Clinical Study

Management of acute optic neuritis: A survey of neurologists and ophthalmologists in Australia and New Zealand

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Abstract

Recent studies suggest that evidence-based medicine is not well translated into everyday practice. Studies of optic neuritis (ON) have generated clear treatment guidelines. Therefore, a survey was mailed to all Australian and New Zealand neurologists and ophthalmologists to evaluate the impact of recent studies on clinical practice. The response rate was 38.9%. Neurologists were more likely to use high dose corticosteroids and disease modifying agents (DMAs), and were more likely to be aware of relevant literature concerning DMAs. Both groups contained a significant minority of practitioners who would use corticosteroids for reasons not substantiated by available evidence. We conclude that most practitioners manage optic neuritis according to existing evidence and guidelines, but many do not. It is essential to instigate high-quality training programs to keep practitioners up-to-date, thereby optimising patient care and justifying the time and expense of large-scale clinical trials.

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1. Background

The assumption behind the current drive towards evidence-based medicine (EBM) is that what evidence there is in the literature should ultimately be translated into clinical practice to optimise patient care. Large randomised clinical trials (RCTs) are expensive and by way of justifying the expense it is important to survey the clinical practice of affected physicians to determine whether their management of patients takes into account new findings relating to clin-

ical efficacy or cost-effectiveness.¹ Several studies in Australia have recently shown that EBM is not well translated into everyday practice in clinical or health promotional settings.^{2,3}

Optic neuritis (ON) is a common cause of visual loss and is recognised as one of the clinically isolated syndromes (CIS) which can precede the development of multiple sclerosis (MS).⁴ Over the past decade several large clinical trials have clarified the natural history of isolated acute ON, among them are the Optic Neuritis Treatment Trial (ONTT),^{5,6} the Controlled High-Risk Subjects Avonex Multiple Sclerosis Prevention Study (CHAMPS),⁷ the Early Treatment of Multiple Sclerosis Study (ETOMS),⁸ the Prevention of Relapses and Disability by Interferon Subcutaneously Study (PRISMS),⁹ and, most recently,

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the Betaferon in Newly Emerging Multiple Sclerosis for Initial Treatment study (BENEFIT).¹⁰ They have also provided strong evidence for and against many of the possible management options for this condition.

On the basis of these trials, treatment guidelines regarding the use of corticosteroids have been published by the American Academy of Neurology,¹¹ and numerous reviews have discussed the optimal management of patients with isolated acute optic neuritis in both the ophthalmology and neurology literature.⁴

The aim of this study was to evaluate the current practice patterns of Australian and New Zealand neurologists and ophthalmologists in the management of acute ON with a view to assessing the impact of recent RCTs on clinical practice.

2. Methods

A four-page survey consisting of 23 questions (Appendix 1) was mailed to all Australian and New Zealand neurologists and ophthalmologists registered with the Australian and New Zealand Association of Neurologists (ANZAN) or the Royal Australian and New Zealand College of Ophthalmologists (RANZCO) in October 2006. The survey included questions related to demographics, the frequency with which patients with acute ON were encountered, practices regarding acute and long-term treatment of ON, the ordering of MRI scans, and the impact of several recent RCTs on patient management. Two follow-up mailings were sent to non-respondents four and eight weeks after the original mailing on the grounds that this was the most efficient way to improve response rate.¹² The study was approved by the ACT Health Human Research Ethics Committee.

A total of 1,335 surveys were mailed out (559 to neurologists [514 in Australia, 45 in New Zealand] and 776 to ophthalmologists [705 in Australia, 71 in New Zealand]). All surveys were returned anonymously by fax or mail to a centre in either Canberra or Auckland, where they were collected and subsequently sent for analysis to Emory University School of Public Health in Atlanta, GA, USA. After individual quality control of each survey, the information was transferred into Statistical Analysis Software v. 9.1 (SAS Institute, Cary, NC, USA). Statistical analysis was performed using Wilcoxon Rank Sum and Chi-square test of independent variables, as appropriate.

3. Results

As shown in Table 1, a total of 185 (33.1%) neurologists and 346 (44.6%) ophthalmologists replied to the survey. The overall response rate was 38.9%.

3.1. Demographic characteristics of respondents

The majority of neurologists who replied worked predominantly in the academic sector rather than in private practice, in contrast to ophthalmologists where the reverse

Table 1
Demographics and clinical practice

	Neurologists	Ophthalmologists	Level of significance
Mailed surveys	n = 559	n = 776	
Received surveys	185 (33.1%)	346 (44.6%)	
Demographics	n = 185	n = 346	
Declared subspecialty	126 (68.1%)	194 (56.1%)	
Fellowship	150 (81.1%)	213 (61.6%)	
Academic practice	124 (67.0%)	89 (25.7%)	p = 0.0018
Private practice	61 (33.0%)	257 (74.3%)	
Contact with ON	143 (77.3%)	252 (72.8%)	
Clinical practice			
Cases/year:	n = 143	n = 252	p = 0.002
0 cases	7 (4.8%)	33 (13.1%)	
1–4 cases	106 (74.1%)	194 (77.0%)	
5–10 cases	20 (14.0%)	21 (8.3%)	
11 + cases	10 (7.0%)	4 (1.6%)	
MRI scans:	n = 143	n = 252	NS
All	109 (76.2%)	106 (42.1%)	
Most	24 (16.8%)	46 (18.2%)	
Some	5 (3.5%)	9 (6.3%)	
None	1 (0.7%)	1 (0.4%)	
No response	4 (2.8%)	90 (35.7%)	
Lumbar puncture	n = 143	n = 252	p < 0.0001
All	8 (5.6%)	1 (0.4%)	
Most	24 (16.8%)	4 (1.6%)	
Some	61 (42.7%)	34 (13.5%)	
None	46 (32.2%)	116 (46.0%)	
No response	4 (2.8%)	97 (38.5%)	

NS = not significant, ON = optic neuritis.

applied. This difference was statistically significant ($p = 0.0018$). Approximately three quarters of both groups saw patients with ON, and the ratio of academic versus private practitioners was preserved in the groups who did and the groups who did not see patient with ON.

The number of practitioners with declared subspecialty interests and fellowship training is shown in Table 1.

3.2. Management of patients with optic neuritis

Approximately 75% of both groups saw 1–4 cases of optic neuritis per year, and this was unaffected by whether the practitioner worked in academic or private sectors. Ninety-six percent of neurologists and 84% of ophthalmologists described themselves as consultants as opposed to primary healthcare providers. Eighty-nine percent of neurologists carried out complete treatment of their patients, 9% would initiate treatment and then refer on, and only 2% would refer patients on immediately. In contrast, only 22% of ophthalmologists indicated that they would carry out complete treatment, 43% referring patients immediately and the remaining 35% initiating management before referral.

3.2.1. Investigations

Of the neurologists, 76% ordered MRI scans on all patients with ON, and the majority of the remainder ordered

scans on most patients. Thirty-six percent of the responding ophthalmologists gave no response to this question; of those that did, 65% ordered MRI scans on all patients and 28% ordered scans on most. This difference was not significant. By contrast, ophthalmologists were significantly less likely to perform lumbar punctures than neurologists ($p < 0.0001$) (Table 1).

3.2.2. Corticosteroids

Neurologists' decision to use corticosteroids was influenced more than that of ophthalmologists by the presence of severe visual loss ($p < 0.0001$), bilateral involvement ($p = 0.0046$), severe pain ($p < 0.0001$) and the presence of abnormalities on cranial MRI scans ($p = 0.0005$) (Table 2).

Ophthalmologists were more often prepared not to use corticosteroids than neurologists ($p < 0.0001$). Both groups tended not to use low dose oral prednisolone, but 28/118 (23.7%) of neurology respondents and 24/131 (18.3%) of ophthalmology respondents would use it. Sixteen (13.6%) out of 118 neurology respondents and 21/131 (16.1%) of ophthalmology respondents indicated they would use high-dose oral steroids, even though this formulation is difficult to obtain in Australia. Neurologists would use significantly more intravenous methylprednisolone than ophthalmologists ($p = 0.0002$).

More neurologists than ophthalmologists would use corticosteroids to shorten the duration of ON symptoms ($p < 0.0001$), but there was no significant difference between groups regarding the eventual effect on visual outcome: 46.3% of responding neurologists and 36.0% ophthalmologists felt that this was a moderate or very important factor governing the decision to use corticosteroids. More ophthalmologists than neurologists felt that corticosteroids would reduce the chance of developing MS in the future ($p < 0.0001$), but a sizeable proportion of both groups felt that this was a moderate to very important effect (38.7% of neurologists and 71.1% of ophthalmologists who responded).

3.2.3. Disease modifying agents

Neurologists were significantly more likely to use disease modifying agents (DMAs) ($p = 0.0003$). Nine percent of neurologists and 25% of ophthalmologists would give DMAs to patients with ON who had normal MRI scans. For patients with abnormal MRI scans, most practitioners would use DMAs in "some" or "most" patients. At the time of the survey, neither Betaferon® nor Copaxone® had a license for use in clinically isolated syndromes, but a sizeable minority of neurologists indicated that they would occasionally use these agents. The number of ophthalmologists responding to this question was too small to permit comment (Table 3).

3.3. Awareness of recent studies in the literature

As shown in Table 4, over 90% of respondents indicated they were aware of the ONTT; there was no significant dif-

ference between groups. Ninety-two percent of neurologists and 99% of ophthalmologists who responded felt that the trial was moderately or very important.

Most responding neurologists had heard of CHAMPS, ETOMS and PRISMS (92.6%, 88.3% and 93.4% respectively), whereas only 37.6%, 18.0% and 23.8% (respectively) of responding ophthalmologists had heard of these studies. These differences between groups were all highly significant ($p < 0.0001$). With regard to importance, only small numbers of ophthalmologists were prepared to comment. Of those that did, 85–95% felt that these trials were moderately important to very important, compared to 81–86% of responding neurologists.

4. Conclusions

This survey achieved an overall response rate of 39%. There were many significant differences in the responses given by neurologists and ophthalmologists. The majority of practitioners appeared to be managing optic neuritis in line with existing evidence and guidelines, but a substantial minority was not. The results of the study are discussed under several headings.

4.1. Corticosteroids

It is gratifying that over 90% of both neurologists and ophthalmologists had heard of the ONTT, and that the vast majority thought this trial was important. Evidence from the trial has clearly shown that low dose oral corticosteroids are not helpful in the management of ON, and that high-dose intravenous corticosteroids will reduce the duration of symptoms but will have no effect on long-term visual outcome, or on the eventual development of MS.^{4,6} Despite these findings, around 20% of both ophthalmologists and neurologists were still using low-dose oral corticosteroids, 40% of both groups felt that treatment with corticosteroids influenced the final visual outcome in patients with ON, and 40% of neurologists and 70% of ophthalmologists felt that the use of corticosteroids decreased the risk of the eventual development of MS. This strongly suggests that the messages of the ONTT are frequently not being translated into clinical practice, even though it is now some 15 years since the first ONTT article was published.⁵

In 1999 Trobe et al. observed that "practitioners may change their practices as a result of a major collaborative trial without having understood some of the important conclusions of that trial".¹³ They found that 65% of neurologists and 45% of ophthalmologists were using steroids to improve final visual outcome, despite the fact that the ONTT "clearly stated that no treatment influences 1 year visual outcome".¹³ Almost a decade later, our study found that nearly 40% of both groups are still using steroids for this reason.

Table 2
Use of corticosteroids

	Neurologists (<i>n</i> = 143) (percentages of respondents)						Ophthalmologists (<i>n</i> = 252) (percentages of respondents)						Level of significance	
	--	–	0	+	++	NR	--	–	0	+	++	NR		
Decision to use steroids:														
Severe visual loss	1 (0.7%)	0 (0.0%)	13 (9.2%)	25 (17.7%)	102 (72.3%)	2	3 (1.8%)	1 (0.6%)	21 (12.7%)	72 (43.6%)	68 (41.2%)	87	<i>p</i> < 0.0001	
Bilateral involvement	1 (0.7%)	3 (2.1%)	17 (12.1%)	30 (21.4%)	89 (63.6%)	3	2 (1.2%)	0 (0.0%)	9 (5.5%)	62 (37.6%)	92 (55.8%)	87	NS	
Severe pain	1 (0.7%)	2 (1.4%)	17 (12.1%)	53 (37.6%)	68 (48.2%)	2	3 (1.8%)	3 (1.8%)	64 (38.8%)	62 (37.6%)	33 (20.0%)	87	<i>p</i> < 0.0001	
MRI abnormalities	0 (0.0%)	2 (1.4%)	64 (45.7%)	41 (29.3%)	33 (23.6%)	3	2 (1.2%)	3 (1.8%)	37 (22.6%)	61 (37.2%)	61 (37.2%)	88	NS	
	All	Most	Some	None	NR		All	Most	Some	None	NR			
Type of steroid treatment:														
None	0 (0.0%)	9 (7.4%)	73 (59.8%)	40 (32.8%)	21	2 (1.4%)	49 (34.3%)	80 (55.9%)	12 (8.4%)	109	<i>p</i> < 0.0001			
Oral prednisolone	1 (0.9%)	7 (5.9%)	20 (17.0%)	90 (76.3%)	25	1 (0.8%)	3 (2.3%)	20 (15.3%)	107 (81.7%)	121	NS			
High-dose oral prednisolone	0 (0.0%)	15 (4.3%)	9 (7.8%)	102 (87.9%)	27	0 (0.0%)	3 (2.4%)	14 (11.0%)	110 (86.6%)	125	NS			
iv Methyl-prednisolone	28 (20.4%)	70 (51.1%)	33 (24.1%)	6 (4.4%)	6	19 (12.3%)	53 (34.2%)	75 (48.4%)	8 (5.2%)	97	<i>p</i> = 0.0002			
	Not important	Mod. important	Very important	NR		Not important	Mod. important	Very important	NR					
Goals of steroid treatment:														
Shorten symptoms	1 (0.7%)	82 (38.2%)	53 (61.0%)	7	20 (12.4%)	88 (54.3%)	54 (33.3%)	90	p < 0.0001					
↑ visual outcome	73 (53.7%)	35 (25.7%)	28 (20.6%)	7	103 (64.0%)	29 (18.0%)	29 (18.0%)	91	NS					
↓ chance of MS	84 (61.3%)	39 (28.5%)	14 (10.2%)	6	47 (29.2%)	54 (33.5%)	60 (37.3%)	91	p < 0.0001					
Patient preference	49 (37.1%)	65 (49.2%)	18 (13.6%)	11	48 (30.4%)	82 (51.9%)	28 (17.7%)	94	NS					

NS = not significant, -- = much less likely, – = less likely, 0 = neither more nor less likely, + = more likely, ++ = much more likely, NR = non-responders, iv = intravenous, MS = multiple sclerosis, Mod = moderately.

Table 3
Disease modifying agents (DMAs)

	Neurologists (<i>n</i> = 143) (percentages of respondents)					Ophthalmologists (<i>n</i> = 252) (percentages of respondents)					Level of significance
	All	Most	Some	None	NR	All	Most	Some	None	NR	
Ever use DMAs	103 (72.0%)					135 (53.6%)					<i>p</i> = 0.0003
Never use DMAs	40 (28.0%)					117 (46.4%)					
Use of DMAs in patients with ON:											
With abnormal MRI	10 (8.2%)	31 (25.4%)	51 (41.8%)	30 (24.6%)	21	8 (15.4%)	14 (26.9%)	24 (46.2%)	6 (11.5%)	200	NS
With normal MRI	0 (0.0%)	1 (0.7%)	12 (8.6%)	127 (90.7%)	3	1 (0.7%)	3 (2.6%)	19 (21.9%)	122 (74.8%)	107	NS
DMA used:											
Always		Usually	Sometimes	Never	NR	Always	Usually	Sometimes	Never	NR	
Avonex®	1 (0.9%)	3 (2.8%)	68 (63.6%)	35 (32.7%)	36	3 (11.5%)	4 (15.4%)	3 (11.5%)	16 (61.5%)	226	<i>p</i> < 0.0001
Rebif®	0 (0.0%)	12 (11.2%)	64 (59.8%)	31 (29.0%)	26	0 (0.0%)	0 (0.0%)	2 (9.2%)	20 (91.9%)	230	<i>p</i> < 0.0001
Betaferon®	3 (2.6%)	30 (26.1%)	59 (51.3%)	23 (20.0%)	28	0 (0.0%)	1 (4.4%)	3 (13.0%)	19 (82.6%)	229	<i>p</i> < 0.0001
Copaxone®	0 (0.0%)	3 (2.8%)	47 (44.3%)	56 (52.8%)	37	0 (0.0%)	1 (4.4%)	1 (4.4%)	21 (91.3%)	229	<i>p</i> = 0.0015

NR = non-respondents, ON = optic neuritis.

4.2. Disease Modifying Agents

The use of disease modifying agents (DMAs) after an attack of acute monosymptomatic ON is still the subject of some debate, from both the standpoints of clinical efficacy and cost-effectiveness: not all agents have yet been shown to be effective in this situation, and the funding of these agents in this situation varies from country to country. In Australia, for example, the Pharmaceutical Benefits Scheme (PBS) will reimburse DMAs only once a clear diagnosis of MS has been made (on the old Poser¹⁴ criteria): it will not reimburse their use after a CIS. Also, at the time of the study (October 2006) only two agents were licensed for use in this situation (Avonex® and Rebif®) in Australia and New Zealand.

Neurologists were considerably more likely than ophthalmologists to have heard of the trials relating to the use of DMAs. Over 80% of those who responded felt that these trials were important. As mentioned above, only Avonex® and Rebif® were licensed for use in CIS (including ON) at the time of the survey, and no DMA was funded for use in CIS in either Australia or New Zealand. It is therefore surprising that 9% of neurologists and 25% of ophthalmologists indicated that they would use DMAs in patients with ON and *normal MRI scans* (for which there is neither evidence nor funding) and that many practitioners were prepared to prescribe Betaferon® and Copaxone®, a practice for which there was, at the time of the study, no published supporting evidence (the BENEFIT study¹⁰ in relation to Betaferon® was first published in October 2006). Again, this suggests that evidence from the literature is not being translated into clinical practice as well as it might be.

4.3. Comparison with other studies

A potential limitation of our study was the 39% response rate. The two previous published questionnaire sur-

veys relating to the management of ON had response rates which were somewhat higher: 47%¹³ and 63%.¹⁵ Trobe et al.¹³ mailed out 1,887 surveys and obtained a response from 47% while Ghosh et al.¹⁵ surveyed 114 local practitioners and obtained a response rate of 63%. Our study incorporated several methods to obtain adequate responses including the option to be an anonymous responder. We also used reminder letters as a method of improving response rate, a technique which has recently been shown to have the most significant effect on improving response rates.¹² Though the final response rate was only 39% of the total, the absolute numbers represented in our responding sample were large enough to be reasonably representative of the population as a whole.

In our survey, 77% of neurologists and 73% of ophthalmologists saw cases of ON. This compares with the figures in a previous study¹³ which found that, respectively, 72% and 70% of practitioners had encountered patients with ON within the last year. As with both previous studies looking at ON,^{13,15} there remains considerable variation in individual practice, despite clear evidence in the literature and the publication of clear guidelines.¹¹

4.4. Overall implications and conclusions

The finding that evidence in the literature is not being optimally applied to patients in day-to-day medical care is not new. Other studies have revealed barriers to application of EBM in practice such as deficient EBM skills, limited access to evidence, lack of time, cognitive and environmental factors.² We share the view that it is essential to instigate high-quality training programs that are universally and easily accessible and which will keep practitioners up-to-date, thus optimising patient care and justifying the time and expense of large-scale clinical trials. We believe our study has added to the weight of evidence that suggests that setting up such programs is an urgent priority.

Table 4
Knowledge of recent studies in the literature

Neurologists (n = 143) (percentages of respondents)				Ophthalmologists (n = 252) (percentages of respondents)			Level of significance		
Know		Don't know	NR	Know		Don't know	NR		
Awareness of studies									
ONTT	125 (90.6%)	13 (9.4%)	5	141 (96.6%)	5 (3.4%)	106	NS		
CHAMPS	126 (92.6%)	10 (7.4%)	7	75 (37.6%)	68 (62.4%)	109	p < 0.0001		
ETOMS	121 (88.3%)	16 (11.7%)	6	50 (18.0%)	91 (82.0%)	111	p < 0.0001		
PRISMS	128 (93.4%)	9 (6.6%)	6	34 (23.8%)	109 (76.2%)	109	p < 0.0001		
Not important		Mod. important	Very important	NR	Not important		Mod. important	Very important	NR
Importance of studies									
ONTT	10 (8.0%)	47 (37.6%)	68 (54.4%)	18	1 (0.7%)	21 (14.9%)	119 (84.4%)	111	NS
CHAMPS	24 (19.1%)	78 (61.9%)	24 (19.1%)	17	7 (9.3%)	27 (36.0%)	41 (54.7%)	177	p < 0.0001
ETOMS	22 (18.25)	73 (60.3%)	26 (21.5%)	22	3 (6.0%)	27 (54.0%)	20 (40.0%)	202	p < 0.0001
PRISMS	18 (14.0%)	67 (52.3%)	43 (33.6%)	15	5 (14.7%)	23 (67.6%)	6 (17.6%)	218	NS

CHAMPS = Controlled High-Risk Subjects Avonex Multiple Sclerosis Prevention Study, ETOMS = Early Treatment of Multiple Sclerosis Study, NR = non-responders, ONTT = Optic Neuritis Treatment Trial, PRISMS = Prevention of Relapses and Disability by Interferon Subcutaneously Study.

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Appendix 1. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.jocn.2008.01.014](https://doi.org/10.1016/j.jocn.2008.01.014).

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