

Effect of magnesium sulphate on the intracranial pressure of preeclampsia patients using ultrasound-guided optic nerve sheath diameter: A pilot study

ABSTRACT

Background: Increased intracranial pressure (ICP) is a known complication of pre-eclampsia with severe features. The use of magnesium sulphate ($MgSO_4$) is the standard treatment and is associated with marked reduction of cerebral perfusion pressure (CPP) and prevention of cerebral damage. Optic nerve sheath diameter (ONSD) ultrasonography is a bedside tool used to reflect changes in the ICP. The aim of this study is to detect the effect of $MgSO_4$ administration on ICP in severe preeclampsia through measuring changes in the ONSDs.

Methods: Thirty pregnant female patients suffering from severe pre-eclampsia were enrolled in this prospective pilot study. Ultrasound measurement of ONSD was measured before the commencement of $MgSO_4$ and after 1, 6, and 24 h after the administration.

Results: There was a significant difference in ONSD measurements between that at baseline and post magnesium administration at 1, 6, and 24 h (P -value 0.001). Additionally, a significant difference in measurements between 1 and 6 and 6 and 24 h after magnesium initiation (P -value 0.001).

Conclusions: Ultrasound ONSD measurement in patients with severe preeclampsia is a non-invasive easy tool to detect increased intracranial pressure and monitor the response to magnesium sulphate infusion.

Key words: Magnesium sulphate; optic nerve diameter sheath; preeclampsia

Introduction

Preeclampsia remains one of the leading causes of maternal morbidity and mortality in pregnant women. Cerebrovascular complications are one of the serious problems in severe preeclampsia. Cerebral edema detected by MRI imaging has been reported to be as high as 71–100% in patients suffering from severe preeclampsia.^[1-3] Early diagnosis and


management of brain edema and increased intracranial pressure (ICP) is of paramount importance.^[4]

The optic nerve with its dural sheath cover is considered a window to central nervous system. The subarachnoid space surrounds the optic nerve and communicates freely with the cerebral subarachnoid space. Changes in the optic

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nerve sheath diameter (ONSD) mirror the changes in the ICP as increases in the ONSD correlates with increase in the ICP.^[5] Bedside ultrasound measurement of the optic nerve has proved to be a simple and effective diagnostic tool to detect the increase in ICP in traumatic and critically ill patients.^[6] Recently, ONSD is used in patients suffering from preeclampsia.^[4,7,8] Researchers showed that changes in ONSD strongly correlate with computed tomography and MRI measurements in patients diagnosed with traumatic brain injury (TBI) and high ICP.^[9-11] A meta-analysis showed a 99% sensitivity and 73% specificity in detecting increased ICP when the ONSD is >5.0 mm.^[6] However, some authors decided to use ONSD of 5.8 mm as cutoff measurement to detect increased ICP in patients suffering from pre-eclampsia.^[4,7]

Magnesium sulphate ($MgSO_4$) is a drug that is routinely used in the treatment of preeclampsia and prevention of eclamptic fits.^[12] Magnesium stabilizes the nerve axons by stimulating the release of glutamate at the neuromuscular junction, thus inhibiting calcium entry at the presynaptic nerve terminal.^[13] A previous work showed a significant association between the magnesium usage and the decrease in intraoperative brain swelling in patients who suffered severe closed traumatic brain injury.^[14] Another work used transcranial Doppler (TCD) to demonstrated the effect of $MgSO_4$ on the cerebral perfusion pressure in patients suffering from severe pre-eclampsia and eclampsia.^[15]

The aim of this study is to determine the effect of $MgSO_4$ on ultrasound measurements of the ONSD as a surrogate measure to intracranial pressure in patients presented with severe preeclampsia.

Methods

Corniche hospital, Abu Dhabi, United Arab Emirates research ethics committee provided ethical approval for this study CH29011702. The study was registered with a clinical trial *registry clinicaltrial.gov* (number NCT032110350) prior to patient enrolment. Written informed consent was obtained for all patients. This study is an observational study according to the guidelines for strengthening the reporting of observational studied in epidemiology (*STROBE*).

Thirty pregnant patients who fulfilled the inclusion criteria of preeclampsia with severe features, as was defined using the American College of Obstetricians and Gynecologist Task Force on Hypertension in Pregnancy recommendation were recruited in this prospective pilot study.^[16] Patients with previous cranial or eye surgeries, or suffering from intracranial pathology, glaucoma, or other eye pathology

were excluded from the study. Additionally, patient who got their $MgSO_4$ medication before the first reading of ONSD were also excluded.

As per our institution's standard protocol, all pre-eclamptic patients on $MgSO_4$ were admitted to high dependency Unit (HDU) for at least 24 h. Invasive blood pressure continuously measured, fluid intake, and urine output were assessed hourly. Blood tests were repeated every 12 h to monitor kidney function, electrolytes, full blood count, liver transaminases, and bilirubin. $MgSO_4$ was used for eclampsia prophylaxis as a 4 g intravenous loading dose, followed by 1 g/h infusion for 24 h. The study patients were recruited at the time of admission in HDU or Emergency suite. Once the decision was made to start $MgSO_4$ the ONSD was measured during the time of $MgSO_4$ preparation to avoid any delay for the initiation of the treatment. Intravenous antihypertensive medications were started also according to our institution policy to keep systolic blood pressure <160 mmHg and diastolic blood pressure <110 mmHg. Measurements of ONSD were repeated 1 h after finishing the $MgSO_4$ loading dose, 6 and 24 h after the start of infusion.

Patients were in the supine position with the head of the bed was less than 20° elevation. A high frequency (7.5 MHz) linear probe of Terason uSmart 3200T was used. The thermal index was kept less than 0.8 and the time of application was between 30 and 60 s to avoid any possible eye injury. The probe was placed gently over each closed eye after liberal application of a sterile gel, the patients were instructed to look forward aligning the optic nerve directly opposite to the probe. The ONSD was measured 3 mm behind the optic disc in both the sagittal and transverse planes of each eye and then an average was calculated and recorded. The ONSD measurement ≥ 5.8 mm was used as a cutoff point to determine increased in the ICP. Hemodynamic variables were recorded at the same times.

Statistical analysis

The results were analyzed using the Statistical Package for Social Science (IBM SPSS Statistics for Macintosh, Version 20.0. Armonk, NY, USA). Normality was tested by Shapiro–Wilk's test. The paired *t*-test was used to compare the mean of average ONDS at the 4 points of measurements. *P* value for this measurement was set on 0.0125 to reduce the risk of type 1 error (Bonferroni correction). As a post-hoc analysis, linear regression was done between ONDS and mean arterial pressure (MAP) at all predetermined measurements points. Numerical data are presented as mean and SD or confidence interval whenever appropriate.

Results

This study included a total of 30 parturient with severe preeclampsia. Patients with an average age 31.9 ± 5.9 years (range 19–43 years), with a mean gestational age 31.8 ± 5.9 weeks (range 22–40 weeks) and body mass index (BMI) 33.5 ± 6.0 kg/m² (range 22.3–47.8 kg/m²). Preeclampsia presentation, mode of delivery, and anesthesia technique are presented in [Table 1]. Data were normality distributed as Shapiro–Wilk’s test for normality was statistically insignificant ($P > 0.05$).

The paired *t*-test was used to compare the mean of average ONDS before and after administration of MgSO₄ [Table 2]. There was a significant difference at ONDS from the baseline at 1, 6, and 24 h after MgSO₄ administration with *P* value of 0.000 [Figure 1]. A second set of comparison of ONDS done between 1 and 6 h and 6 and 24 h from MgSO₄ administration, these comparisons were statistically significant with a *P* value of 0.000.

A simple linear regression was performed to predict the correlation between ONDS and MAP at all predetermined measuring points. At the baseline measurement insignificant regression equation was found ($F(1,28) = 1.35, P 0.254$), with an *R*² of 0.046. At 1 h of measurement; insignificant regression was found with equation ($F(1,28) = 0.042, P 0.839$), with an *R*² of 0.034. Furthermore; correlation done at 6 h were insignificant with regression equation of ($F(1,28) = 0.326, P 0.573$), with an *R*² of -0.024. At 24 h, the regression was insignificant with the following equation ($F(1,28) = 0.014, P 0.905$), with an *R*² of -0.035. All of this is indicative of negative correlation between drop in ONDS and MAP.

Discussion

The present work demonstrated that ONSD could be used to detect an increase in the ICP and monitor the effect of magnesium in patients with severe preeclampsia. The study also showed that there was no correlation between the ONSD and MAP at any measured time point.

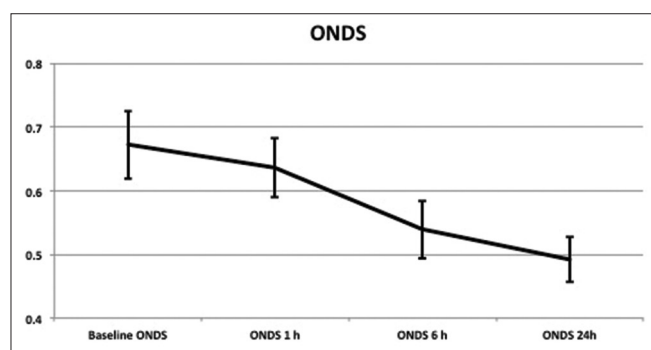


Figure 1: Optic nerve diameter sheath (ONDS) over time

Baseline measurements of ONSD was marked increase in all parturient participated in the current study, this was in the agreement with previous work done by Simenc *et al.*, Aduagi *et al.*, Singh and Bhatia, and Bala *et al.* that showed the correlation between increased ICP and increased ONSD in patients suffering preeclampsia and eclampsia when they used ultrasound technique.^[4,7,8,17] Furthermore, increased ICP was also supported by MRI in a studies carried out by Loureiro *et al.*, Schwartz *et al.*, and Zeeman *et al.* that showed evidence of brain edema in 100%, 71%, and 92%, respectively, in patients suffering from eclampsia and severe preeclampsia.^[1-3]

Table 1: Patients presentation, Mode of delivery and anesthesia technique

	Number (percent)
Preeclampsia presentation:	
Neurological manifestations	21 (70%)
Eclamptic fit before admission	1 (3%)
Abdominal pain	10 (33%)
HELLP syndrome	3 (10%)
Postnatal preeclampsia	3 (10%)
Mode of delivery:	
Caesarean section	20 (67%)
Vaginal delivery	8 (27%)
Intrauterine fetal death IUFD	2 (7%)
Anesthesia technique:	
Spinal anesthesia	19 (63%)
Epidural anesthesia	3 (10%)
General anesthesia	3 (10%)
Vaginal delivery without analgesia	4 (13%)
Delivered outside our hospital	1 (3%)

Table 2: Effect of magnesium sulphate on optic nerve diameter sheath

	Mean (SD) N = 30		95% confidence interval	t statistic (df)	P
	Time 1	Time 2			
Baseline ONDS & 1 h after magnesium	0.67 (0.05)	0.63 (0.04)	0.018 - 0.05	4.12 (29)	0.000
Baseline ONDS & 6 h after magnesium	0.67 (0.05)	0.53 (0.04)	0.018 - 0.15	11.3 (29)	0.000
Baseline ONDS & 24 h after magnesium	0.67 (0.05)	0.49 (0.03)	0.15 - 0.02	15.4 (29)	0.000
ONDS 1 & 6 h after magnesium	0.63 (0.04)	0.53 (0.04)	0.08 - 0.11	14.0 (29)	0.000
ONDS 6 & 24 h after magnesium	0.53 (0.04)	0.49 (0.03)	0.03 - 0.05	8.7 (29)	0.000

SD = Standard deviation & df = degree of freedom

The diagnostic accuracy of ONSD was validated in patients with traumatic brain injury. A meta-analysis of Aduayi *et al.* documented that ONSD measurements of >5.0 mm can detect increased ICP by computed tomography (CT) with 99% sensitivity and 73% specificity.^[6] Furthermore, another study compared ONSD by US to direct measurement of ICP showed that using 5.0 mm can be used as a cutoff limit to detect ICP >20 cm H₂O with 88% sensitivity and 93% specificity.^[18] In the current study, 5.8 mm was used as the cutoff point, based on the previous studies done on patients suffering preeclampsia and eclampsia.^[4,7,17] The current study showed that ONSD measurements were above the cutoff point in 100% of patients compared to the study carried by Simenc *et al.* which showed a 43% of baseline ONSD measurement above the cutoff point.^[4] This difference could be attributed to the difference in percentage of patients presented with neurological manifestations which is higher in our patients (70%) compared to 53% in Simenc study.

To our knowledge, this is the first study that attempts to correlate the relationship between MgSO₄ therapy and the ONSD as a surrogate to ICP in patients suffering from severe preeclampsia/eclampsia. A previous study by Dhandapani *et al.* used MgSO₄ in treatment of severe closed traumatic brain injury showed a significant decrease in intraoperative brain swelling and improved neurological output in relation to the control group.^[14]

There are some limitations in our study. Firstly, the confounding effect that antihypertensive drugs might have an effect on the ONSD measurements where it is unethical to withhold the antihypertensive drugs to such group of patients and this could also explain the negative correlation between drop in ONSD and MAP. Secondly, still the effect of the anesthesia on the ONSD needs further evaluation. Thirdly, there is no studied showed the correlation between ONSD and direct ICP measurements in patients suffering from pre-eclampsia, so most of the data used in the study were derived from previous work done on patients with traumatic brain injury.

Conclusions

Ultrasound ONSD measurement in patients with severe preeclampsia may provide a noninvasive, easy and reliable tool to detect increased intracranial pressure and to monitor the response to MgSO₄ therapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other

clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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