICP. The subarachnoid spaces surrounding the optic nerve communicate with the intracranial cavity and changes in cerebrospinal fluid pressure are transmitted along the optic nerve sheath.²⁰ In the anterior part of the optic nerve and particularly in the retrobulbar segment, the nerve is only surrounded by orbital fat. The retrobulbar optic nerve sheath is therefore distensi-

ble and can inflate in case of raised cerebrospinal fluid pressure. Comparing ocular ultrasonography with gold standard measures of ICP (invasive devices), values of ONSD above 5.8 mm have been shown to be associated with a 95% risk of raised ICP (*i.e.*, more than 20 mmHg).¹³ Such values were obtained in 19% of our preeclamptic patients, suggesting a substantial incidence of raised ICP in this population. However, we were not able to show any relationship between preeclampsia severity and the magnitude of ONSD enlargement. This can be the result of the relatively small sample size, with 26 preeclamptic patients in total, and only 13 severe patients among them. This can also be the result of the small proportion of patients presenting with neurologic signs. In our population, preeclampsia was classified as severe mainly due to renal dysfunction (27% of all preeclamptic and 54% of the severe preeclamptic patients) rather than to neurologic symptoms. Moreover, the medical management of our patients included urgent cesarean section in case of neurologic abnormalities, leaving few time to evaluate patients with such symptoms. Analysis of patients with a greater incidence of neurologic symptoms might be needed to establish a relationship with ONSD enlargement.

Using transcranial doppler, Oehm *et al.* showed in one severe preeclamptic and in 3 eclamptic patients that brain edema decreases noticeably 5 to 6 days after delivery.²⁵ In the present study, using ocular ultrasonography, we found a very similar evolution during the first 7 days after delivery.

There are some limitations for the use of ocular ultrasonography in the detection of raised ICP. First, inexperience with ultrasonography may be an important limitation of this method. As mentioned by Tayal *et al.*, the slope of the learning curve seems to be steep: an experienced sonologist needs as few as 10 measurements and three abnormal scans to obtain adequate results, whereas for novice sonologists, 25 scans may be needed.²⁶ Variability in ultrasonographic measurement of ONSD seems to be limited, as the median intraobserver and interobserver variations have been shown to be respectively less than 0.2 and 0.3 mm.^{13,27} In the present study, the difference in ONSD between preeclamptic and healthy pregnant women is 0.9 mm, a difference which was therefore very unlikely to be related to intra- or interobserver variations.

Conclusion

Using noninvasive assessment of intracranial pressure with ocular ultrasonography and ONSD measurement in preeclamptic and healthy pregnant women, we demonstrated a significantly higher ONSD in preeclamptic women. In about 20% of them, ONSD reaches values compatible with ICP above 20 mmHg. This noninvasive estimate of the incidence of raised ICP may be of interest for the care of these patients, when considering the risk of neurologic complications of preeclampsia. In this small pilot study, we were not able to show any relationship between ONSD enlargement and neurologic signs during severe preeclampsia. A study in a

larger cohort of preeclamptic patients with and without neurologic symptoms would be of great interest to study the usefulness of ONSD measurement to estimate the risk of significant brain edema.

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