Optic Nerve Sonography in the Diagnostic Evaluation of Pseudopapilledema and Raised Intracranial Pressure: A Cross-Sectional Study

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Received 28 September 2014; Revised 21 December 2014; Accepted 9 January 2015

Academic Editor: Mamede de Carvalho

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Introduction. Differentiating pseudopapilledema from papilledema which is optic disk edema and a result of increased ICP (intracranial pressure) is important and can be done with noninvasive methods like orbital ultrasound examination. Method. This was a cross-sectional study in which patients with optic nerve head swelling were referred for LP exam after optic nerve head swelling diagnosis confirmation and having normal brain imaging (CT scan). Before LP (lumbar puncture) exam the patients were referred for optic nerve ultrasound test of both eyes. Results. Calculating accuracy validity of ONSD measurement in detecting pseudopapilledema is 90% for the right eye and 87% for the left eye. Conclusion. Our study demonstrated a close correlation between optic nerve sheath dilation on ocular ultrasound and evidence of elevated ICP with optic disk swelling. With the aid of noninvasive diagnostic tests we can avoid unnecessary concerns along with expensive and invasive neurological investigations while targeting the correct diagnosis in bilateral optic disk swelling. Our study showed optic nerve sonography as a reliable diagnostic method for further usage.

Clinical Study

1. Introduction

While papill edema is Optic Nerve Head (ONH) edema secondary to increased intracranial pressure (ICP), pseudopapilledema is apparent ONH swelling that stimulates some features of papill edema but is secondary to an underlying, usually benign, process which can be congenital anomalies associated with the disk elevation, hyperopic disk, or ONH drusen.

Acquired disk edema includes papilledema as well as other causes of optic disk edema such as optic neuritis, anterior ischemic optic neuropathy, malignant hypertension, infiltrative optic neuropathies, and compressive optic neuropathy [1].

ONH drusen accounts for 75% of clinical cases of pseudopapilledema, occurs in up to 2% of general population, and is congenitally inherited; it has the same prevalence between men and women and is usually bilateral. Patients with ONH drusen are usually asymptomatic but visual field defects can be present.

Diagnosis is most reliably made by orbital ultrasound examination [1].

Clinical features in pseudopapilledema differ from papilledema; pseudopapilledema patients usually have no visual
symptoms while papilledema patients can have the follow-
ing symptoms: transient visual obscurations, blurring of
vision, diplopia, decreased color perception, and so forth.
Also papilledema is almost always bilateral while pseudopa-
pilledema can be either bilateral or unilateral. Furthermore
there are some funduscopic assessment features seen in true
papilledema which can help to distinguish it from pseudopa-
pilledema, such as hyperemia of the optic disk with surface
telangiectatic vessels, congested vasculature, and associated
flame hemorrhages, optic disk elevation, and blurring of the
disk margin associated with obscuration of the retinal vessels
that traverse it. Lack of spontaneous venous pulsations at disk
margin suggests true papilledema, but it is not diagnostic [1].

ONH elevation tends to be the most intimidating ocular
finding especially when it presents bilaterally. The fore-
most clinical aim is to differentiate pseudopapilledema from
acquired disk edema. Papilledema is ONH edema as a result
of increased ICP, which bears specific etiologic implications.
The most important entity to consider in cases of increased
ICP is a space occupying lesion of the brain. A through
history and a dilated fundus examination with use of current
diagnostic technologies can facilitate the diagnosis. Orbital
ultrasound examination is reported to be a useful noninvasive
way which increase our ability to diagnose and manage these
challenging case scenarios [2–5].

The purpose of this paper is to provide clinical strategies
that will enhance clinicians’ assessment of bilateral disk
elevations. In addition, this topic is important to review
because effective management will reduce over referrals for
neurological evaluations, thus decreasing health care costs
while avoiding LP, which is the gold standard test for ICP
measuring, and other expensive imaging technologies.

2. Method

This was a cross-sectional study in 2013–2014, in which 32
(64 eyes) patients with bilateral ONH swelling whom had
visited the ophthalmology or neurology clinic of Firoozgar
Hospital, located in Tehran, Iran, were included. We excluded
patients who had contraindication for LP such as increased
intracranial pressure due to brain mass, bleeding diathesis
such as coagulopathy and thrombocytopenia, skin infection
at puncture site, sepsis, abnormal respiratory pattern, focal
neurologic deficit, and loss of consciousness. Ophthalmic
evaluation was done by expert ophthalmologist to rule out
other causes. Also computerized tomography (CT) scan was
done for all of the patients; if it did show any mass or
abnormality which could be the reason for optic disk edema,
the patient must be excluded.

We explained the process of our research for all included
patients before starting data gathering. We asked them to
sign written testimonials if they accept being included; also
they had the choice to stop cooperating with our project
whenever they want. Furthermore we have to point that
our study was noninvasive and did not harm any body and
we respected Helsinki declaration all along our project. We
obtained ethical approval and it was not a part of routine care.

The patients were referred for LP exam after ONH
swelling diagnosis confirmation and normal brain imaging.
Before LP exam we had measured the vertical and horizontal
diameters of the optic nerves of both eyes by ultrasonography
(US) in supine position. The probe was placed on the superior
and lateral aspect of the orbit against the upper eyelid with
the eye closed and angled slightly caudally and medially
until the optic nerve was visualized as a linear hypoechoic
structure with clearly defined margins posterior to the globe.
The probe was always placed gently on the closed eyelid
without any contact with the cornea or sclera. Contact with
the eye was gentle and pressure never directly applied on the
globe with the probe, as this can theoretically result in nausea,
vomiting, and a vagal response. The ONSD was measured
3 mm behind the retina; the measurements were done by
wetting the closed eyelids and using a 7.5 MHz linear probe.
All of the measurement in optic sonography was done by
expert and particular person. We compare the ultrasound
results with the LP results as the gold standard of measuring
ICP for each patient.

Statistical Analysis. All analysis and comparisons were done
with SPSS version 16. The mean of right and left eyes ONSD
(optic nerve sheath diameter), OND (optic nerve diameter),
and CSF pressure were calculated. A receiver operating
characteristic (ROC) curve was constructed to determine the
optimal ONSD and OND cut-off to detect ICP > 20 mmHg.
We calculated the sensitivity and specificity of this cut-off
with 95% confidence intervals for the detection of ICP >
20 mmHg. Also the sensitivity, specificity, positive predictive
value, negative predictive value, and accuracy validity of
optic sonography were calculated for detecting of pseudopap-
pilledema. At last we calculate the diagnostic accuracy which
is in fact a criterion that considers sensitivity and specificity
together for determination of optic sonography value in
diagnosis of pseudopapilledema.

3. Results

We performed ocular sonography on 29 female and 3 male
patients with swelled optic disk. The mean age of patients was
35.44 ± 13 (19–75 years old), 19 patients were below 35 years
old and 13 were older than 35 (Table 1).

According to the literatures we set 5.7 mm and 20 mmHg
as the cut-off values for ONSD and CSF pressure, respectively.
We measured CSF pressure, RT.ONS, and LT.ONS in
patients. Results show that 68.8% (22 patients) of the patients
had CSF pressure more than 20 mmHg, and for 81.4% (26

<table>
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<tr>
<th>Table 1: Results (RT = right, LT = left, OND = optic nerve diameter, and ONSD = optic nerve sheath diameter).</th>
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<tr>
<td>CSF pressure</td>
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Table 2: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy validity of optic sonography in diagnosis of PPE.

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<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy validity</th>
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<tbody>
<tr>
<td>RT.ONSD</td>
<td>100</td>
<td>84</td>
<td>60</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>LT.ONSD</td>
<td>100</td>
<td>88</td>
<td>70</td>
<td>100</td>
<td>87</td>
</tr>
<tr>
<td>Both eyes together</td>
<td>100</td>
<td>83</td>
<td>55</td>
<td>100</td>
<td>86</td>
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patients) and (25 patients) 78% of patients RT.ONSD and LT.ONSD were more than the chosen threshold, respectively. 
Due to our measurements, patients with high ICP had significantly larger ONSD comparing to the patients with normal ICP (right ONSD, OR: 5.2 mm, \( P = 0.001 \), Kappa: 0.67 and for left ONSD OR: 4.1 mm, \( P = 0.002 \), Kappa: 0.76). Additionally comparing OND of patients with high ICP with ones with normal ICP demonstrates the significantly higher OND in patients with high ICP (RT OND, OR: 1.15, \( P = 0.000 \) and for LT OND OR: 1.20, \( P = 0.000 \)).

Considering 5.7 mm as the upper limit for normal ONSD, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy validity of optic sonography in diagnosis of PPE are shown in Table 2.

Due to the lack of enough male subjects we could not assess the accuracy validity of ONSD measurement in detecting pseudopapilledema based on gender. Based on the measurements age did not affect accuracy validity of optic sonography for detecting pseudopapilledema (RT.ONSD sig: 0.497 and LT.ONSD sig: 0.21).

The area under the curve (AUC) for RT.ONSD and LT.ONSD is 0.8 and 0.91 (\( P < 0.01 \) for AUC = 0.5), respectively. The best RT.ONSD cut-off value for detection of invasive ICP > 20 mmHg is 5.95 mm with 86% sensitivity and 70% specificity. The best LT.ONSD cut-off value for detection of invasive ICP > 20 mmHg is 5.86 mm. The sensitivity of this cut-off is 90% and the specificity is 80%. The best ONSD cut-off for both eyes together is 5.91 mm (sensitivity 86%, specificity 75%, AUC 0.85, \( P < 0.000 \)) (Figure 1).

The best RT.OND cut-off for the detection of invasive ICP > 20 mmHg is 3.15 mm (sensitivity 78%, specificity 66%, AUC 0.8, \( P < 0.01 \)). The best LT.OND cut-off for the detection of invasive ICP > 20 mmHg is 3.19 mm (sensitivity 85%, specificity 63%, AUC 0.74, \( P < 0.04 \)). We also calculated OND cut-off for both eyes together that was 3.19 mm (sensitivity 82%, specificity 59%, AUC 0.77, \( P < 0.001 \)).

4. Discussion

Our study demonstrates that optic nerve ultrasound with measurement of ONSD (optic nerve sheath diameter) is a highly accurate noninvasive technique for detection of intracranial hypertension. The literature, supporting our data, has reports of correlation between ONSD and intracranial hypertension among intracranial hemorrhagic patients [2] and based on considering 7.3 mm as the upper limit of normal ONSD [3]. Correspondingly some reports show that optic nerve ultrasound can be delightfully helping for ICP raising diagnosis when other imaging methods or invasive neurological testing is contraindicated in patients [4, 5].

Also in our research based on considering 5.7 mm as the upper limit of normal ONSD for detecting ICP more than 20 cm Hg, the sensitivity and negative predictive value of optic nerve ultrasound in diagnosis of pseudopapilledema for the right and left eyes were 100%. There are different reports for sensitivity and negative predictive values among literatures; Rajajee et al., by assessing ONSD in 56 patients with head trauma, intracranial hemorrhage, ischemic stroke, and cranial tumor, found that ICP raising correlates with ONSD in optic nerve ultrasound. With ROC curve and analysis they demonstrated that the optimal cut-off for ICP > 20 cm Hg is 4.8 cm for both eyes with 96% sensitivity and 94% specificity [6]. Moreover, Major et al. assessed ONSD in 26 patients. They showed that the optimal ONSD cut-off for increased ICP is 5 mm with 86% sensitivity and 100% specificity [7]. There are different sensitivity and specificity values for different cut-off chosen for ONSD demonstrating increased ICP among literatures [8, 9]. These different reports could be as a matter of fact that each research has different population with different epidemiologic features and also different number of subjects; furthermore choosing lower measures for ONSD cut-off in optic nerve ultrasound can affect the statistical values in this regard. To the authors’ knowledge, there are not many reports for assessing a reliable ONSD cut-off among Iranian population [10]; also there are not many reports for assessing correlation between ONSD and ICP raising among literature which make our research novel.
There are some reports among literature which chose their cut-off 5.7 mm in the same way as we did [11, 12]. On the other hand, there are many of reports that chose a lower cut-off which has a wide threshold among different researches from 4 mm to more than 5 mm [8, 9]. Besides we found some different data for ONSD and OND in detecting of raised ICP in comparison of left and right eye together that was not considered in other researches. All these different reports contribute to one similar conclusion; optic nerve ultrasound is a reliable diagnostic test for detecting raised ICP.

One limitation of our study was our sample size; there would be lower measure for our ONSD cut-off if we chose a larger sample size. Another limitation was that only suspected pseudotumor cerebri patients were included with normal neuroimaging and hence more female patients were included. We could not find any relationship between gender and ONSD because about 90% of our subjects were female. This issue could be considered for further researches that female's and male's ONSD cut-off could be different or not.

5. Conclusion

Our study demonstrated a close correlation between optic nerve sheath dilation on ocular ultrasound and evidence of elevated ICP with optic disk swelling. As mentioned before ONH swelling has many differential diagnoses but the critical one is true papilledema which could be a sign of raised ICP and a serious brain problem which need urgent intervention. Hence, clinicians must rule out pathological presentations that can be misinterpreted as swollen anomalous nerves which are called pseudopapilledema. Our study showed optic nerve sonography as a reliable diagnostic method in this regard for further usage.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors’ Contribution

Masoud Mehrpour carried out the overall studies and participated in the design of the study and had active role in acquisition of data. Fatemeh Oliaee Torshizi participated in the design of the study, performed the statistical analysis and participated in data gathering, and had given final approval of the version to be published. Shooka Esmaeeli drafted the paper, participated in the data gathering and helped in performing the statistical analysis. Salameh Taghipour participated in the design of the study and coordination and helped to draft the paper and, she also participated in the sequence alignments. Sahar Abdollahi helped to draft the paper, participated in performing the statistical analysis, and helped in data gathering. All authors read and approved the final paper.

Acknowledgment

The authors thank the Firoozgar Hospital Ophthalmology Department who refer the patients with whit optic disk edema to our department.

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