ORIGINAL ARTICLE

Management of Optic Neuritis in Canada: Survey of Ophthalmologists and Neurologists

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ABSTRACT: ***Background:*** Acute isolated optic neuritis is often the first manifestation of multiple sclerosis (MS), and its management remains controversial. Over the past decade, with the advent of new disease-modifying agents, management of isolated optic neuritis has become more complicated. ***Objectives:*** To evaluate the current practice patterns of Canadian ophthalmologists and neurologists in the management of acute optic neuritis, and to evaluate the impact of recently published randomized clinical trials. ***Design:*** Mail survey. ***Methods:*** All practicing ophthalmologists and neurologists in Canada were mailed a survey evaluating the management of isolated acute optic neuritis and familiarity with recent clinical trials. Surveys for 1158 were mailed, and completed surveys were collected anonymously through a datafax system. Second and third mailings were sent to non-respondents 6 and 12 weeks later. ***Results:*** The final response rate was 34.5%. Although many acute optic neuritis patients initially present to ophthalmologists, neurologists are the physicians primarily managing these patients . Ordering magnetic resonance imaging, and treating with high dose intravenous steroids has become the standard of care. However, 15% of physicians (14% of ophthalmologists and 16% of neurologists) continue to prescribe low dose oral steroids, and steroids are being given for reasons other than to shorten the duration of visual symptoms by 73% of ophthalmologists and 50% of neurologists. More neurologists than ophthalmologists are familiar with recent clinical trials involving disease-modifying agents. ***Conclusion:*** Although the management of acute optic neuritis has been evaluated in large clinical trials that were published in major international journals, some ophthalmologists and neurologists are not following evidence-based recommendations.

RÉSUMÉ: Traitement de la névrite optique au Canada : enquête auprès des ophtalmologistes et des neurologues. ***Contexte :*** La névrite optique aiguë isolée est souvent la première manifestation de la sclérose en plaques (SEP) et son traitement demeure controversé. Au cours des dix dernières années, le traitement de la névrite optique isolée s'est compliqué à cause de l'apparition sur le marché de nouveaux agents qui modifient l'évolution de la maladie. ***Objectifs :*** Le but de cette étude était d'évaluer les habitudes de pratique actuelles des ophtalmologistes et des neurologues canadiens en ce qui concerne le traitement de la névrite optique aiguë et d'évaluer l'impact des essais cliniques randomisés publiés récemment. ***Plan d'étude :*** Il s'agit d'une enquête postale. ***Méthodes :*** Un questionnaire portant sur le traitement de la névrite optique aiguë isolée et sur la familiarité avec les essais cliniques récents a été posté à tous les ophtalmologistes et neurologues du Canada. Mille cent cinquante-huit questionnaires ont été postés et les réponses ont été recueillies anonymement au moyen d'un système datafax. Un deuxième et un troisième envoi ont été faits aux non-répondeurs 6 et 12 semaines plus tard. ***Résultats :*** Le taux de réponse final a été de 34,5%. Bien que plusieurs patients atteints de névrite optique aiguë consultent initialement un ophtalmologiste, ce sont principalement les neurologues qui traitent ces patients. On procède à une imagerie par résonance magnétique et le traitement standard actuel est l'administration intraveineuse de stéroïdes à haute dose. Cependant, 15% des médecins (14% des ophtalmologistes et 16% des neurologues) continuent à prescrire des stéroïdes à faible dose par voie orale et les stéroïdes sont prescrits pour d'autres raisons que pour diminuer la durée des symptômes visuels par 73% des ophtalmologistes et 50% des neurologues. Plus de neurologues que d'ophtalmologistes connaissent les essais cliniques récents sur les agents modifiant l'évolution de la maladie. ***Conclusion :*** Bien que le traitement de la névrite optique aiguë ait été évalué par des essais cliniques de grande envergure, publiés dans des revues internationales importantes, certains ophtalmologistes et neurologues ne suivent pas les recommandations de médecine factuelle.

Can. J. Neurol. Sci. 2008; 35: 179-184

Acute optic neuritis is a common cause of visual loss in the young and is recognized as one of the clinically isolated syndromes heralding multiple sclerosis (MS).[1] Over the past decade, several large clinical trials, including the Optic Neuritis Treatment Trial (ONTT),[2-4] the Controlled High Risk Avonex Multiple Sclerosis Study (CHAMPS),[5-7] the Early Treatment of Multiple Sclerosis Study (ETOMS),[8] and the Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment Trial (BENEFIT),[9] have helped clarify the natural history and

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Received April 12, 2007. Final Revisions Submitted December 21, 2007.

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management options for clinically isolated syndromes, such as isolated optic neuritis.[1,10-12] The American Academy of Neurology has published guidelines,[13] and numerous reviews have discussed the management of patients with isolated acute optic neuritis in both the ophthalmologic and neurologic literature, thereby clarifying the "optimal" management of acute idiopathic optic neuritis.[1,14-18] These publications have emphasized that high-dose steroids shorten the duration of visual loss, but do not change the long-term visual prognosis or the risk of MS in patients with isolated acute optic neuritis.[13] Treatment with low-dose prednisone in the ONTT doubled the risk of recurrent optic neuritis, and therefore should not be prescribed to patients with acute isolated optic neuritis. Obtaining a brain MRI can be recommended to assess the risk of subsequent MS in this population and to define a subgroup of high-risk patients who may benefit from early treatment with disease modulating agents. However, the impact of these studies on the behaviour of each clinician varies greatly, and many issues regarding the acute and long-term management of patients with isolated acute idiopathic optic neuritis remain debated.

A few years after the publication of the ONTT results, a survey of American ophthalmologists and neurologists[19] showed that most physicians did not fully understand the results of the ONTT. However, this survey also showed that the ONTT had led to a dramatic reduction in the use of oral prednisone alone in the treatment of acute optic neuritis. A shorter survey was performed in the northwest of England in 2002[20] that showed several significant differences in practices between ophthalmologists and neurologists. More neurologists chose to treat with intravenous methylprednisolone, more ophthalmologists chose no steroid treatment, and each group rarely selected the use of oral steroids. Other trials such as CHAMPS,[5-7] ETOMS,[8] and BENEFIT[9] studies have since suggested that the prescription of disease-modifying agents such as interferon beta-1a and beta 1-b after an episode of isolated optic neuritis delays the development of clinically definite MS in magnetic resonance imaging (MRI) defined high-risk patients. The open label CHAMPIONS study even suggested that such treatment should be initiated early after the first attack of optic neuritis.[21] The long-term effects of these treatments remain unknown.

The objectives of our study were to evaluate the current practice patterns of Canadian ophthalmologists and neurologists in acute optic neuritis management, and to evaluate the impact of the results of recent randomized clinical trials on clinical practices.

Methods

An anonymous 24-question survey was mailed to all Canadian ophthalmologists and neurologists registered with the Canadian Ophthalmology Society and the Canadian Neurological Society. Two follow-up mailings were sent to non-respondents at intervals of 6 and 12 weeks. This study was approved by the University of Saskatchewan Ethics Review Board, and by the Emory University School of Medicine (USA) Institutional Review Board.

The survey included questions related to physicians' demographics (e.g., certification, medical school affiliation, gender, years since completion of residency, fellowship training, and subspecialty), the frequency of their encounters with patients with isolated acute optic neuritis (without a prior diagnosis of MS), practices regarding acute and long-term treatment of optic neuritis, ordering of lumbar punctures and MRI scans, and the impact of several recent clinical trials on their treatment practices. Only respondents who saw at least one patient with acute optic neuritis per year completed the survey questions on diagnosis and management.

Statistical Analyses

All information was returned anonymously via fax where it was directly entered into a Datafax at Emory University Rollins School of Public Health in Atlanta, GA, USA. After a quality check of each survey, the information was transferred into SAS 9.1 (SAS Institute, Cary, NC, USA). Statistical analyses comparing ophthalmologists to neurologists were performed using Wilcoxon Rank Sum tests for ordinal variables and Chi-Square tests of independence for nominal variables.

Results

A total of 1158 surveys were mailed (672 to ophthalmologists and 486 to neurologists). The response rate after three mailings was 34.5% (ophthalmologists, 37%; neurologists, 32%) after excluding incomplete surveys, and unreachable, retired, or resident physicians. The majority of neurologists and ophthalmologists who responded to the survey reported that they were sub-specialists or had completed a fellowship (Table 1). The majority of ophthalmologists' patients were seen in private practice, whereas the majority of neurologists' patients were seen in academic centers (Table 1). Among these respondents, 71% of ophthalmologists and 66% of neurologists saw at least one acute optic neuritis patients per year (Table 1). Only physicians who saw at least one optic neuritis patient per year were asked to complete the questions regarding diagnosis and treatment of optic neuritis. Not all physicians responded to all questions, and some responders who declared not seeing optic neuritis patients within the past year, still chose to fill in some questions on the

Table 1: Response rate of surveyed Canadian ophthalmologists and neurologists and demographic characteristics of respondents

	Total	Ophthalmologists	Neurologists	p value
Questionnaires mailed	1158	672	486	
Useable responses	399	245	154	
Final response rate	**34.5%**	**37%**	**32%**	NS
Academic Center	220	46% (111)	71.2% (109)	p<0.01
Subspecialty	233	57.4% (136)	67.4% (97)	p=0.05
Completed fellowship	252	57.6% (141)	73.5% (111)	p<0.01
Saw at least 1 acute optic neuritis patient per year, and completed most questions in the survey	69.5% (277)	71% (175)	66% (102)	p=0.01
-Saw 1 to 4 acute optic neuritis patients per year		84% (147)	65.5 (67)	
-Saw more than 4 acute optic neuritis patients per year		16% (28)	34.5% (35)	

NS: non significant

https://doi.org/10.1017/S031716710000860X Published online by Cambridge University Press

survey regarding diagnosis and treatment. We considered that if they chose to fill in these questions on the survey, it indicated that they had opinions on the diagnosis and management of optic neuritis based on past experience or that they anticipated caring for optic neuritis patients in the future; therefore, we included all responses in our results.

Practice pattern of physicians who see optic neuritis patients

More neurologists (73%) than ophthalmologists (26%) reported initiating and completing treatment, whereas more ophthalmologists (29%) than neurologists (19%) reported initiating treatment prior to referral (p<0.001). Ophthalmologists (45%) reported having a greater tendency to refer without initiating treatment than neurologists (8%) (p<0.001).

Diagnostic practices

There were significant differences between the responses regarding diagnostic practices of ophthalmologists and neurologists (Table 2). More neurologists than ophthalmologists said they would recommend or obtain a lumbar puncture. Similarly, more neurologists than ophthalmologists reported ordering a baseline MRI in all or most patients with acute isolated optic neuritis. More neurologists recommended ordering follow-up MRIs in patients with a first episode of optic neuritis and an initial normal brain MRI (Table 2).

Table 2: Diagnostic practices of ophthalmologists and neurologists who saw at least one patient with optic neuritis per year*

	Ophthalmologists n=116				Neurologists n=102				
	All	Most	Some	None	All	Most	Some	None	p value**
Would recommend a lumbar puncture	2%	5%	15%	78%	4%	6%	52%	38%	p<0.01
Would obtain an initial MRI	54%	20%	15%	11%	72%	23%	5%	0%	p<0.01
	>1/year	Yearly	<1/year	Never	>1/year	Yearly	<1/year	Never	
Would recommend follow up MRI	3%	15%	24%	58%	11%	20%	37%	32%	p<0.01

* Survey questions regarding diagnosis and treatment were only filled out by ophthalmologists and neurologists who saw at least one patient with optic neuritis per year; ** p values refer to the significance of the difference between the responses of ophthalmologists and neurologists.

Steroid treatment practices

Ophthalmologists indicated being less inclined than neurologists to treat acute optic neuritis with steroids (Table 3). Although the majority of ophthalmologists and neurologists reported never prescribing low dose oral prednisone (1 mg/kg/day) for the treatment of isolated acute optic neuritis, 14% of ophthalmologists and 16% of neurologists indicated that they continue to do so. The use of high dose intravenous methylprednisolone was less prevalent among ophthalmologists than neurologists. A small percentage of ophthalmologists and neurologists said they would recommend or prescribe high dose oral steroids for the treatment of acute optic neuritis. There was

Table 3: Steroid treatment practices of ophthalmologists and neurologists who treated at least one patient with optic neuritis per year and completed the corresponding survey questions*

	All	Most	Some	None	All	Most	Some	None	P value
	Ophthalmologists n=103				Neurologists n=90				
No steroid treatment	4%	43%	43%	10%	0%	17%	59%	24%	P<0.01
	Ophthalmologists n=95				Neurologists n=85				
Low dose oral prednisone	1%	2%	11%	86%	2%	5%	9%	84%	P=0.68
	Ophthalmologists n=86				Neurologists n=86				
High dose oral prednisone	2%	4%	28%	66%	5%	8%	32%	55%	P=0.08
	Ophthalmologists n=113				Neurologists n=99				
High dose intravenous methylprednisolone	16%	22%	49%	13%	25%	39%	26%	10%	P<0.01

* Not all surveyed physicians completed all questions. This is why the denominator number of ophthalmologists and neurologists varies from question to question

Table 4: Reasons for prescribing steroids and factors influencing the decision, among physicians who treated at least one patient with optic neuritis per year and completed the corresponding survey questions*

	Ophthalmologists n=120	Neurologists n=102	
	More likely	More likely	p value**
Severe visual loss	84%	90%	p<0.01
Severe pain	65%	81%	p<0.01
Bilateral involvement	88%	90%	p=0.29
Abnormal brain MRI	59%	52%	p=0.22
	Very Important	Very Important	P value
Shorten duration of visual symptoms	32%	65%	p<0.01
Affect visual outcome	13%	27%	p<0.01
Reduce future MS	36%	12%	p<0.01
Patient preference	24%	11%	p=0.42

*Not all surveyed physicians completed all questions. This is why the denominator number of ophthalmologists and neurologists varies from question to question; ** p values refer to the significance of the difference between the numerical value of the responses of ophthalmologists and neurologists

https://doi.org/10.1017/S031716710000860X Published online by Cambridge University Press

Table 5: Disease modifying agent (DMA) treatment practices among physicians who treated at least one patient with optic neuritis per year and completed the corresponding survey questions*

	Ophthalmologists n=106				Neurologists n=101				P value**
Likelihood of using a DMA	All	Most	Some	None	All	Most	Some	None	
With a normal MRI	1%	4%	12%	83%	0%	3%	6%	91%	P=0.05
With an abnormal MRI	14%	26%	42%	18%	11%	33%	41%	15%	P<0.01
	Choice of disease modifying agent								
	Ophthalmologists n=11				Neurologists n=69				
Interferon beta 1-a (Avonex)	0%	17%	41%	42%	7%	18%	56%	19%	p<0.01
Interferon beta 1-a (Rebif)	0%	9%	54%	37%	0%	12%	67%	21%	p<0.01
Interferon beta 1-b (Betaseron)	0%	9%	54%	37%	1%	11%	64%	24%	p<0.01
Glatiramir acetate (Copaxone)	0%	0%	50%	50%	0%	6%	66%	28%	p<0.01

*Not all surveyed physicians completed all questions. This is why the denominator number of ophthalmologists and neurologists varies from question to question; ** p values refer to the significance of the difference between the numerical value of the responses of ophthalmologists and neurologists

Table 6: Impact of trials on treatment practices among physicians who treated at least one patient with optic neuritis per year and completed the corresponding survey questions*

	Ophthalmologists n=99			Neurologists n=102			
	Not Important	Moderately Important	Very important	Not Important	Moderately Important	Very important	P value** (trend)
ONTT (Optic Neuritis Treatment Trial)	1%	13%	86%	5%	41%	54%	P<0.01
CHAMPS (Controlled High Risk Avonex Multiple Sclerosis Study)	12%	40%	48%	6%	51%	43%	P=0.78
ETOMS (Early Treatment of Multiple Sclerosis Study)	13%	41%	46%	11%	64%	25%	P=0.11

*Not all surveyed physicians completed all questions. This is why the denominator number of ophthalmologists and neurologists varies from question to question; ** p values refer to the significance of the difference between the numerical value of the responses of ophthalmologists and neurologists

no statistically significant difference between the two groups regarding the use of either low or high-dose oral steroids (Table 3).

Symptoms of severe visual loss, severe pain, and bilateral involvement were features that made both ophthalmologists and neurologists more likely to treat with steroids (Table 4). Both groups reported that an abnormal MRI was not as influential on the decision to treat or not to treat with steroids, but would still make the decision to treat with steroids more likely. Table 4 shows that steroids were still being given for other reasons than shortening the duration of visual symptoms, and fewer ophthalmologists (32%) than neurologists (65%) considered shortening the duration of visual symptoms to be very important.

Treatment with disease-modifying agents

Most ophthalmologists (83%) and neurologists (91%) indicated there was no likelihood of their recommending a disease-modifying agent to patients with acute idiopathic optic neuritis who have a normal baseline MRI (Table 5). However, 17% of ophthalmologists and 9% of neurologists responded that they consider prescribing a disease-modifying agent if the MRI is normal. For patients with acute idiopathic optic neuritis and an abnormal MRI, 82% of ophthalmologists and 85% of neurologists felt that a disease-modifying agent may be indicated. Only a minority of ophthalmologists and neurologists who treated patients with optic neuritis responded that there would be no likelihood of prescribing a disease-modifying agent with an abnormal MRI. Thirty-six percent of neurologists and 80% of ophthalmologists said they never use disease modifying agents in the treatment of optic neuritis, regardless of MRI findings (Table 5).

Many ophthalmologists and neurologists choose disease-modifying agents for which there is not yet published evidence for their use in patients with clinically isolated syndromes (Table 5).

Impact of trials on treatment practices

More ophthalmologists than neurologists were unfamiliar with the results of ETOMS (61% vs 18%) and CHAMPS (39% vs 9%). Conversely, more neurologists (9%) than ophthalmologists (4%) were unfamiliar with the main findings of the ONTT. Among the physicians who reported knowing the results of these clinical trials (Table 6), more ophthalmologists than neurologists considered the ONTT to be a very important study in terms of its impact on treatment practices.

Discussion

The results of our survey reveal some confusion and inconsistency on the part of both ophthalmologists and neurologists in the diagnosis and treatment of isolated acute optic neuritis. Three results of this survey are particularly concerning: 1) despite evidence in the literature that treatment with low-dose prednisone is associated with an increased risk of recurrence of optic neuritis,[1] 15% of respondents would still at least occasionally use this short-term intervention (Table 3); 2) despite no evidence in the literature to support the efficacy of steroids on ultimate visual outcome or reduction in MS activity,[1] more than 40% of respondents are using steroids for those indications (Table 4); and, 3) despite a lack of published evidence, 17% of ophthalmologists and 9% of neurologists feel that a disease-modifying agent would be indicated to treat patients with normal MR scans (Table 5). These responses highlight the need for such a survey of current practices, as well as the need for clearer guidelines. Because evidence-based

https://doi.org/10.1017/S031716710000860X Published online by Cambridge University Press

medicine is now dominating our daily practice, it is essential to evaluate and understand the impact of important clinical trials.

Although our response rate was only 34.5%, this is consistent with other surveys,[22] and was felt sufficient to draw valid conclusions. A limitation of this type of clinical audit is that responses may reflect idealized rather than actual practice. The tendency of ophthalmologists to immediately refer demonstrates that acute optic neuritis has largely become a disease managed by subspecialists, and may explain why our response rate was relatively low compared with a 1999 survey.[19] A higher response rate would have countered possible non-response bias, but the consistency of responses among the three mailings makes it unlikely that a higher response rate would have substantially altered our conclusions. It would be helpful to know the demographic and practice characteristics of the non-responders, but this information is not available since the survey was anonymous.

The survey results indicate that 73% of neurologists who see at least one optic neuritis patient per year initiate and complete treatment. This option includes all possible short-term and secondary prevention options, including the option of no treatment; however it likely does not reflect long-term management and follow-up of all optic neuritis patients who are often followed by MS specialists, particularly when their initial brain MRI is abnormal.

Not surprisingly, most neurologists order a brain MRI in patients with isolated acute optic neuritis, and neurologists are more likely to obtain follow-up MRIs. The fact that ophthalmologists order fewer MRIs, especially follow-up MRIs, may relate to an expectation that the neurologists to whom they refer will order them. Even though the diagnosis of acute isolated optic neuritis is mostly clinical, our survey confirms that ordering a brain MRI has become the standard of care in Canada. This likely reflects an evolving understanding of the relationship between clinically isolated syndromes and MRI criteria for the diagnosis of MS.

The survey also shows that neurologists are more likely to consider a lumbar puncture in some patients. However, lumbar puncture for CSF analysis is usually not necessary in patients with typical acute optic neuritis, particularly when the brain MRI is abnormal.[1,4,23] In Canada, ophthalmologists who feel a lumbar puncture may be indicated generally refer to a neurologist for this procedure. It is not surprising; therefore, that more ophthalmologists never order lumbar punctures, even if they feel it may be indicated. The responses indicating that 22% of ophthalmologists would "order" a lumbar puncture can reasonably be interpreted to mean that ophthalmologists who do not perform this procedure themselves would recommend it, or refer the patient to a neurologist.

In our survey, 47% of ophthalmologists compared to 17% of neurologists choose no treatment, most or all of the time, which is an entirely acceptable option based on results from the ONTT.[1,2] These percentages are not significantly different from those reported in 1999.[19] Currently, the use of high dose intravenous methylprednisolone is less prevalent among ophthalmologists than neurologists; 38% of ophthalmologists and 64% of neurologists report using this regimen in more than 50% of cases ($p<0.01$).

As emphasized by the American Academy of Neurology practice parameter on the treatment of acute optic neuritis,[13] oral prednisone in conventional doses of 1mg/kg per day should not be used in the treatment of idiopathic acute optic neuritis. Currently, 86% of ophthalmologists and 84% of neurologists never prescribe low dose oral prednisone alone in the treatment of acute optic neuritis (Table 3). This is an improvement compared to 74% of ophthalmologists and 68% of neurologists in 1999 in the U.S.[19]

Our study showed that neurologists have a greater tendency to treat with high dose oral steroids; 6% of ophthalmologists and 13% of neurologists choose this option in more than 50% of cases. Many MS centers in Canada now routinely use high dose oral prednisone (1250 mg) once daily for three to five days; however, supportive evidence is lacking, and no trial comparing intravenous high dose to oral high dose has been performed for the treatment of isolated optic neuritis.

In Canada, chronic management of clinically isolated syndromes with disease-modifying agents is the domain of the academic subspecialist neurologist, and this is reflected in our survey. Provincial formularies have different reimbursement criteria for MS drug products. Only Ontario and Quebec currently provide coverage for the use of interferon in clinically isolated syndromes, providing there is documentation of an abnormal MRI. It is not clear whether this has translated into more frequent use of interferons in these provinces. The practices of the remaining provincial MS drug eligibility review panels vary regarding reimbursement for the use of interferon in patients with MS, and rely heavily on specialist assessment. In some provinces only certain neurologists and MS subspecialists are allowed to prescribe disease-modifying agents, and there is considerable variability in MS care across the country. It would be very rare for ophthalmologists to be directly involved in the long-term management of MS and initiation of treatment with disease modifying agents in Canada. Indeed, this likely explains the very low number of ophthalmologists (n=11) who responded to the survey question regarding choice of disease-modifying agents (Table 5), Accordingly, neurologists are more familiar with recent trials involving clinically isolated syndromes and disease-modifying agents. A contributing factor may be that trials looking at the role of interferon have been primarily published in neurology rather than ophthalmology journals. The BENEFIT[9] trial was not included in our survey, since results from this trial were not available at the time of mailing.

In summary, the main findings of our survey are that: 1) most ophthalmologists refer acute optic neuritis patients to neurologists for treatment; 2) brain MRIs are routinely performed on isolated optic neuritis patients; 3) the reasons for prescribing steroids for optic neuritis are often not evidence-based; and 4) low-dose oral prednisone treatment is still being used at least occasionally by 15% of respondents. Many ophthalmologists and neurologists are not following evidence-based recommendations for the management of isolated acute optic neuritis.

Acknowledgements

This study was supported in part by a resident research divisional grant (Division of Neurology, University of

Saskatchewan, Saskatoon, Canada), and in part by a departmental grant (Department of Ophthalmology) from Research to Prevent Blindness, Inc, New York, New York, and by core grant P30-EY06360 (Department of Ophthalmology) from the National Institutes of Health, Bethesda, Maryland. Dr Newman is a recipient of a Research to Prevent Blindness Lew R. Wasserman Merit Award.

References

1. Atkins EJ, Biousse V, Newman NJ. The natural history of optic neuritis. Rev Neurol Dis. 2006;3:45-55.
2. Beck RW, Cleary PA, Anderson MM Jr, Keltner JL, Shults WT, Kaufman DI, et al. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. N Engl J Med. 1992;326:581-8.
3. Beck RW, Cleary PA, Trobe JD, Kaufman DI, Kupersmith MJ, Paty DW, et al. The effect of corticosteroids for acute optic neuritis on the subsequent development of multiple sclerosis. The Optic Neuritis Study Group. N Engl J Med. 1993;329:1764-9.
4. Rolak LA, Beck RW, Paty DW, Tourtellotte WW, Whitaker JN, Rudick RA, Optic Neuritis Study Group. Cerebrospinal fluid in acute optic neuritis: experience of the optic neuritis treatment trial. Neurology. 1996;46:368-72.
5. Jacobs LD, Beck RW, Simon JH, Kinkel, RP, Brownscheidle, CM, Murray TJ, et al. Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. CHAMPS Study Group. N Engl J Med. 2000;343:898-904.
6. CHAMPS Study Group. Interferon β-1a for optic neuritis patients at high-risk for multiple sclerosis. Am J Ophthalmol. 2001; 132:463-71.
7. Beck RW, Chandler DL, Cole SR, Simon JH, Jacobs LD, and the CHAMPS Study Group. Interferon β-1a for early multiple sclerosis: CHAMPS trial subgroup analyses. Ann Neurol. 2002;51:481-90.
8. Comi G, Filippi M, Barkhof F, Durelli, L, Edan, G, Fernandez, O, et al. Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study (ETOMS). Lancet. 2001;357:1576-82.
9. Kappos L, Polman C, Freedman M, Edan G, Hartung H, Miller D, et al. Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. Neurology. 2006;67:1242-9.
10. Brex P, Ciccarelli O, O'Riordan J, Sailer M, Thompson A, Miller D. A longitudinal study of abnormalities on MRI and disability from multiple sclerosis. N Engl J Med. 2002;346:156-64.
11. Soderstrom M, Ya Ping J, Hillert J, Link H. Optic neuritis, prognosis for multiple sclerosis from MRI, CSF, and HLA findings. Neurology. 1998;50:708-14.
12. Ghezzi A, Martinelli V, Torri V, Zaffaroni M, Rodegher M, Comi G, et al. Long-term follow-up of isolated optic neuritis: the risk of developing multiple sclerosis, its outcome, and the prognostic role of paraclinical tests. J Neurol. 1999;246:770-5.
13. Kaufman DI, Trobe JD, Eggenberger ER, Whitaker, JN. Practice parameter: the role of corticosteroids in the management of acute monosymptomatic optic neuritis. Neurology. 2000;54: 2039-44.
14. Balcer L. Optic neuritis. New Engl J Med. 2006;354:1273-80.
15. Frohman E, Frohman T, Zee D, McColl R, Galetta, S. The neuro-ophthalmology of multiple sclerosis. Lancet Neurol. 2005;4: 111-21.
16. Miller D, Barkhof F, Montalban X, Thompson A, Filippi M. Clinically isolated syndromes suggestive of multiple sclerosis, part I: natural history, pathogenesis, diagnosis, and prognosis. Lancet Neurol. 2005;4:281-8.
17. Miller D, Barkhof F, Montalban X, Thompson A, Filippi M. Clinically isolated syndromes suggestive of multiple sclerosis, part II: non-conventional MRI, recovery processes, and management. Lancet Neurol. 2005;4:341-8.
18. Arnold AC. Evolving management of optic neuritis and multiple sclerosis. Am J Ophthalmol. 2005;139:1101-8.
19. Trobe JD, Sieving PC, Guire KE, Fendrick AM. The impact of the optic neuritis treatment trial on the practices of ophthalmologists and neurologists. Ophthalmology. 1999;106: 2047-53.
20. Ghosh A, Kelly S, Mathews J, Cooper PN, MacDermott N. Evaluation of the management of optic neuritis: audit on the neurological and ophthalmological practice in the north west of England. J Neurol Neurosurg Psychiatry. 2002;72:119-21.
21. CHAMPIONS Study Group. IM interferon β-1a delays definite multiple sclerosis 5 years after a first demyelinating event. Neurology. 2006;66:678-84.
22. Hikmet N, Chen S. An investigation into low survey response rates of information technology users in health care organizations. Int J Med Inform. 2003;72:29-34.
23. Cole SR, Beck RW, Moke PS, Kaufman DI, Tourtellotte WW. The predictive value of CSF oligoclonal banding for MS 5 years after optic neuritis. Optic Neuritis Study Group. Neurology. 1998;51:885-7.