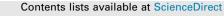
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HIGHLIGHTS

- The optic nerve diameter (OND) was thicker in the affected eye compared with its unaffected fellow or controls.
- An increased OND was found in 78–100% and papilledema in 6–43% of patients.
- B-mode transorbital ultrasonography provides promising support for the clinical diagnosis of acute optic neuritis.

ABSTRACT

Objective: In patients with acute optic neuritis (AON) transorbital sonography may reveal a thickening of the retrobulbar portion of the optic nerve. Our aim was to systematically review the diagnostic accuracy of ultrasonography of optic nerve diameter (OND) for assessment of AON.

Methods: MEDLINE, EMBASE (1966–October 2014) was searched to identify studies reporting data on patients with AON (with/without multiple sclerosis) assessed by B-mode transorbital ultrasonography. Thereafter, the studies retrieved were screened based on predefined inclusion and exclusion criteria. Data were extracted and the quality of the included studies was evaluated.

Results: Seven studies (162 patients) were included. The OND was significantly thicker in the affected eye compared with its unaffected fellow or controls. An increased OND was found in 78–100% of patients. Four studies determined papilledema in 6–43% of patients.

Conclusions: Transorbital sonography is a sensitive, highly accessible and user-friendly technique for the detection of significant optic nerve thickening on the side affected by AON and represents an adjunctive tool for the diagnosis of AON. Compared to visual evoked potentials, TOS may provide different, though complementary, information on the pathophysiology of AON.

Significance: B-mode transorbital ultrasonography provides promising support for the clinical diagnosis of AON.

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Abbrevations: OND, optic nerve diameter; ONS, optic nerve sheath; AON, acute optic neuritis; ODE, optic disc elevation; TOS, transorbital sonography; BBB, blood-brain barrier; CSF, cerebrospinal fluid.

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1. Introduction

Acute optic neuritis (AON) is the most common optic neuropathy in young adults and displays a 3:1 female/male ratio. The most common symptoms are unilateral subacute vision loss, periocular and retrobulbar pain, abnormal color vision (dyschromatopsia) a relative afferent pupillary defect and in the involved eye (Optic

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Neuritis Study Group, 1991; Bradley and Whitthy, 1967). AON is usually idiopathic, but in temperate latitudes and Caucasian population it is the presenting symptom of multiple sclerosis (MS) in 25% of cases (Heussinger et al., 2013). It can also occur as a result of other inflammatory, vasculitic or toxic processes (Petzold et al., 2014).

The diagnosis of AON is primarily clinical. Further investigation is needed in the event of atypical warning signs such as severe periorbital pain as well as simultaneous or rapidly sequential bilateral visual loss. To date, the afferent visual pathway has been mostly studied using visual evoked potentials, magnetic resonance imaging, and the optical coherence tomography (Halliday et al., 1972; McKinney et al., 2013; Costello et al., 2006).

Transorbital sonography (TOS) is reliable for the diagnosis of increased intracranial pressure in neurocritical patients (Rajajee et al., 2012) and has also been used to support that of AON (Dees et al., 1995; Elvin and Andersson, 1998; Gerling et al., 1997; Stefanović et al., 2010; Karami et al., 2012; Dehghani et al., 2012; Neroev and Karlova, 2001; Lochner et al., 2014), especially with regard to the prediction of visual outcome (Elvin and Andersson, 1998) and the differentiation of anterior ischemic optic neuropathy and idiopathic AON (Gerling et al., 1997; Stefanović et al., 2010; Karami et al., 2012; Dehghani et al., 2012). The typical TOS finding in AON is a significant thickening of the optic nerve diameter (OND) of the affected side (Dees et al., 1995; Elvin and Andersson, 1998; Gerling et al., 1997; Stefanović et al., 2010; Karami et al., 2012; Dehghani et al., 2012; Neroev and Karlova, 2001; Lochner et al., 2014), probably due to inflammation with subsequent increased perineural subarachnoid fluid (Dees et al., 1995).

TOS employs two methods: amplitude-mode (A) scan, that provides simple displays plotted as a series of peaks whose height represents the depth of echoing structure from transducer; and Brightness (B) scan that produces a two-dimensional image of the tissue under study by combining A-mode signals from various directions through mechanical transducer scanning (Ossoinig, 1979; Schroeder, 1976). Only B scan studies are reviewed in this article. We aimed to systematically search and critically assess the literature evaluating the role of this method in the diagnosis of AON. Introductive sections are focused on the optic nerve anatomy and pathophysiology of AON, and on a description of sonographic assessment of the optic nerve.

1.1. Anatomy of the optic nerve and its involucre and pathophysiology of acute optic neuritis

The sheath of the optic nerve is composed of the dura, the arachnoid and the pia mater, which borders a small amount of cerebrospinal fluid (CSF) in the subarachnoid space. The nerve is not totally constrained within its sheath, but closely linked to it by a multitrabeculated connective tissue network of arachnoidal septa and pillars. There is thus a continuum between the optic nerve sheath (ONS) and the dura mater that allows free CSF communication between the optic nerve and the intracranial subarachnoid spaces within a layer usually 0.1–0.2 mm thick (Hayreh, 1984).

The overall length of the optic nerve ranges from 35 to 55 mm from the eyeball to the chiasma, namely the intraorbital segment constituting its anterior half (25 mm) (Duke-Elder and Wybar, 1961).

The OND narrows slightly from the posterior to the anterior head, while the anterior segment of the optic nerve (papilla) protrudes into the vitreous body of the eye. Because of the greater amount of elastic fibers in the connective matrix, a short portion of the optic nerve marked by a strong distensibility is identifiable at a depth of 3 mm (Fig 1) (Duke-Elder and Wybar, 1961;

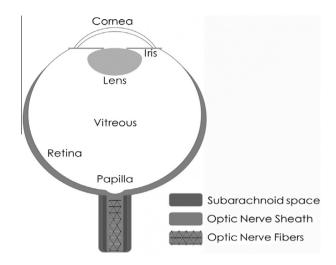


Fig. 1. Schematic drawing of anterior and posterior pole of the eye. The main anatomical structures are depicted: iris, lens, vitreous, retina papilla, optic nerve fibers, optic nerve sheath, subarachnoid space.

Hayreh, 1964). In the retrolaminar region the OND is about twice that of the optic disc (i.e. 3–4 mm), because the nerve fibers are myelinated (Hayreh, 1984).

Acute optic neuritis is caused by inflammation of the optic nerve whose earliest detectable abnormality is increased permeability of the blood-brain barrier (BBB) revealed by Gadoliniumdiethylenetriaminepentacetate (DTPA) enhancement in all patients examined at an early stage (Youl et al., 1991). This is gradually followed by edema (Willoughby et al., 1989), that usually lasts a few weeks and then diminishes to the point of restoring the normal permeability of the BBB, as suggested by the disappearance of its enhancement after one month in most patients (Youl et al., 1991). The intensity of this inflammation explains the severity of the clinical features (visual loss, field defects, afferent pupillary defect and pain).

Recovery usually begins a few weeks after the onset of symptoms (Optic Neuritis Study Group, 1991). Most patients fully recover, whereas a few are left with a persistent visual reduction/loss due to the interaction of several factors, including nerve atrophy, failed remyelinization, and possibly ophthalmic artery ischemia via the optic canal due to edema and compression of the artery itself (Malik et al., 2014).

1.2. Technical and safety considerations of transorbital sonography

TOS uses most modern Color Duplex ultrasound systems equipped with a high-frequency linear-array transducer endowed with an emitted frequency at least equal or superior to 7.5 MHz and a lateral axial spatial resolution <0.4 mm (Bäuerle et al., 2012). All parameters, such as time-gain-compensation or gray scale, are individually adjusted to achieve the best image qualities.

The mechanical index must be decreased to 0.23 and, according to the ALARA (as low as reasonably achievable) principle, the procedure time must be as short as possible to avoid damage to the lens, choroid and retina because of cavitation and heating depending on insonation time mechanical bioeffects from diagnostic ultrasound (Fowlkes and Holland, 2000). Since most examinations last less than 5 min per eye the possibility of thermal damage is slight.

Subjects lie supine with the upper part of their body and head raised 20–30°. A thick layer of gel is applied on the temporal part on the closed upper eyelid prior to pressure-free placement of the probe. The transducer is placed on the temporal side and the patient is asked to look straight ahead with close eyes for better

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