Recovery of demyelinating optic neuritis after treatment with equivalent high doses of oral vs. intravenous corticosteroids: a randomized single blinded clinical trial

Objectives

The objective of this study is to determine if there is a difference in the recovery of optic nerve function after an episode of acute demyelinating optic neuritis when treated with equivalent doses of oral and IV corticosteroids.

Specific Aims

1) To compare the recovery of nerve conduction on visual evoked potentials (VEP) after treatment for acute demyelinating optic neuritis at 1 and 6 months when treated with either 1250mg oral prednisone or 1000mg IV methylprednisolone daily for three days.

2) A secondary aim will be to compare the functional recovery of vision via visual acuity and contrast sensitivity of the two treatment modalities.

3) Another secondary aim will be to compare safety and tolerability associated with each treatment modality.

Hypothesis

The null hypothesis of this study is that there is no difference in recovery of the visual evoked potential (VEP) P100 latency when comparing 1000mg daily for 3 days of IV methylprednisolone to 1250mg daily for 3 days of oral prednisone for the treatment of acute demyelinating optic neuritis.

Abbreviations:

MS Multiple Sclerosis
ON Optic Neuritis
VEP Visual Evoked Potential
IV Intravenous
ON Optic Neuritis
ONTT Optic Neuritis Treatment Trial
CIS Clinically Isolated Syndrome
CNS Central Nervous System

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Background and Rationale

Multiple sclerosis (MS) is a chronic neurologic disease, in which damage to myelin (demyelination) occurs due to inflammation in the central nervous system (CNS) (1). Canada has one of the highest rates of MS in the world with a prevalence 240/100,000 (1). MS is one of the most common neurological diseases in young adults with a mean age of onset of 30 years and a peak onset of 24 years in women and 25 years in men, affecting more women than men in a 3.2:1 ratio (2, 3). In 85% cases, MS presents as a relapsing-remitting course (RRMS), which is characterized by the sub-acute onset of neurological symptoms (relapses) that resolve over time, albeit not always completely, with periods of relative stability in between (4). These relapses present as focal or multi-focal neurological signs and symptoms lasting for at least 24 hours; most tend to progress over a few days to a week, reach a nadir which can plateau for days to weeks, and then slowly recover. The diagnosis of MS requires clinical symptoms suggestive of demyelination combined with MRI imaging confirming demyelination as well as evidence of dissemination in space (multiple areas of the brain and spinal cord affected) and time (evidence of ongoing demyelination with changes over time). A common presentation is a patient with the first episode of demyelination who does not meet the dissemination in time criteria, and thus cannot yet be diagnosed with MS but is at risk of developing MS. This presentation is called clinically isolated syndrome (CIS).

An acute relapse in MS is defined as an episode of neurological signs and symptoms due to an inflammatory or demyelinating lesion in the CNS (5). For diagnostic purposes, the symptoms should last for at least 24 hours with an acute or sub-acute onset and not caused by another underlying cause, such as increased body temperature or infection (a pseudo-exacerbation), and can be either mono- or multifocal in nature (5). The MRI correlate of an acute relapse is a gadolinium enhancing lesion, which represents a breakdown of the blood-brain barrier, allowing myelin-reactive T-cells to enter the CNS and cause a cascade of changes that lead to edema and direct damage to the myelin, and possibly the axon itself, in a well-circumscribed area (6). Gadolinium enhancing lesions resolve within two to six weeks, which is similar to the period in which clinical recovery begins.

A common anatomical area affected by a relapse is the optic nerve, resulting in acute demyelinating optic neuritis (ON). Optic neuritis occurs at some point during the course of MS in 50% of RRMS patients, and is the presenting demyelinating event in 15-20% of patients who go on to develop MS (7, 8). However, only 38% of those who present with optic neuritis will develop MS in the next 10 years (9). As with most demyelinating events, ON usually presents as a decline in vision over several days associated with painful eye movements (10). On physical examination, a reduction in visual acuity (the eye's ability to perceive sharp outlines of small objects at high contrast

(11)) in the central visual field is present, and there may be associated impairment of contrast sensitivity (the ability to perceive minor changes in luminance between regions without definite borders) and a relative afferent pupillary defect (12). Recovery of vision is expected to start within 30 days of the symptom onset, corresponding to the resolution of optic nerve inflammation (13). Recovery of colour vision and subjective visual improvement have been noted as early as three weeks, which can be accelerated to as early as one week with high dose corticosteroids (14). Most recovery occurs within six months (10).

Corticosteroids have been used to treat acute demyelinating events, as a part of an MS or CIS diagnosis, including ON for many years. The evidence suggests that corticosteroids improve the speed of functional recovery, but not the eventual outcome as the prognosis is the same with or without treatment, for all demyelinating events of the CNS, including ON. Corticosteroids reduce blood brain barrier breakdown, as demonstrated by reduction in the intensity or complete resolution of gadolinium enhancing lesions on MRI, leading to accelerated recovery from the acute relapse (15). To date, no long-term functional benefit of treating acute relapses with corticosteroids. Equivalent functional recoveries were demonstrated at six and 12-month time points whether the subjects were treated with corticosteroids or placebo (12, 16). Further, the American Academy of Neurology Practice parameter for the treatment of acute optic neuritis cites Class II evidence supporting the lack of long-term benefit for visual function with the use of high dose corticosteroids, but Class I evidence that it does hasten the speed and degree of recovery of visual function in optic neuritis (17). Not all demyelinating events in CIS or MS are treated with corticosteroids since, as described previously, this treatment only hastens the speed and degree of recovery in the short term, but has no long-term benefit on recovery of visual function. Survey studies in the past have shown that neurologists treat only 25-50% of relapses with corticosteroids (18, 19). Relapses that are not causing functional impairment are often not treated as the risks and/or adverse events associated with corticosteroids outweigh the low level of benefit expected (20). However, optic neuritis is most often treated as it is causing a functional impairment (loss of vision).

Corticosteroid treatment administered intravenously (IV) became the standard of practice based on the results of the Optic Neuritis Treatment Trial (ONTT) (12). In this study, the IV methylprednisolone group had a greater rate of return of vision than the placebo group and the oral prednisone group. Additionally, the group treated with oral prednisone had a higher risk of recurrent optic neuritis than either the IV or the placebo groups. However, the treatment groups were not pharmacologically equivalent in terms of corticosteroid dose. The IV group received 1000mg of methylprednisolone daily for three days followed by an oral taper over 11 days, while the prednisone group consisted of a much lower daily dose: 1mg/kg daily for 14 days; equivalent to 56mg of IV methylprednisolone for an average 70kg man. Other studies demonstrated a better response to high ($\geq$1.0 gram) doses of corticosteroids on MRI outcomes (resolution of gadolinium enhancing lesions). This supports the findings of the ONTT that high dose treatment should be standard of care, but it still does not address whether the route of medication delivery plays a role (21). Yet, these results influenced how physicians

treated optic neuritis, as demonstrated by a survey performed 6 years after the publication of ONTT, which found that 95% of neurologists had reduced the use of oral prednisone, with 65% stating high dose IV methylprednisolone was the most effective way to hasten visual recovery and 53% believing that IV methylprednisolone reduced future neurologic events of MS (22).

Present State of Knowledge

More recent evidence supports high dose oral corticosteroids, given as prednisone in dose equivalent to the IV methylprednisolone dose, as an alternative to IV therapy. Oral prednisone has the advantage of being less expensive, more convenient, more accessible for patients living in remote areas without easy access to IV treatment and is preferred by patients (23, 24). We previously demonstrated bioequivalence of 1250mg of oral prednisone and 1000mg of IV methylprednisolone in MS patients (25). A recent survey found that MS specialists in Canada are using both high dose oral and IV corticosteroids for relapse treatment (18). Furthermore, compliance with oral therapy is not an issue, as demonstrated by a survey study we performed which found a 98% compliance rate with this preparation and 2/3 of subjects indicating a preference for oral treatment (26). A 2009 Cochrane review found no significant differences between short term outcomes ($\leq$ 6 weeks) of MS relapse treatment with oral vs. IV corticosteroids but the statistical conclusions were limited by the relatively small subject pool and methodological issues of the trials reviewed (27).

None of these studies addressed the longer-term impact of equivalent high doses of corticosteroids for the treatment of MS relapses. To date, it is unknown if the rate and/or degree of recovery is influenced by the route of administration. The fact that fewer neurologists use oral corticosteroids as the first line treatment may be influenced by this lack of evidence and the impact of the ONTT trial conclusions, despite the lack of dose equivalency between the two treatments.

Visual evoked potentials (VEPs) measure the occipital cortical response to visual stimulation in the centre of the visual field and are used to detect anterior visual conduction abnormalities (10). The most common VEP morphology used is the pattern-reversal VEP, which is a checkerboard stimulus and has less variability in waveform morphology and latency of the cortical response than other methods for VEP stimuli (28). The cortical waveform consists of an initial negative peak (N75) followed by a large positive peak (P100) and then another negative peak (N145) (29). The P100 peak is the most prominent with little within-subject or inter-rater variation and is used as the primary outcomes when interpreting VEPs (28). The mean latency of the P100 peak is 100 milliseconds (ms) with a standard deviation of 5 ms (30-33). The upper limit of normal is commonly defined as two SD above the mean (30, 31, 33) or approximately 110ms. The sensitivity of a prolonged P100 latency has been found to be as good as 88% for severe ON and 68% for mild or moderate ON (31) and, along with contrast sensitivity, is considered to be one of the most sensitive tests to detect clinical and subclinical demyelinating lesions affecting the optic nerve (34). VEPs have been found to be a reliable measure of the integrity of the visual conducting pathway, with VEP

latencies correlating with the VEP waveform amplitude, visual acuity and recovery of visual fields in ON (31, 35). Finally, studies have shown an increase in the VEP waveform amplitudes, suggesting improved conduction, approximately 30 days after onset of symptoms (36), closely mirroring the inflammatory MRI findings and clinical recovery noted.

Thus, VEPs are an ideal method for assessing recovery from an acute demyelinating event affecting the optic nerve when treated with equivalent high doses of oral versus IV corticosteroids. In this study, we propose to evaluate the recovery of optic nerve function after acute optic neuritis with VEPs as the primary outcome, and functional recovery, assessed by visual acuity and contrast sensitivity, as secondary outcome measures when treated with equivalent doses of oral and IV corticosteroids. Contrast sensitivity has been found to be a sensitive measure of visual function in demyelinating lesions when focusing on recovery, even in patients with high contract visual acuity of 20/20 or better (37) and correlated with vision specific health-related qualify of life measures (38) . Additionally we will evaluate the adverse events in both treatment groups to monitor safety. Although clinical recovery is the most relevant outcome, VEPs allow a standardized and objective measure of damage due to demyelination and recovery over time and is more sensitive to changes in visual function than clinical measures and has been found to correlate well with low contrast sensitivity scores (39). Limiting the study population to those with demyelinating events only in the optic nerve eliminates the difficulty of contending with the heterogeneous spectrum of clinical presentation and problems with objective assessment of function with demyelination (relapses) outside of the optic nerves.

Study Design

This will be a single-blind, randomized comparison study between 1000mg IV methylprednisolone daily for three days and 1250mg oral prednisone daily for three days of the recovery of optic nerve function in acute demyelinating optic neuritis. We will be comparing assessments at baseline, prior to corticosteroid treatment, with assessments at one and six months post corticosteroid treatment.

Patient Population

We propose to study patients with acute demyelinating optic neuritis where treatment with high dose corticosteroids is being considered. This presentation can be either the first presentation of a demyelinating event (CIS) or in a patient with a previous diagnosis of CIS or MS but must be the first presentation of ON in the affected eye.

Subjects will be recruited from out-patients assessed for acute demyelinating optic neuritis by neurology, ophthalmology, neuro-ophthalmology at London Health Sciences Center and St. Joseph's Health Care Center in London, Ontario. Subjects will be included only if the first visit takes place within 14 days of symptom onset. Only subjects where the physician who identifies/diagnoses the optic neuritis is considering corticosteroid treatment will be contacted for potential screening and enrollment. To

ensure treatment is chosen based on the clinical judgement of physician diagnosing ON, the investigators will only contact potential subjects after the decision to use corticosteroids has been made by the patient's treating physician.

Sample Size

The sample size was based on the data provided above (normal distribution of the VEP P100 mean latency with standard deviation of five (5) ms) and an estimated clinically significant difference between the two groups to be one standard deviation (a difference of -2.5 to 2.5). Based on a 1:1 randomization, a probability (power) of 0.08 and an alpha of 0.005 (the type I error probability (the risk of rejecting a true null hypothesis, that the two treatments are equal) 38 subjects are needed. Assuming a potential dropout rate of 20% before the third follow-up visit, we plan on recruiting 46 subjects in total.

Primary and Secondary Endpoints

The primary measure will be the P100 latency of the Visual Evoked Potential in the affected eye at six months. Secondary measures will include high contrast visual acuity and contrast sensitivity at one and six months post corticosteroid treatment and the P100 latency at one-month post corticosteroid treatment.

Visual Evoked Potentials
VEPs will be recorded with Teca Synergy equipment (Viasys Healthcare). To ensures consistency in technique, the same technician will perform all three assessments (day 0, 30 and 180) on the same patient. The subject's skin will be cleaned for electrode placement. The scalp electrodes will be placed relative to bony landmarks, as per International Society for Clinical Electrophysiology of Vision (ISCEV) standards (40). The electrodes will be positioned 5 cm above the inion for Oz (active), mid-forehead for Fz (reference) and on the right arm for the ground, following ISCEV guidelines (28). The patient will be positioned comfortably in a chair with the eye at a distance of 1 meter from a 17-inch cathode ray tube (CRT) monitor, which has been found to be superior to an LCD monitor as the latter can cause a delay in the latency (41). The room will be darkened to minimize extraneous light that produce responses in the visual cortex and interfere with the VEP response. The same room will be used for every VEP in this study. The subject will be monitored for fixation as poor fixation can affect the P100 peak time (28) and an eye patch used to isolate vision from one eye only. Monocular stimulation will occur at a frequency of 2 Hz, beginning with the unaffected eye, averaging 200 individual responses for each trial. A minimum of two trials per eye will be performed as per ISCEV guidelines (28). Further averaging of additional trials may be done if there are obvious technical problems (with visual fixation for instance). As the test is dependent on subject compliance, the following will take place to maximize compliance and technical aspects of the recording: talking and gum chewing will be prohibited; the subject will be instructed to relax all muscles of the head and neck specifically the jaw; feet will be resting flat on the floor with hands relaxed in the subject's lap; coaching will take place to help diminish any anxiety; the importance of fixation will be emphasized and the need to resist following the changes in colour of the

checkerboard pattern and to continue fixating on the red fixation square in the centre of the monitor will be explained. The interpretation of the VEPs will be done by an assessor blinded to the treatment arm received.

Visual Acuity
Visual acuity will be measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts and standard protocol as it the gold standard for ophthalmology clinical trials using visual acuity as an outcome (42). Testing acuity occurs initially at 4 meters initially and only testing at 2 meters if there are no abnormalities noted at 4 meters.

Contrast Sensitivity
Contrast sensitivity will be measured using the Low Contrast Sloan Letter Charts that was found to be valid and reliable for the MS population (43, 44).

Inclusion criteria

Patients will be eligible for the study if they fulfill all inclusion criteria specified below.

1. Males/Females who are ≥ 18 years old and < 65 years old and are capable of understanding and complying with the protocol
2. Have a diagnosis of unilateral acute demyelinating optic neuritis and will be treated with high dose corticosteroids
3. Are within 14 days of symptom onset
4. Have a visual acuity in the affected of eye of ≥ 20/40
5. Have not received corticosteroids in the last thirty (30) days
6. Medications that could potentially affect the VEP P100 amplitude or may cause drowsiness/difficulty with visual fixation are allowed if there has been no change in dose within 30 days of study enrollment or anytime during the study. These medications include:
    a. Carbamazepine or other anticonvulsants (45)
    b. Benzodiazepines
    c. Opioid and opiates
    d. Barbiturates
    e. Sleep aids such as zopiclone or trazadone
    f. Tricyclic antidepressants
7. Have given written informed consent prior to any study related procedure not part of normal medical care, with the understanding that consent may be withdrawn by the subject at any time without prejudice to his/her future medical care

Exclusion criteria

Patients will be excluded from the study if they meet any one of the exclusion criteria specified below.

1. Have another medical condition that could affect the visual outcomes, such as, but not limited to, diabetes retinopathy, glaucoma, cataracts and optic neuropathy not due to a demyelinating lesion
2. Have had optic neuritis in the same eye previously

Study Procedures

Day 1
At the screening visit, Day 1, informed consent will be obtained from the subject, prior to any study procedure taking place.
After informed consent, the following will take place:

a. Demographics, including age/date of birth, past CIS or MS diagnosis, past medical history, current medication use will be documented
b. Neurological and physical examination

If the subject qualifies for the trial the following will be performed by the evaluating physician and VEP technician:

a. VEPs on each eye
b. Visual acuity of both eyes individually using ETDRS charts (42)
c. Contrast sensitivity of both eyes individually using the Low Contrast Sloan Letter Charts (37)

Randomization and Treatment
Next, the subject will be randomized by a computer generated pattern, using block randomization based on first demyelinating event (presenting as CIS) vs. previously diagnosed CIS (2^{nd} demyelinating event) vs. MS diagnosis, to either IV or oral treatment. The subject and the treating physician will not be blinded to his or her treatment, but the evaluating physician, technician performing the VEPs and physician interpreting the VEPs will be blinded.

The subjects randomized to the IV group will be treated with 1000mg IV methylprednisolone daily for three (3) days as an outpatient in a hospital clinic or, if possible, at home. The subjects randomized to the oral group will be treated with 1250mg of oral prednisone daily for three (3) days. No taper will be used, as previous research has shown that this has no effect on short or long term outcomes (46) but can be used if the subject experiences rebound symptoms, at the discretion of the treating physician.

Adverse events
Within one week of corticosteroid administration, the subject will be contacted by phone by the treating physician, unblinded to the treatment allocation, to assess adverse events. If any adverse events are reported prior to this one week follow-up, they will be dealt with by the treating physician on a case by case basis, which is the standard of practice in MS clinics in Canada (18).

Phone call reminders
One week and also one day prior to each of visits two (at 30 days) and three (at 180 days), the subject will be contacted by phone to remind them about the upcoming appointment and discuss/resolve any potential barriers to completing the study visits.

Visit 2 and 3

The same procedures that were performed on Day 1/Screening visit will be performed by the blinded evaluating physician and blinded VEP technician 30 (+/- 5 days) and 180 (+/- 5 days) after the high dose corticosteroid treatment is completed. The subject will be reminded prior to the appointment that the evaluating physician is to be blinded to the route of corticosteroid administration. Additionally at visit 3, a physical and neurologic examination will also take place.

	Screening	Visit 1	Phone contact	Visit 2	Phone Contact	Visit 3
Demographics	X					
Medical History (incl. medications)	X	X		X		X
Informed Consent	X					
Neurologic and Physical Exam	X					X
Visual Evoked Potentials		X		X		X
Visual Acuity		X		X		X
Contrast Sensitivity		X		X		X
Adverse Events			X	X	X	X

Statistical Analysis

The general approach will be Analysis of Covariance (ANCOVA) where the baseline measures are employed as covariates to assess the significance of between group differences at Day 30 and Day 180. Where significant linear relationships are found between the outcomes and potential covariates (i.e. age, gender) these variables will also be included in these models. Linear trends in the data (i.e. baseline to Day 30 and 180) will be evaluated using mixed factor ANOVA. Further analysis will include comparison of the proportion of subjects with improvement, as well as degree of improvement (percent change) on the various outcomes included, between the two treatment groups.

REB

This protocol will be submitted to the University of Western Ontario's Health Sciences REB for approval prior to initiating the study. We will follow all applicable laws and codes of ethics in conduction this research, in accordance with the International Conference on Harmonization and Good Clinical Practice (GCP).

Timelines

We anticipate enrollment to occur over 16-20 months, based on enrollment of 1-3 subjects per month. The entire study would thus be complete in 22-26 months, based on a 6 month follow-up period.

Citations

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Budget and Budget Justification

Budget Items & Rationale (items not fully justified with rationale will not be considered)	Year 1 $	Year 2 $	Total $
Personnel (describe type/role of personnel and indicate amount of time per week or month)			
• Visual Evoke Potential Administration and Interpretation Support for the electrophysiology laboratory technician to administer the full VEP protocol on Days 1, 30 and 180 (approximately 1 hour/session/patient) and for analysis and interpretation by the qualified neurologist. MOHLTC fee for performing and interpreting one VEP session = $129.95.	8,251.83	8,251.82	16,503.65
• Research Assistant ($25/hour +23%) In charge of screening/consenting potential subjects, administrative duties (organization of charts, booking appointments organizing/reminding subjects of appointments, answering phone questions etc.) Estimated time commitment: 4 hours/subject for the initial visit/enrollment, 2.5 hours for the 2nd and 3rd visit. Hourly rate for a research assistant is $25 +23%.	5,942.44	5,942.44	11,884.88
• Treating Physician (unblinded) In charge screening/consenting subjects, supervising the research staff, liaising with other staff for recruitment, managing adverse events. Compensation: $50/visit. • Examining Physician (blinded) Will perform the physical/neurological exam at Visit 1 & 3; assess visual acuity and contract sensitivity at Visits 1, 2 & 3. Compensated $85.00 for visit 1, $65.00 for visit 2&3based on MOHLTC cost for neurologist limited consultation and medical specific assessment = $84.95 and $65.65 respectively.	3,175.00 4,587.50	3,175.00 4,587.50	6,350.00 9,175.00
Total Personnel	21,956.77	21,956.76	43,913.53
Equipment (describe type and quantities and how will be used for study)			
• EDTRS illuminator box and charts	1,350.00	---	1,350.00
• Low Contrast Sloan Letter Charts	250.00	---	250.00
• (Shipping and handling – 16%)	256.00	---	256.00
Total Equipment	1,856.00		1,856.00
Materials & Supplies (describe type and quantities required and how will be used for study			
• Pharmacy – see budget justification	5,324.00	4,324.00	9,648.00

• IV infusion – see budget justification	3,852.50	3,852.50	7,705.00
• Incidentals (charts, photocopying etc.)	750.00	250.00	1,000.00
Total Materials & Supplies	9,926.50	8,426.50	18,353.00
Knowledge Translation Activities (publications/ conference presentations) (maximum $1500 per grant)			
• Presentation at International Scientific Meeting	---	1,000.00	1,000.00
• Publication and Reprints		500.00	500.00
Total Knowledge Translation Activities	---	1,500.00	1,500.00
Other Expenses (full detailed description, quantities and amounts must be provided below)			
• Parking ($12/visit) 38 subjects 8 drop-outs	 684.00 78.00	 684.00 78.00	 1,368.00 156.00
• Advertising and Recruitment – see budget justification	1,000.00	500.00	1,500.00
Total Other Expenses	1,762.00	1,262.00	3,024.00
TOTAL PROJECT BUDGET REQUESTED (maximum $85,000 per year for up to two years)	35,501.27	33,145.26	68,546.53

Budget Justification

The budget is based on a planned 2 year study with 46 recruited subjects based on a sample size of 38 and a 20% (8 subjects) dropout rate. We anticipate subjects are more likely to drop out after they feel they have recovered functionally (between one and six months), thus we will budget for 3 drop-outs after visit 1/before visit 2 and 5 drop-outs after visit 2/before visit 3.

Treatment
Since participation in this study and allocation to either IV or oral treatment is above the usual standard of care, we are requesting coverage of the cost of IV methylprednisolone, its administration, and the cost of oral prednisone.
Pharmacy: The cost of each mini bag of IV methylprednisolone is $62.00 with a $50.00 dispensing fee, for a total of $112 per day per subject. This is a total of $7,728.00 for 23 patients (subjects randomized to IV treatment). The cost of each prednisone tablet is $0.20. One dose of 1250mg is 25 tablets (75 tablets for 3 doses = $15.00). If all 3 doses are dispensed at once, the dispensing cost is $25.00, for a total of $920.00 for 23 subjects. Additionally, pharmacy requires $1000.00 in administration fees for the following:
- Initial protocol review, close-out
- Liaison with the study co-coordinator & PI

- Preparation of a procedure for use by pharmacy staff
- Preparation of appropriate Dispensing Logs and Inventory Records
- Provision of medication storage space within the Pharmacy Department
- Discussion with study personnel concerning procedures and documentation requirements
- Procurement of drug supply
- Development of research prescription vial label in accordance with GCP
- Preparation of a computer code for outpatient order entry
- Preparation of protocol summary for use by pharmacy staff
- Research pharmacy staff availability within normal work hours of 0700 - 1500 (M - F)

IV infusion: The London Health Sciences Center pharmacy and infusion center estimate the cost of IV methylprednisolone treatment for 3 days in total to be $335.00. This total is based on 4.5 hours of RN time (1.5 hours/visit, based on $45.49/hour + 23%) and supplies need for IV infusion of $87.50.

Advertisement and Recruitment

Acute optic neuritis is often evaluated by the general ophthalmologist/ophthalmology resident on call or the neurologist/neurology resident on call. Further, these physicians may initiate treatment prior to referring to either a neuro-ophthalmologist or an MS neurologist. To improve recruitment, we plan on initiating education sessions with the above mentioned staff (presentation at grand rounds and/or resident teaching sessions), as well as posting flyers in the appropriate clinical settings.