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Research report

Time is vision in recurrent optic neuritis

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ABSTRACT

In optic neuritis (ON) inflammation precedes onset of demyelination and axonal loss. The anti-inflammatory properties of corticosteroids may be most effective in the early inflammatory phase, but rapid patient recruitment remains a logistic challenge. The aim of the study was to review the effect of time to initiation of treatment on visual outcome in recurrent ON.

A retrospective case note review of patients known to our centre with recurrent ON. The primary clinical outcome was change of best corrected high contrast visual acuity (BCVA). The secondary outcome was the change of optical coherence tomography (OCT) thickness of the peripapillary retinal nerve fibre layer (pRNFL) and macular ganglion cell layer (mGCL) from baseline and after a minimum of 3 months following the episode of recurrent ON.

Of 269 patients with a previous episode of ON, 54 experienced recurrent ON. In total 40 OCT documented episodes of relapsing ON were captured in 19 patients. Treatment within <2 days led to better recovery of the BCVA (+0.02) and mGCL (−2.4 μm) if compared to delayed treatment (BCVA −0.2, p = 0.036, mGCL −25.6 μm, p = 0.019) or no corticosteroids treatment (BCVA −0.2, p = 0.045, GCL −5.0 μm, p = 0.836).

These data suggest a beneficial effect of hyperacute corticosteroid treatment. A pragmatic approach for a prospective treatment trial should consider patients with recurrent ON for logistic reasons.

1. Introduction

The North American optic neuritis treatment trial (ONTT) has influenced the medical management of optic neuritis (ON) (Group and others, 1991; Beck et al., 1992a). Over the past 25 years new developments have changed the clinical spectrum and diagnostic work up. Whilst testing for syphilis was mandatory in 1992 (Beck et al., 1992b), contemporary diagnostic work up includes testing for autoantibodies such to aquaporin 4 (AQP4) and myelin glycoprotein (MOG) (Asgari et al., 2011; Petzold et al., 2014). In addition, retinal axonal degeneration has been established as a key pathological feature quantifiable by retinal optical coherence tomography (OCT), a technique not included to the ONTT (Petzold et al., 2010). One conclusion of the ONTT, superiority of intravenous compared to oral corticosteroid treatment, has been refuted by a recent non-inferiority trial (Le Page et al., 2015). In view of these new developments it is worthwhile to remember that the failure of the ONTT to include any pharmacokinetic data and the lack of a biological plausible explanation to why oral corticosteroids should be harmful compared to intravenous corticosteroids had already been debated in 1992 (Achiron et al., 1992; Moskopp, 1992).

Experimentally, inflammation of the optic nerve precedes demyelination and axonal degeneration by two days (Shindler et al., 2008). Irreversible damage to the axonal cytoskeleton will occur within 5–7 days (Zhu et al., 1999). Therefore the time window for successful treatment initiation is narrow. Corticosteroids have anti-inflammatory and neuroprotective properties (Rosenberg-Schaffer & Lucas, 1993; Banik et al., 1997; Sapolsky et al., 2000). Targeting the inflammatory phase of optic neuritis requires rapid patient recruitment, a logistic challenge for the ONTT and all subsequent ON trials (Petzold, 2017). Recurrent episodes of ON occur frequently in NMO and CRION, but also affect about 5.5% of patients with multiple sclerosis (MS) (Nikoskelainen, 1975; Burman et al., 2011; Petzold et al., 2014).

Therefore is interesting to note that two studies demonstrated hyperacute corticosteroid treatment to improve outcome in patients with Chronic Relapsing Inflammatory Optic Neuropathy (CRION) and neuromyelitis optica (NMO) (Nakamura et al., 2010; Plant et al., 2011). Here we review the outcome of this practise

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in patients with recurrent ON for (1) speed of treatment initiation, (2) outcome of visual acuity and (3) outcome of retinal layer atrophy.

2. Results

The inclusion and exclusion of patients from the hospital database to our study is summarised as a flow-chart (Fig. 1).

The hospital database had 269 patients registered with ON. Of these OCT scans were recorded in 101. Revision of these 101 patients revealed that 47 did not have a diagnosis of optic neuritis according to diagnostic criteria (Petzold et al., 2014). Of the remaining 54 patients ON was monophasic in 35. Taken together 19 patients experienced recurrent episodes of ON whilst under our care. These 19 patients had a total of 40 episodes of OCT documented recurrent episodes of ON.

The median age of these 19 patients was 31 years (IQR 26-44). The baseline characteristics are presented in Table 1. A majority of these patients suffered from RION (n = 9), followed by MSON (n = 4), CRION (n = 4) and NMO-ON (n = 2).

The clinical subgroups were comparable for age and gender. As expected, patients with RION, CRION and NMO-ON had more recurrent episodes of ON compared to MSON (Table 2).

Table 1
Baseline characteristics of patients with recurrent episodes of ON (pooled). n = number, IQR = Inter Quartile Range, M = Male, F = Female, RION = relapsing isolated optic neuritis, CRION = Chronic Relapsing Inflammatory Optic Neuropathy, MSON = Multiple Sclerosis associated Optic Neuritis, NMO-ON = Neuromyelitis Optica associated ON.

Patients, n		19
Median age (IQR), years		31.0 (26–44)
M:F ratio		4:15
Ethnicity, %	Caucasian	90%
	Asian	5%
	Afro-Caribbean	5%
Median time follow-up (IQR),	Months	22 (13–33)
AQP4, n	Positive	2
	Negative	17
Episodes, n		
Total		40
Type, n	RION	9
	CRION	4
	MSON	4
	NMO-ON	2

The median interval of onset of symptoms and administration of corticosteroids was one day (IQR 1–5 days). Fig. 2 summarises the timing of episodes and treatment initiation per patient.

In total, 14 episodes were treated within two days, 15 episodes received delayed treatment and 11 episodes were not treated with

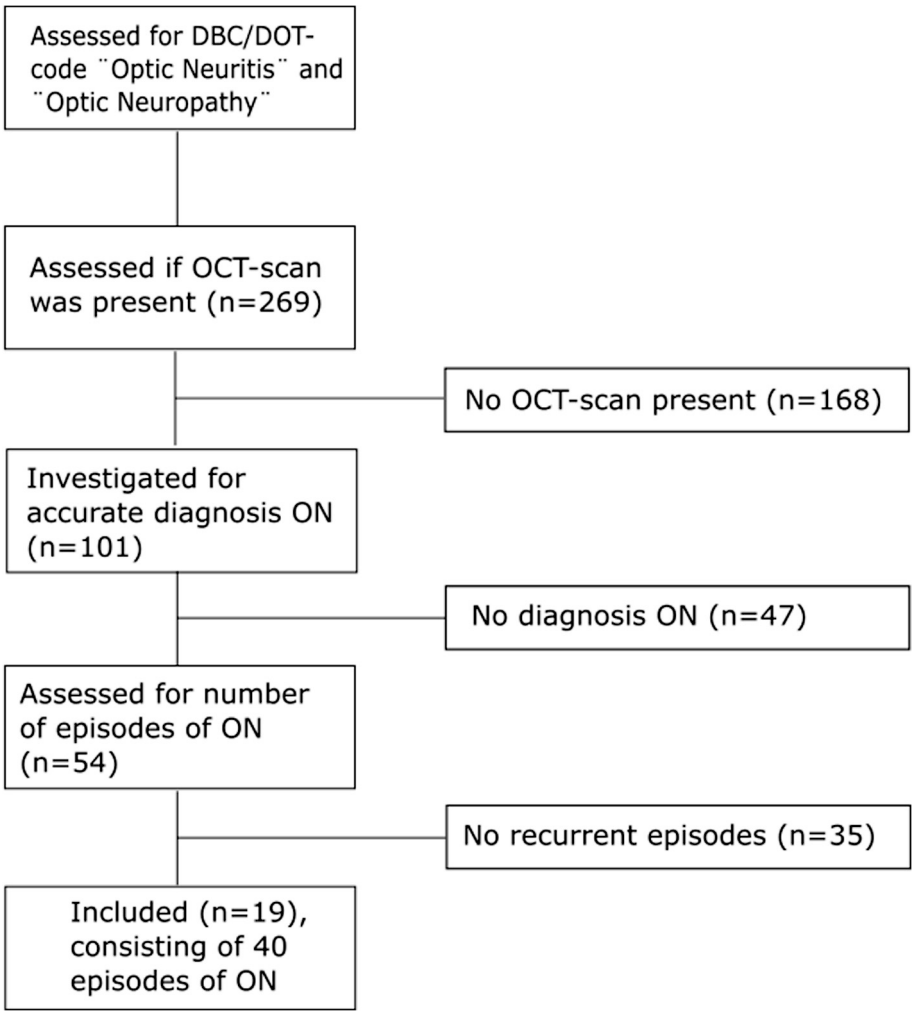

Fig. 1. Overview of the patient selection process. In total 40 episodes of recurrent ON occurring in 19 patients had appropriately timed OCT investigations to qualify for inclusion.