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The predictor factor of final visual acuity (VA) of acute retrobulbar neuritis patients receiving optic neuritis treatment trial (ONTT) regiment

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ABSTRACT

The study aimed to investigate the efficacy of intravenous optic neuritis treatment trial (ONTT) regiment on the treatment of patients with acute retrobulbar neuritis. This was a cross sectional study using medical records data of patients diagnosed with unilateral or bilateral retrobulbar neuritis by normal funduscopic findings and typical optic neuritis perimetry results within 14 days of onset from the Neuro-ophthalmology Clinic, Department of Ophthalmology, Dr. Sardjito General Hospital, Yogyakarta from January to December 2015. Medical records data of patients who received 1000 mg methylprednisolone IV per day for 3 days followed by 11 days 1 mg/kg body weight oral prednisolone were reviewed. Visual acuity (VA) at onset, final VA at time of follow up, delta VA improvement and time of follow up were included in the analyses. Twenty data of patients aged 33.95±8.07 years with VA at onset of 1.96±0.81 (~ 1 m CF) were analyzed in this study. Significantly improvement in final VA after treatment to be 1.39±1.12 (~ 5 m CF) was reported (p=0.001). The VA at onset was a predictive factor for final VA (p <0.001). Every 1.17 increase of final VA for every one-point decreased VA at onset (p<0.001). Time follow up showed to be trend (p=0.059), however, age and sex were not a predictive factor of final VA (p>0.05). In conclusion, there is VA improvement after the treatment of ONTT regiment. The VA at onset is a predictive factor of final VA on patients with acute retrobulbar neuritis.

ABSTRAK

Penelitian ini bertujuan mengkaji efektivitas regimen *optic neuritis treatment trial* (ONTT) intravena pada pengobatan pasien dengan neuritis retrobulbar fase akut. Penelitian potong lintang ini menggunakan rekam medis pasien yang didiagnosis neuritis retrobulbar unilateral atau bilateral dengan temuan funduskopi normal dan hasil perimetri neuritis optik yang khas dalam waktu 14 hari setelah onset dari Klinik Neuro-oftalmologi, Departemen Oftalmologi, Rumah Sakit Umum Pusat Dr. Sardjito, Yogyakarta dari Januari-Desember 2015. Data rekam medis pasien yang menerima 1000 mg metilprednisolon IV per hari selama 3 hari diikuti oleh prednisolon oral selama 11 hari dengan dosis 1 mg/kg berat badan dianalisis. Ketajaman visual (VA) saat onset, VA akhir saat tindak lanjut, peningkatan VA, dan waktu tindak lanjut dianalisis. Sebanyak 20 data pasien berumur 33,95 ±8,07 tahun dengan VA saat onset 1,96 ±0,81 (~ 1 m CF) dianalisis dalam penelitian ini. Perbaikan VA akhir menjadi 1,39±1,12 (~ 5 m CF) dilaporkan (p=0,001). Ketajaman visual saat onset merupakan factor predictor VA akhir (p<0,001). Setiap peningkatan VA akhir sebesar 1,17 menurunkan satu poin VA saat onset (p<0.001). Waktu tindak lanjut cenderung menjadi factor prediktor (p=0,059), namun demikian usia, jenis kelamin bukan factor predictor VA akhir (p>0,05). Dapat disimpulkan, terdapat peningkatan VA pasien setelah pengobatan regimen ONTT. Ketajaman visual saat onset merupakan faktor prediktor VA akhir pada pasien dengan neuritis retrobulbar akut.

Keywords:
retrobulbar neuritis;
optic neuritis;
visual acuity;
optic neuritis treatment trial;
treatment;

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INTRODUCTION

Optic neuritis is defined as an inflammation affecting the optic nerve. It is a frequent cause of acute optic nerve injury in children and adults.[1] Optic neuritis commonly related to demyelinating optic neuritis, which ultimately evolve into multiple sclerosis (MS). The other form of optic neuritis is severe immune-mediated demyelinating disease that injured the optic nerves as part of neuromyelitis optica spectrum disease (NMOSD).[2,3] The estimated lifetime prevalence of optic neuritis was 0.6/1000, and the incidence that adjusted to the age and sex was 1–5/100000.[4,5] Several studies reported that young female Caucasian frequently suffered from optic neuritis with the mean age of onset is 31–32 years.[6-8] The female predominance also mentioned in study from Asia, with the mean age of 40 years old.[9]

According to the involved location, optic neuritis can be differed as a retrobulbar neuritis (most of cases) that appeared with normal optic disc; papillitis, which appeared to have a swollen disc; perineuritis, in which optic nerve sheath was involved with normal or swollen optic disc; and neuroretinitis with prominent macular star sign and swollen optic disc.[10,11] The MS was predominantly associated with retrobulbar neuritis and papillitis. Meanwhile, the perineuritis and neuroretinitis were commonly involved in infectious or inflammatory pathologies.[11,12]

Retrobulbar neuritis is an inflammation affecting the optic nerve behind the eyeball characterized by a sudden onset of unilateral or bilateral visual loss with normal disc appearance. Most of the case of retrobulbar neuritis are idiopathic in nature, but it could be associated with demyelinating lesions (multiple sclerosis). Other less common etiologies include infectious and para-infectious causes and inflammatory responses.[11] The optic neuritis treatment trial (ONTT), was the first major study that found that patients treated with intravenous corticosteroids had faster recovery of vision but that visual recovery in patients treated with an oral placebo was as good after 1 year of follow-up as visual recovery in patients treated with either intravenous or oral corticosteroids.[13] The aim of this study was to investigate the efficacy of intravenous ONTT regiment in treating acute retrobulbar neuritis.

MATERIALS AND METHODS

Patients

This is a retrospective, cross-sectional study that approved by the Institutional Review Board in accordance with the Declaration of Helsinki and was approved by the Medical and Health Research Ethic Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada / Dr. Sardjito General Hospital, Yogyakarta (KE/FK/0749/EC/2017). The data from medical records of patients diagnosed with unilateral or bilateral retrobulbar neuritis from the Neuro-ophthalmology Clinic, Department of and Ophthalmology, Dr. Sardjito General Hospital, Yogyakarta from January to December 2015 were reviewed. The data were then derived from the patients who diagnosed with unilateral and bilateral retrobulbar neuritis.

Protocol of study

Diagnosis of retrobulbar neuritis was based on clinical symptom sudden visual loss with normal funduscopy findings and typical optic neuritis perimetry results within 14 days of onset. All the patients received 1000 mg methylprednisolone IV per day for 3 days followed by 11 days 1 mg/kg body

weight oral prednisolone. Demographic data including gender and age of onset were recorded. The best corrected visual acuity (BCVA) was examined by Snellen chart and converted into logarithm of the minimal angle of resolution (LogMAR) units for statistical analysis. Visual acuity (VA) at onset, final VA at time of follow up, delta VA improvement and time of follow up were included in the analyses. Patients with age less than 18 years old were excluded.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA). Predictive factors associated with final VA were analyzed using ANOVA regression analysis. *p*-values < 0.05 were considered statistically significant.

RESULTS

Twenty patients were included in this study. Their mean age was 33.95 ± 8.07 years (range 21-49 years). Eleven (55%) patients were female. The mean time of follow up was 0.8750 ± 0.59 months. Visual acuity at onset ranged from 20/32 to light perceptionwith mean initial VA was 1.96 ± 0.81 (~ 1 m CF). The predictive factors for treatment results are shown in TABLE 1. Significantly improvement in final VA post therapy to be 1.39±1.12 (~ 5 m CF) was reported (p=0.001). The VA at onset was founds as a predictive factor for final VA (p <0.001), while age and sex were not a predictive factor of final VA post ONTT (p> 0.05). It was also reported that in every 1.17 increase of final VA was associated with 1-point decrease of VA at onset. There was no association between time of follow up with final VA, but time of follow up were shown trend (p=0.059). Thus, VA at the onset of acute retrobulbar neuritis was a strong predictive factor that important to determine the prognosis of VA after ONTT.

TABLE 1. Predictive factors for treatment results

Variables	Value	*p*	PR	95% CI
Sex [n (%)]				
• Male	9 (45)	0.549	0.314	-0.766 – 1.395
• Female	11 (55)			
Age (mean ± SD)	33.95±8.07	0.974	0.001	-0.068 – 0.070
VA at onset (mean ± SD)	1.96±0.81	<0.001*	1.117	0.707 – 1.527
Time of follow up (mean ± SD)	0.8750±0.59	0.059	-0.815	-1.663 – 0.034

PR: Prevalence Ratio

DISCUSSION

This study identified that VA at onset was the only factor associated with final VA. Every 1.17 increase of final VA was associated with 1-point decrease of VA at onset. This finding showed the efficacy of the ONTT regiment in acute retrobulbar neuritis. Previous study conducted by Sheti *et al.*,[14] to evaluate the efficacy and safety profile of intravenous dexamethasone showed that the intravenous pulse dexamethasone led to rapid recovery of vision in acute optic neuritis, without any serious side effects. However, another study reported that, ONTT indeed proven to be effective in accelerate the visual recovery in acute optic neuritis, but may not affect the final VA.[15] This might happen in patient with the worst VA at the onset of optic neuritis. Another study conducted by

Menon *et al*.,[16] reported that intravenous dexamethasone to be as effective as mega-dose intravenous methylprednisolone therapy recommended by the ONTT study, with the added advantage of being easier to administer and less costly (costing one sixth of injection methylprednisolone).

In some cases, the benefit of corticosteroids treatment might relatively subtle when it is present.[17] Several studies reported no serious adverse effects were found during ONTT.[18-20] Approximately 50% of patients with ONTT were reported to experience insomnia.[21] Concordantly, other studies also reported several adverse effects, such as hyperglycemia, hyperlipidemia, headache, weight gain, facial flushing, and fever.[21,22] Because of this adverse effects, the clinician should also consider the adverse effect of corticosteroids before delivering ONTT.

We also compared the demographic data and predictive factors of ONTT treatment results. The mean age of onset was 33.95 ± 8.07 years. This finding was similar to other study reported by Zhou *et al*.[23] (mean 34.6 years, range 18-55 years) and Hansapinyoand Vivattanaseth,[24] (mean 39.1 years, range 18-73). The majority of the patients in this study were female (55%). However, sex was not predictive factor of final VA (p= 0.549). This finding was different with the study conducted by Hansapinyo and Vivattanaseth[24] which showed that female-male ratio was higher in patients with NMOSD.

The retrospective design of this study, incomplete and varied data documentation, and small sample size were limitations in this study. Future prospective studies to determine the appropriate diagnostic and treatment protocol of retrobulbar neuritis should be performed by using experimental study design.

CONCLUSION

There isVA improvement after the treatment of ONTT regiment. The VA at onset is a predictive factor of final VAon patients with acute retrobulbar neuritis.

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