Journal of Critical Care 31 (2016) 168–171

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Ultrasound assessment of optic nerve sheath diameter in healthy volunteers☆

Patrick Goeres, BSc [a], Frederick A. Zeiler, MD [a], Bertram Unger, MD, PhD [b], Dimitrios Karakitsos, MD, PhD, DSc [c], Lawrence M. Gillman, MD, MMedEd, FRCSC, FACS [a,*]

[a] Department of Surgery, University of Manitoba, Winnipeg, MB, Canada
[b] Department of Medical Education, University of Manitoba, Winnipeg, MB, Canada
[c] Department of Internal Medicine, University of South Carolina, Columbia, SC

ARTICLE INFO

Keywords:
Point of care ultrasound
Optic nerve sheath diameter
Ultrasound
Intracranial pressure

ABSTRACT

Background: Ultrasound assessment of optic nerve sheath diameter (ONSD) has been suggested as a non-invasive measure of intracranial pressure. Numerous small studies suggest its validity; however, discrepancy exists around normal values for ONSD. In this study we sought to define a normal value range for ONSD in a population of healthy adult volunteers.
Methods: ONSD was measured in healthy adult volunteers and a normal range was defined using descriptive statistics. A regression analysis was used to determine relationship between ONSD measurements and sex, age, height and weight.
Results: One hundred twenty adults were recruited (age 18-65 [mean 29.3]) with 55 male and 65 female subjects. Mean ONSD was 3.68 mm (95% confidence interval [CI], 2.85-4.40). Upon regression analysis, mean ONSD did not vary with age, weight, or height but did vary with sex. Mean ONSD measurements for men were 3.78 mm (95% CI, 3.23-4.48) compared with 3.60 mm (95% CI, 2.83-4.11) for women.
Conclusion: This study has defined the range of ONSD in a healthy cohort of volunteers. The lack of relationship to age, weight and height is similar to other studies but this is the first study to find a difference depending on sex suggesting the possible need for separate reference ranges for men and women.

1. Introduction

Ultrasound assessment of optic nerve sheath diameter (ONSD) has been suggested as a non-invasive measure of intracranial pressure (ICP) and was first described in 1987 [1]. Elevated ICP is associated with worse outcomes in head injured patients. Hence, close ICP monitoring is a fundamental strategy enabling prompt and aggressive therapy [2]. Current literature supports the correlation between increased ONSD and increased ICP in a variety of adult and pediatric patient populations [3], including those with traumatic brain injury, mass lesions, infection, and in transplant recipients with reperfusion injury [4–8].

Invasive ICP monitoring via intra- parenchymal or ventricular monitors is the gold standard method in assessing ICP, but carries risks such as infection and bleeding [9]. Other techniques, such as detection of papilledema via fundoscopy, have significant limitations including high operator dependence, and only qualitative rather than quantitative results [7]. Studies supporting ONSD measurements show low inter and intra observer variability [10–13]. Numerous small studies suggest its validity however discrepancy exists around thresholds for elevated ONSD and normal reference ranges, as most measurements are derived from unhealthy subjects who have abnormal invasive ICP measurements [7,14–17] Potential exists for a clinically useful and rapid assessment of ICP by ocular ultrasound, although a well defined, large control population has yet to be studied. In this study, we sought to define a normal value range for ONSD in a large population of healthy adult volunteers.

2. Methods

2.1. Subjects

Healthy volunteers (not patients) over the age of 18 were recruited via email and print advertisement to participate in this study. Subjects were excluded if they had any history of ocular disease/pathology or intra-cranial pathology. All subjects signed a consent form in accordance with the University of Manitoba Health Research Ethics Board.

☆ Presented as a podium presentation at the Trauma Association of Canada (TAC) Meeting in Calgary, Alberta, April 2015.

* Corresponding author at: Z3053-409 Tache Avenue, Winnipeg, Manitoba, Canada, R2H 2A6. Tel.: +1 204 258 1408; fax: +1 204 237 3429.
E-mail addresses: goeresp@myumanitoba.ca (P. Goeres), umzeiler@cc.umanitoba.ca (F.A. Zeiler), bertram.j.unger@gmail.com (B. Unger), karakitsosdimitrios@gmail.com (D. Karakitsos), gillmanlm@yahoo.ca (L.M. Gillman).

http://dx.doi.org/10.1016/j.jcrc.2015.10.009
0883-9441/

2.2. Sample size

Based on a previous study [10] we predicted a standard deviation of 0.5 in our sample and therefore power sample analysis revealed that 120 subjects would be required to predict the population's ONSD mean to an accuracy of +/− 0.1 mm. In addition, research in laboratory medicine has shown that a sample of 120 participants is adequate to determine the normal range of a population for a given test [18]. Previous research of Magnetic Resonance Imaging measurements of ONSD had shown that ONSD in adults does not vary significantly by age and therefore a balanced sample covering all age ranges was felt to be unnecessary and thus 120 random subjects were sought [19].

2.3. Measurement technique

All measurements were performed by a single trained expert (LG). All patients were placed in a supine position with no elevation of the head of the bed and images were obtained through a closed eyelid using a generous amount of ultrasound gel. Utilizing a standard technique most widely reported in the literature [7,20], a 13-6 MHz linear array ultrasound transducer (L25x transducer with a Sonosite M-Turbo Ultrasound Machine, SonoSite Inc, Bothell, WA) was used to measure the ONSD, in 2 planes for each eye, 3 mm behind the optic nerve head, for a total of 4 measurements per subject.

2.4. Statistical analysis

Mean ONSD, SD, and 95% confidence interval (CI) were calculated for each of the ONSD measurements, mean of all 4 measurements, and the maximum of all 4 measurements. Each of the 4 ONSD measurements was compared for agreement by analysis of variance (ANOVA) and Bland Altman Plot. Main effect linear regression modeling was used to compare the relationship between mean ONSD and sex, weight and height. Analysis was completed using both the Statistical Analysis Software version 9.3 (SAS Institute, Cary, NC) and R Statistical Library (R Core Team, 2013).

3. Results

Subjects included 65 men and 55 women. Mean age was 29.3 (range, 18-65). Overall mean ONSD measurement was 3.68 (95% CI, 2.85-4.40) (Table 1). Overall, there were no significant differences between any of the 4 measurements ($P = 0.87$) (Fig. 1). Bland-Altman Plot did not demonstrate any evidence of systematic bias within the data (data not shown). However, intraclass correlations (ICC) between each of the 4 individual measurements revealed an overall ICC of 0.765 (95% CI, 0.705-0.818) (Table 2). Linear regression revealed a relationship between mean ONSD and sex but no change with age, weight or height (Table 3). By gender, the mean ONSD was significantly different ($P = .0001$); 3.54 (95% CI, 2.83-4.11) for women and 3.80 (95% CI, 3.23-4.48) for men (Fig. 2).

Table 1
Mean ONSD, SD and 95% CI for each eye in both the saggital and horizontal plane, as well as mean and maximum of each of the 4 measurements per subject

Measurement	Mean (mm)	SD	95% CI (mm)
Left horizontal	3.66	.42	2.80 – 4.50
Left saggital	3.69	.39	2.80 – 4.40
Right horizontal	3.66	.39	2.80 – 4.40
Right saggital	3.70	.39	2.90 – 4.40
Overall mean	3.68	.36	2.85 – 4.40
Maximum	3.86	.38	3.00 – 4.50

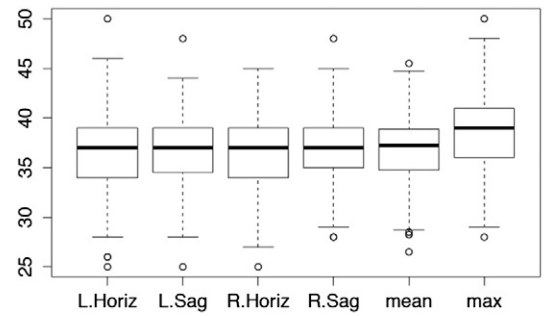

Fig. 1. Boxplot demonstrating relationship between ONSD measurement in 4 planes, mean of the 4 measurements and the maximum (largest) of the 4 measurements.

4. Discussion

Ultrasound measurement of ONSD appears to be a promising, rapid, non-invasive bedside tool for identification of elevated ICP. There are a number of other novel, non-invasive technologies for ICP measurement including HeadSense (Headsense Medical Ltd, Netanya, Israel) and Vittamed 205 (UAB Vittamed, Kaunas, Lithuania). While HeadSense remains still early in development and testing phases with no current published trials, Vittamed on the other hand has shown some success in a number of smaller prospective trials [21,22]. Despite this, ONSD measurement remains the most widely studied, noninvasive technique for ICP estimation and has the advantage of not requiring any proprietary software or hardware and can be carried out using equipment already widely available in many emergency departments. However, an accurate cut-off value for normal versus elevated ICP has yet to be conclusively established. To date, most studies advocate a threshold of 5 mm [14–17] with some studies suggesting thresholds as high as 5.7 to 5.9 mm [5,7,20,23]. However, this has been based mainly on small studies in non-healthy individuals and the true range of ONSD measurements in a healthy population is still not known. In our study, overall mean ONSD measurement was 3.68 mm (95% CI 2.85-4.40), which is consistent with other European studies [12] but lower than a recent Bangladeshi population [24]. The authors of the Bangladeshi study wondered if the difference could be related to ethnicity. Unfortunately, we did not record ethnic origin as part of our data, though our Canadian population would likely be very similar in diversity to the other European study populations. Another reason for the lower mean measurements could relate to the technique. The technique we utilized is often referred to as the "black stripe" technique and is the most common technique currently advocated in the literature [5,7,14,20,21,16,17,23]. However, new quality criteria recently introduced (following the data collection for this study) by Sargsyan et al [25] may help eliminate some of this variation in results. Studies comparing these criteria to the standard "black stripe" technique have yet to be published however and this is an exciting area in need of further study.

Our current findings suggest that the ONSD range in the general healthy population is reasonably wide and this could have implications for the clinical utility of ONSD ultrasound. The extent of nerve sheath dilation with increased ICP has not been clearly demonstrated; however, acute increases during transplant reperfusion are shown to be approximately 0.4 mm [8]. Therefore, if a patient's baseline ONSD was at the lower end of our demonstrated range, an increased ONSD may not be

Table 2
Intraclass correlations between each of the 4 measurements of ONSD

	Left horizontal	Left sagittal	Right horizontal	Right sagittal
Left horizontal	1.0000	0.8107	0.7634	0.7735
Left sagittal	0.8107	1.0000	0.7734	0.7523
Right horizontal	0.7634	0.7734	1.0000	0.7160
Right sagittal	0.7735	0.7523	0.7160	1.0000