Comparison of Efficacy Between Steroid Therapy and Observation Therapy in the Treatment of Traumatic Optic Neuropathy-a Meta-analysis

Peipei Zhang

Tianjin Fifth Central Hospital: Peking University BinHai Hospital

Chao Xue

Tianjin Eye Hospital

Ying Chen

Tianjin Eye Hospital

Xuening Su (✉ 316280020@qq.com)

Tianjin Fifth Central Hospital: Peking University BinHai Hospital

Research

Keywords: traumatic optic neuropathy, steroid therapy, meta-analysis

Posted Date: July 26th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-736728/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background: Until now, the exact pathophysiology of traumatic optic neuropathy(TON) is still unclear, its management has remained controversial. The effect of steroid in TON remains unclear. The purpose of this study is to compare the effect of steroid therapy with observation therapy in the treatment of traumatic optic neuropathy(TON).

Methods: A systematic literature search was performed in data sources including CENTRAL, PubMed, EMBASE, Web of Science, Cochrane Library, MEDLINE, Chinese databases including Wanfang and China National Knowledge Infrastructure for to find relevant studies. The statistical analysis was performed by RevMan 5.3 software.

Results: Eight studies including 263 eyes were enrolled in this study. The rate of improvement of VA in the steroid group was not better than that of the observation group (OR=2.17, 95%, CI=1.23-3.83, P=0.007), with no heterogeneity ($I^2=0$, P=0.43).

Conclusions: Patients with TON receiving steroid treatment may not have a better visual recovery than observation therapy. Steroid therapy is not recommend in patients with TON. Further larger randomized clinical trials are needed to evaluate the effect of steroid therapy for TON in the future.

Background

Traumatic optic neuropathy (TON) describes an injury to the optic nerve following either blunt or penetrating trauma.[1] Until now, the exact pathophysiology of TON is still unclear, its management has remained controversial. Treatment options include observation alone, corticosteroid administration, and/or surgical decompression.[2]

Since the early 1980s, steroid have been used in an attempt to reduce the abnormal swelling that follows an injury to the optic nerve and improve visual recovery. [3]In a study by Anderson et al[3], it was found that some patients who were administered corticosteroids shortly after injury recovered some vision within 6 hours of treatment initiation. [4]However, others found no clear benefit of corticosteroid therapy.[5] The effect of steroid in TON remains unclear.

The purpose of this systematic review was to examine the effect of steroid and to make recommendations for best practice in the treatment of TON.

Materials And Methods

Search strategy

We searched the following databases: CENTRAL, PubMed, EMBASE, Web of Science, Cochrane Library, MEDLINE, Chinese databases including Wanfang and China National Knowledge Infrastructure from database inception through until July 20, 2020. There were no language restrictions. The following search terms were used: “(Optic Nerve[MeSH] OR Optic Nerve Diseases[MeSH] OR Optic Nerve Injuries[MeSH] OR optic nerve* OR optic neuropath* OR optic injur* OR optic trauma* OR optic contusion* OR optic compress* OR optic avulsion* OR optic transection* OR optic damage*) AND (Steroids[MeSH] OR steroid* OR Prednisolone[MeSH] OR prednisolone OR Prednisone[MeSH] OR prednisone OR Methylprednisolone[MeSH]) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh])”. In addition, we manually searched the reference of research articles, reviews, meta-analyses and book chapters on TON to reduce the chance of omitting relevant studies.

Eligibility Criteria

We planned to include all the studies of TON in which any steroid regime was compared to observation group. Animal studies, conference proceedings, editorials, abstracts and studies with incomplete data were excluded.

Data collection and analysis

Two review authors independently screened and reviewed the titles and abstracts resulting from all retrieved records. We obtained full-text articles of studies that appeared to meet the inclusion criteria. Both authors then assessed the articles to ensure that they met our inclusion criteria. Any disagreement was resolved by discussion and a consensus opinion was reached. The reports that did not completely fulfill the inclusion criteria were excluded.

We used Review Manager software (version 5.3, Cochrane Collaboration, Oxford, UK) for all the statistical analyses.

Before carrying out a meta-analysis we assessed heterogeneity by examining the characteristics of the study, the forest plot of results in the studies, and the results of the Chi^2 statistic and I^2 value for statistical heterogeneity.[6] $P < 0.05$ was considered statistically significant.

Results

Selection of Studies And Characteristics of the Included Studies

The original searches identified 315 reports of studies. We read the titles and abstracts of these studies for potential inclusion in the review. The full-text articles of studies that appeared to meet the inclusion criteria were obtained. In addition, references from these articles were reviewed to ensure that no potentially relevant studies were missed. Finally, eight studies[4, 5, 7–12] including 263 eyes were enrolled in this analysis. Characteristics of included studies are presented in Table 1. Of these studies, three were performed in China, two in USA, one in Iran, Malaysia and Singapore respectively(Table 1).

Table 1
Characteristics of studies of steroids vs. observation group included in the meta-analysis

Year	First Author	No. of eyes	Application method for steroids	Definition of Visual Improvement	Steroids group		Observation group		Country
					improved	not improved	improved	not improved	
1996	Chou PI ⁷	33	intravenous dexamethason:1-3mg/kg/day, oral prednisolone:60-80mg/day	Snellen chart: one line or better	13	10	0	10	China
2007	Entezari M ⁸	31	250 mg methylprednisolone intravenously every 6 h for 3 days, then 1 mg/kg prednisolone orally for 14 days	decrease of at least 0.4 logMAR	11	5	8	7	Iran
2010	Lee KF ⁴	27	intravenous methylprednisolone 250mg for 3 days without commencement of oral prednisolone, intravenous methylprednisolone 250mg for 3 days followed by oral prednisolone 1 mg/kg for 11 days	Snellen chart: at least 1 line improvement of visual acuity	12	6	7	2	Malaysia
1999	Levin LA ⁵	71	according to the initial daily dose of methylprednisolone	≥ 3 lines improvement	33	31	4	3	USA
2001	Li Z ⁹	18	intravenous dexamethasone 0.5-1mg/kg/day, then reduced the dose after 2-3days to 14 days. First dose of intravenous methylprednisolone 30mg/kg, then 500mg/8 h for 2-3 days, followed by oral prednisolone 1mg/kg/day, gradually reduce the dose to 14 days	VA was improved after treatment	8	2	5	3	China

Year	First Author	No. of eyes	Application method for steroids	Definition of Visual Improvement	Steroids group		Observation group		Country
					improved	not improved	improved	not improved	
2000	Ma ZZ ¹⁰	26	intravenous dexamethasone 1mg/kg/d for 3 days, followed by oral dexamethasone 7.5mg, then gradually reduce the dose to 14 days. intravenous methylprednisolone for patients who started treatment within 3 days after injury, first dose was 30mg/kg, then 5.4mg/kg/h for 23h, 250mg/6h in 24-48h.(for patients who started treatment more than 3 days after injury, first dose was 1000mg, then 500mg bid for 2 days). from 3rd day, oral prednisolone 50mg/d, gradually reduce the dose to 14 days	VA was improved after treatment	8	3	7	8	China
2002	Yip CC ¹²	21	125–250 mg methylprednisolone 6-hourly intravenously	improvement of 2 or more Snellen lines	4	5	4	8	Singapore
1990	Seiff SR ¹¹	36	1 mg/kg of intravenous dexamethasone per day	lines improved over initial acuity	13	8	5	10	USA

Outcomes of the Meta-analysis

Figure 1 showed forest plots comparing the results of the steroid group with observation group: the rate of improvement of VA in the steroid group was not better than that of the observation group (OR = 2.17, 95%CI = 1.23–3.83, P = 0.007), with no heterogeneity ($I^2 = 0$, P = 0.43).

Discussion

Traumatic optic neuropathy (TON) was first described by Hippocrates in 500 BC.[13] It mainly affects young, economically active males and is a rare cause of visual loss following blunt or penetrating head trauma with a reported incidence of 0.7–2.5% in previous studies.[14–16] The pathophysiology of TON is likely to be multifactorial, and the concept of primary and secondary injury has been proposed[16–18]: Following trauma, there is an immediate shearing of a proportion of retinal ganglion cell axons, an irreversible process that results in neuronal loss. There is then a degree of optic nerve swelling within the tight confines of the optic canal secondary to direct mechanical trauma and vascular ischemia. The ensuing compartment syndrome further impairs the already compromised blood supply to surviving retinal ganglion cells, setting up a downward spiral toward apoptotic cell death. This two-stage model of TON forms the basis for optic nerve decompression by medical or surgical means, in order to break this vicious

cycle and to preserve the remaining retinal ganglion cells that survived the initial insult. It is caused by the transmission of forces to the optic nerve from a distant site, without any overt damage to the surrounding tissue structures. TON could result in partial to complete loss of vision. The loss of visual acuity is usually instantaneous and, without treatment, permanent.[19]

The treatment of TON is still controversial because it is a challenge to perform large, randomized controlled trials in the relatively small patient population of TON.

Steroid treatment was used from the findings from the Second National Acute Spinal Cord Injury Study (NASCIS-II).[20] It is supposed that large doses of steroid may slow the cell degenerative process, increase the blood supply to the injured area, and decrease cell damage secondary to ischemia and hypoxemia.[21] The use of steroid to treat TON injuries was first reported by Anderson et al in 1982.[3]

One study by Cook et al[22] concluded that treatment with corticosteroids was significantly better than no treatment. However, other literatures have not shown any significantly better visual outcome in the steroid than observation.[23, 24] The results of steroid interventions have still shown to be uncertain.[5, 8]

In the studies included in this meta-analysis, only the results of Lee et al[4] and Levin et al[5] favored experimental group who receiving intravenous steroid had a better visual recovery as compared with observation group. The others[7–12] all favored observation group. When we took all the studies into meta-analysis, the result didn't showed a better visual recovery in patients receiving steroid treatment compared with observation therapy.

There are a few limitations in the present study. Parts of studies including into this meta-analysis failed to be RCT, the application method for steroid and definition of visual improvement in different studies were not consistent.

Conclusions

In conclusion, to the best of our knowledge, this is the first meta-analysis to compare the effect of steroid therapy to observation therapy in the treatment of TON. The result don't show a better visual recovery with steroid treatment. Considering the complication of steroid, steroid therapy is not recommend in patients with TON. Further larger randomized clinical trials are still needed to evaluate steroid therapy for TON in the future.

Abbreviations

TON: traumatic optic neuropathy

OR: Odds ratio

CI: Confidence interval

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors have no proprietary or commercial interest in any of the materials discussed in this article.

Funding

None.

Authors' contributions

Peipei Zhang, Chao Xue reviewed the literature and contributed to manuscript drafting; Ying Chen reviewed the literature reviewed the literature and designed the methods; Xuening Su were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

Acknowledgements

None.

References

1. Chaon BC, Lee MS: Is there treatment for traumatic optic neuropathy? *Current opinion in ophthalmology* 2015;26:445-449.
2. Cook MW, Levin LA, Joseph MP, Pinczower EF: Traumatic Optic Neuropathy: A Meta-analysis. *Arch Otolaryngol Head Neck Surg* 1996;122:389-392.
3. Anderson RL, Panje WR, Gross CE: Optic nerve blindness following blunt forehead trauma. *Ophthalmology* 1982;89:445-455.
4. Lee KF, Muhd Nor NI, Yaakub A, Wan Hitam WH: Traumatic optic neuropathy: a review of 24 patients. *International journal of ophthalmology* 2010;3:175-178.
5. Levin LA, Beck RW, Joseph MP, Seiff S, Kraker R: The treatment of traumatic optic neuropathy: the International Optic Nerve Trauma Study. *Ophthalmology* 1999;106:1268-1277.
6. Yu-Wai-Man P, Griffiths PG: Steroids for traumatic optic neuropathy. *The Cochrane database of systematic reviews* 2013:Cd006032.
7. Chou PI SA, Chen YC, Su WY, Lin SZ, Lee CC.: Clinical experiences in the management of traumatic optic neuropathy. *Neuro-ophthalmology* 1996;16:325-336.
8. Entezari M, Rajavi Z, Sedighi N, Daftarian N, Sanagoo M: High-dose intravenous methylprednisolone in recent traumatic optic neuropathy; a randomized double-masked placebo-controlled clinical trial. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2007;245:1267-1271.
9. Li Z DY, Guo H, Zhang HY: Therapeutic efficacy of traumatic optic neuropathy treated with different protocol. *Chin J Ocul Traum Occupat Eye Dis* 2001;23:396-397.
10. Ma ZZ LT, Wei SB, Wang RG, Zhang MN, Huang YF, Li CH.: Assessment of surgical and high-dose corticosteroid treatment in traumatic optic neuropathy. *Chin J Ocul Fundus Dis* 2000;16:75-77.
11. Seiff SR: High dose corticosteroids for treatment of vision loss due to indirect injury to the optic nerve. *Ophthalmic surgery* 1990;21:389-395.
12. Yip CC, Chng NW, Au Eong KG, Heng WJ, Lim TH, Lim WK: Low-dose intravenous methylprednisolone or conservative treatment in the management of traumatic optic neuropathy. *European journal of ophthalmology* 2002;12:309-314.
13. Miliaras G, Fotakopoulos G, Asproudis I, Voulgaris S, Zikou A, Polyzoidis K: Indirect traumatic optic neuropathy following head injury: report of five patients and review of the literature. *Journal of neurological surgery Part A, Central European neurosurgery* 2013;74:168-174.
14. Pirouzmand F: Epidemiological trends of traumatic optic nerve injuries in the largest Canadian adult trauma center. *The Journal of craniofacial surgery* 2012;23:516-520.
15. Cockerham GC, Goodrich GL, Weichel ED, Orcutt JC, Rizzo JF, Bower KS, Schuchard RA: Eye and visual function in traumatic brain injury. *Journal of rehabilitation research and development* 2009;46:811-818.
16. Yu-Wai-Man P: Traumatic optic neuropathy-Clinical features and management issues. *Taiwan journal of ophthalmology* 2015;5:3-8.
17. Levkovitch-Verbin H: Animal models of optic nerve diseases. *Eye (London, England)* 2004;18:1066-1074.

18. Osborne NN, Chidlow G, Layton CJ, Wood JP, Casson RJ, Melena J: Optic nerve and neuroprotection strategies. Eye (London, England) 2004;18:1075-1084.
19. Kitthaweesin K, Yospaiboon Y: Dexamethasone and methylprednisolone in treatment of indirect traumatic optic neuropathy. Journal of the Medical Association of Thailand = Chotmai het thangphaet 2001;84:628-634.
20. Bracken MB, Shepard MJ, Collins WF, Holford TR, Young W, Baskin DS, Eisenberg HM, Flamm E, Leo-Summers L, Maroon J, et al.: A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the Second National Acute Spinal Cord Injury Study. The New England journal of medicine 1990;322:1405-1411.
21. Braughler JM, Hall ED: Current application of "high-dose" steroid therapy for CNS injury. A pharmacological perspective. Journal of neurosurgery 1985;62:806-810.
22. Cook MW, Levin LA, Joseph MP, Pinczower EF: Traumatic optic neuropathy. A meta-analysis. Archives of otolaryngology-head & neck surgery 1996;122:389-392.
23. Steinsapir KD, Goldberg RA: Traumatic optic neuropathy. Survey of ophthalmology 1994;38:487-518.
24. Singman EL, Daphalapurkar N, White H, Nguyen TD, Panghat L, Chang J, McCulley T: Indirect traumatic optic neuropathy. Military Medical Research 2016;3:2.

Figures

Figure 1

Forest plots comparing the results of the steroid group with observation group