Management of Traumatic Optic Neuropathy: A Systematic Review

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Abstract

Traumatic optic neuropathy (TON) is indeed a rare cause of vision loss that can be caused by head or periorbital injury. Unfortunately, TON's consequences can be severe, especially when both optic nerves are affected. Interestingly, about 20% of cases occur during childhood, even though most patients are young adult males. The diagnosis of TON is typically easy to make based on clinical history and examination findings that suggest optic neuropathy. TON management is controversial in medicine. Some prefer monitoring; others use steroids, surgery, or both. Patients managed conservatively have high spontaneous recovery rates, so the intervention's adverse effects must be carefully weighed. After conducting a thorough database search on traumatic optic neuropathy (TON), articles written in English with abstracts and full text were selected. Good visual acuity is the most important predictor of recovery in TON patients.

Keywords: *Trauma, Optic Nerve, Neuropathy, Steroids, Observation, Visual Outcome.*

Introduction

Traumatic optic neuropathy (TON) is usually a medical condition characterized by an acute injury to the optic nerve resulting from trauma to the head or periorbital area. The damage to the optic nerve can vary from simple contusion to complete avulsion, resulting in partial or total loss of vision. Still, the consequences can be devastating when involving both optic nerves.[1,2]When TON is suspected, performing neuroimaging studies like computed tomography scans (CT scans) or magnetic resonance imaging (MRI) is crucial. The main treatment modalities for TON typically involve systemic corticosteroids and surgical optic nerve decompression, which can be used alone or in combination, depending on the case.[2,3]Optic nerve damage can result in swelling and fluid accumulation, which contributes to further deterioration and reduced blood flow. Surgical optic canal decompression and steroids may help alleviate these effects.

Classification

Traumatic optic neuropathy (TON) can be classified based on the location of the injury (optic nerve head, intraorbital, intracanalicular, or intracranial) or traditionally according to the mode of injury (direct or indirect) or depends upon retinal features (Optic disc avulsion, anterior optic neuropathy or posterior optic neuropathy).[3,4] The optic nerve is most vulnerable to traumatic injury within the canal, but the orbit portion is also at risk of injury.5,6 An indirect injury (Fig 1) to the optic nerve often happens due to the transmission of forces to the optic canal from a distant site, resulting from blunt trauma to the head, forehead, or the globe. On the other hand, direct TON occurs due to anatomic disruption of optic nerve fibres caused by penetrating orbital trauma at high velocity (Fig. 2), nerve sheath hematomas, or bone fragments within the optic canal. Direct trauma can cause optic nerve avulsion.[1,3]

Blunt trauma can cause stress on the skull, which

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is concentrated in the optic canal region. The optic nerve's intracanalicular segment is vulnerable to this type of injury due to the dural sheath's tight adherence to the periosteum in this area.[7-9]The optic nerve within the intracranial portion near the falciform dural fold is at the next highest risk of injury.[10]

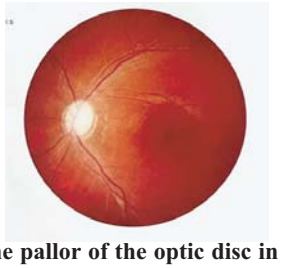

Figure 1: The pallor of the optic disc in the left eye due to blunt indirect trauma, was observed 3 weeks later of indirect traumatic optic of the left eye. The patient's vision was not improved and subsequently vision lost on follow-up and developed primary optic atrophy.

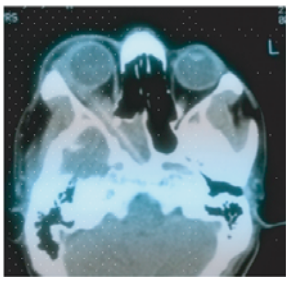

Figure 2: a 46-year-old male patient gave a history of accidental penetrating trauma at high velocity to his right globe. CT-Scan of the orbit shows a hyperdense elongated foreign body from lateral aspect of the right orbit, just below the globe to the sphenoid sinus, with variable number of densities of tissues suggestive of an old wooden foreign body with inflammatory changes of the surrounding tissue.

Epidemiology

Traumatic optic neuropathy occurs rarely and causes visual loss permanently following penetrating or blunt trauma to the head or periorbital area.[11-13] It affects about 0.7% to 2.5% of the population.[5 ,14] As per Gise et al., TON is the most frequent (86.1%) visual pathway injury among children in the USA from 2008 to 2014.[15] The minimum prevalence of TON is one among the one million population.[16] Studies have shown that the leading causes of TON is road traffic accidents (motor vehicle and bicycle, 43-49%), falls (27-35%), and assaults (13%). The incidence of traumatic optic neuropathy (TON) in the context of a closed traumatic head injury varies from 0.5% to 5%.[16,17] TON is more common in males (79-89%) with a mean age of 34 (Fig. 3).[1,16,17,18]. In children, most TON cases are usually caused by falls (50%) and accidents on the road (40%).[19] Additionally, TON has also been associated with penetrating orbital trauma (e.g., stab wounds, pellet and gunshot injuries, foreign bodies) and sports-related injuries (e.g., cricket ball injury).[2]

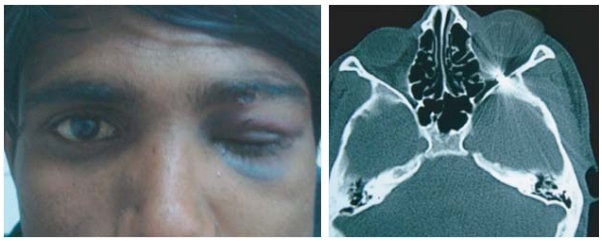

Figure 3: A 25-year-old male patient gave a history of gunshot injury to his left eye three days ago. The left upper eyelid shows a round entry point of a wound with periocular ecchymosis. The CT-Scan of the orbit (bone window) shows a round metallic foreign body with artifact in the posterior aspect of the left orbit. The diagnosis was the direct traumatic optic neuropathy of the left eye.

Pathophysiology

Traumatic optic neuropathy (TON) is believed to be caused by various factors, and some researchers have suggested that there could be both primary and secondary mechanisms of injury involved.[20,21] Primary and secondary mechanisms of injury can cause traumatic optic neuropathy (TON). Indirect TON (Fig. 3) occurs due to shearing forces transmitted to the nerve fibres or the vascular supply of the optic nerve, which can lead to ischemic injury to the retinal ganglion cells in the optic canal. Optic nerve swelling after the acute injury can exacerbate retinal ganglion cell degeneration by compromising the vascular blood supply through increased intraluminal pressure or reactive vasospasm. Forces delivered to the axons by the shifting of the brain following head trauma can damage the intracranial segment of the optic nerve. It has been found through various studies that when forces are exerted on the frontal bone and malar eminences, they tend to get transferred and concentrated in the region situated close to the optic canal. The optic nerve's dural sheath tightly adheres to the periosteum within the optic canal, making this nerve segment highly susceptible to deformative stresses from skull bones.[22]

Diagnostic Procedures

The Diagnosis of Traumatic optic neuropathy (TON) is primarily based on a clinical evaluation, including detailed ophthalmic and neurologic examinations with a recent history of head or periorbital trauma (Fig. 4). Symptoms include sudden visual field or vision loss. Ophthalmic Signs included reduced vision, impaired coloured vision, decreased visual field, and afferent pupillary defect (APD). Traumatic optic neuropathy (TON) can cause unilateral vision loss due to head or periorbital trauma. It is worth noting that if a patient is unconscious or has other injuries related to the trauma, such as a traumatic brain injury, the diagnosis of TON may be delayed. This delay could hinder the presentation and subsequent evaluation of any ophthalmologic injury.

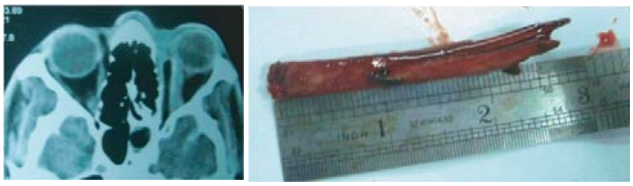

Figure 4: A 29-year-old-male patient presented with Optic Nerve avulsion of the left eye due to periorbital trauma accidentally by a long bamboo stick. Axial CT image of the orbit shows a long hypo dense lesion with surrounding heterogeneous hyper densities due to tissue oedema and inflammatory changes suggestive of the wooden foreign body in the left orbit.

A detailed examination record should also be maintained for the future medicolegal proceedings of the patients. Conscious and cooperative patients may experience the following features: i. Unilateral or bilateral Ocular involvement ii. Variable amount of vision loss even if there is no perception of light, iii. impaired colour vision, iv. a relative afferent pupillary defect (RAPD), assessed by swinging-flashlight test or afferent pupillary defect (APD). It is important to note that an eye with a unilateral optic nerve injury will demonstrate an APD, which can help verify the presence of traumatic optic neuropathy (TON). In the rare case of a bilateral TON (Fig. 5), a relative APD may not be seen if the injury is symmetric between the two sides, and both pupils may be dilated and nonreactive to light if the injury is profound. v. The variable degree of visual field defect. The funduscopic examination is a diagnostic tool that can be performed using a direct ophthalmoscope, indirect ophthalmoscope, or slit lamp biomicroscope.[1-4,18,19, 23-25]

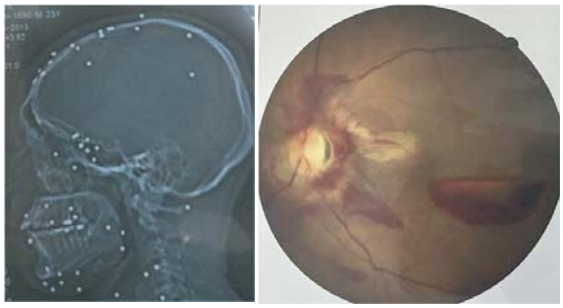

Figure 5: Direct Traumatic optic neuropathy in both eyes by a gunshot injury throughout the head- face & neck region. Figure 6: Colour fundus photography (CFP) shows partial Avulsion of the optic nerve with pre-retinal haemorrhage in the left eye.

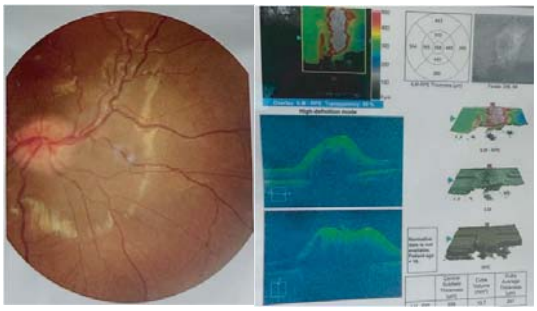

Figure 7: CFP of the left eye shows the optic disc swelling, and OCT macula shows the macular oedema in the same eye following a head trauma and vision was only perception light initially.

In cases of traumatic optic neuropathy (TON), where the injury is typically located in the posterior orbit or optic canal, the optic disc may often appear normal during the initial funduscopic examination. Optic nerve atrophy can develop 3-4 weeks after a traumatic event, causing the disc to become pale. Direct injuries to the optic nerve can also cause changes like an avulsed optic nerve head with haemorrhage (Fig. 6) or optic disc swelling with macular oedema (Fig. 7).[10,18,19]

Neuro-imaging studies

Neuroimaging is important for assessing suspected traumatic optic neuropathy (TON). In post-trauma cases, CT scanning (1 mm slice) is the most suitable method for displaying an optic canal fracture. This bony fragment has moved out of place, causing pressure on the optic nerve, a metallic foreign object in the orbit (Fig. 8), orbital emphysema, or a hematoma on the optic nerve sheath. MRI of the brain and orbit (Fig. 9) can

determine neurovascular haemorrhage or optic neuropathy causes. TON patients usually have optic nerve injury within the optic canal and normal anterior visual pathways on neuroimaging. A fracture in the area surrounding the optic canal can be observed.[1,2,25,26] A study by Bodanapally et al. found that hyperintensity of the optic nerve on diffusion-weighted imaging (DWI) due to diffusion restriction can aid in diagnosing traumatic optic neuropathy (TON).[27] Reddy et al. found that TON patients with intraconal or optic nerve hematoma on CT scans had poor visual acuity on admission.[28]

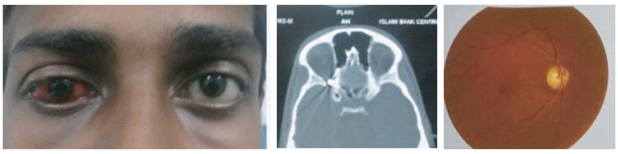

Figure 8: Direct Traumatic Optic neuropathy A. The CT scan of the orbit shows a round metallic foreign body (pellet) is impacted in the most posterior part of the right orbit. B. The patient's anterior segment was subconjunctival hemorrhage and a conjunctival entry wound at temporal aspect. Posterior segment shows normal study. C. The color fundus photograph shows the pallor of the optic disc after 6 weeks of injury. The patient's visual acuity was no-perception of light, but optic disc showed normal initially.

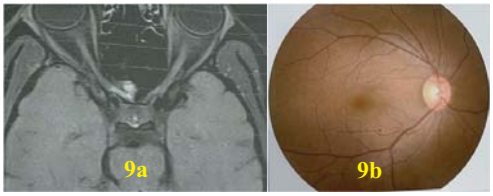

Figure 9: T1 weighted image of the MRI shows high intensity at distal part of the right optic nerve and adjacent ethmoid air cells. CSF intensity is not seen around the optic nerve. The MRI features suggestive of contusion of the right optic nerve along with tear of overlying dura matter due to fracture of right posterior ethmoid air cells. The CFP of the right eye shows normal appearance at presentation.

Other Tests:

Automated visual field perimetry is only possible for patients with adequate vision. Patients with poor visual acuity (<20/200) can be assessed with Goldmann perimetry or confrontational visual field testing.[29] No specific visual field loss pattern is diagnostic for TON, but dense central scotoma or hemianopia field defects may be seen.[30] Recovery can be tracked with serial visual field testing.[31]

Visual evoked potential (VEP) helps detect TON in unconscious or injured patients and monitors recovery. VEP is diagnostically useful for patients with nerve damage of unknown time, unreliable pupillary responses, and bilateral TON. Patients with better VEP responses have higher chances of vision recovery.[32,33] However, logistical difficulties limit its use. Flash VEP amplitude ratio >0.5 predicts a good outcome in unilateral TON. No VEP amplitude indicates little visual recovery.[34-36]

Retinal nerve fibre layer (NFL) imaging can assess and monitor axonal loss of the retinal NFL through scanning laser polarimetry and optical coherence tomography during the follow-up period.[26, 37,38]

Doppler Sonography Ultrasound Doppler has been advocated for assessing hemodynamic indices of TON patients' central retinal arteries. The TON eye is usually showing the reduction of peak systolic velocity (PSV), end-diastolic velocity (EDV), and time-average mean velocity (TAMX).[39,40]

Medical Treatment

The TON management controversy aside, no evidence supports any treatment option over observation.[1,25] The main treatment options for TON are: 1. Medical- Corticosteroids of varying doses and durations; 2. Surgical- Optic canal decompression, 3. Combination of Corticosteroids and optic canal decompression, 4. Only observation.[41-43] Indirect TON is expected to recover 50% visually with conservative management, where baseline VA predicts Outcome.[9, 44]

Steroids can be used alone or in combination with surgical optic nerve decompression, either preoperative, perioperatively, or postoperatively.[2] Steroid therapy for TON has not been extensively studied, and the available data supports the initial daily dose of steroid used; steroid regimes can be classified as (1) low dose (< 100 mg), (2) moderate dose (100–499 mg), (3) high dose (500–1999 mg), (4) very high dose (2000–5399 mg), or (5) megadose (> 5400 mg). The most used steroid protocol for TON involves a course of intravenous methylprednisolone in very high (1 gm per day) to megadose ranges.[1,2,10,45-47]

Steroids have been a common treatment for traumatic central nervous system injury since the early 1980s.[10] Animal models suggest they

protect neurons via antioxidants and inhibit infusion lipid peroxidation by free radicals.[45] Bracken and colleagues reported on high-dose methylprednisolone in NASCIS II (1990).[46] NASCIS II trials evaluated placebo, methylprednisolone, and naloxone on spinal cord injury patients. Administering methylprednisolone (30 mg/kg loading dose, followed by 5.4 mg/kg/h for 23 hours) within 8 hours of injury significantly improved motor and sensory function.[46,47] In NASCIS-III, administering steroids within 8 hours post-injury for 48 rather than 24 hours resulted in greater motor and functional recovery.[48]

Cochrane systematic review found only one RCT comparing high-dose IV steroids to placebo in patients with indirect TON diagnosed within seven days of injury.[49] As part of a clinical trial, 31 patients with 31 eyes were split into two groups. One group of 16 eyes was given 250 mg of intravenous methylprednisolone every six hours for three days, followed by 14 days of prednisolone at a dose of 1 mg/kg. The other group of 15 eyes received a placebo. The study reported no significant difference in visual acuity improvement between the two groups.[50] The final visual Outcome was not significantly different between the two groups, indicating that steroids did not have a significant therapeutic effect.[49,50]

The MRC-CRASH (Corticosteroid Randomization After Significant Head Injury) trial 2005 raised concerns about high-dose steroids in traumatic brain injury (TBI).[44,51] The use of steroids in traumatic brain injury was discontinued early due to a higher mortality rate in patients who received high-dose steroids (25.7%) compared to those who received placebos (22.3%) at six months follow-up. When managing TON with concurrent brain injury, consider the study's findings since the cause of the increased risk of death is unknown.[51,52] Spinal cord injury studies may not apply to traumatic optic neuropathy (TON) due to significant differences in histology. The optic nerve is pure white matter, while the spinal cord comprises grey and white matter. Repair mechanisms of optic nerve axons and spinal cord injuries may differ significantly.[6,53,50]The International Optic Nerve Trauma Study (IONTS) study compared visual outcomes for patients with traumatic optic neuropathy treated with observation, systemic steroids, or optic canal decompression. In 1999, 133 patients were treated within a week of their traumatic event. Most were given corticosteroids (n=85) or underwent surgical optic canal decompression (n=33). After surgery, 32% of patients had improved visual acuity by over three lines. Increases were 52% and 57% for those treated with corticosteroids and under observation, respectively. However, the study was not randomized or controlled and had limited statistical power due to a small observation group (n=9).[1] No clear link was found between higher steroid doses or earlier treatment initiation and improved visual recovery rates. Although some case series suggest better improvement rates with steroids, most published figures are like IONTS (44-62%).[18,23, 54,55]

Currently, there is no evidence to support the use of corticosteroids as a therapeutic option for TON management. If considering steroids for TON, avoid use with concomitant traumatic brain injury or in patients presenting eight or more hours after injury. The literature does not clearly define whether clinicians should use mega doses or lower doses of steroids for selected cases of TON. The NASCIS studies used high-dose steroids to show benefits in some patients, but the CRASH study found serious complications in trauma cases. Animal studies have shown that increasing doses of steroids can lead to the death of retinal ganglion cells.[6,56-58]

According to the study, a high-dose intravenous methylprednisolone (1 g/day) had a significant positive impact on the final visual acuity. The results showed a p-value of 0.013, indicating a strong level of statistical significance. The study found that the duration between the injury and the start of treatment was a crucial factor affecting the outcome of treatment in patients with traumatic optic neuropathy. Specifically, 61.9% of patients who received treatment within the first seven days of injury showed improvement in their vision. Among the patients who were presented between 8 days and 1 month after injury, 21% improved their vision with treatment. Finally, 10.2% of patients who received treatment after one month of injury experienced an improvement in their vision due to traumatic optic neuropathy.[17] A maximum daily dose of 1 g of intravenous methylprednisolone has been recommended for managing TON to reduce the risk of neurotoxicity.[59]

A recent study conducted on 42 patients with maxillofacial trauma and traumatic optic neuropathy (TON) has found that administering high doses of intravenous methylprednisolone within three days of TON diagnosis, along with optic nerve decompression surgery, leads to better improvement rates. According to the study, the initial visual acuity and receiving treatment within seven days of injury were the most significant factors in achieving better outcomes.[60]

In a study of 21 patients with traumatic optic neuropathy (TON), 8 received dexamethasone and 13 received methylprednisolone. 7 out of 9 patients in the dexamethasone group and 12 out of 13 patients in the methylprednisolone group experienced improved vision.[61]

Erythropoietin can be used in the treatment of indirect traumatic optic neuropathy as an adjunctive modality with steroids. In a 2011 pilot study, seven patients with indirect TON were treated with intravenous injections of 10,000 IU erythropoietin (EPO) per day for three days and compared to 8 patients who received no treatment.[62] In Another study on Traumatic Optic Neuropathy Treatment Trial (TONTT), 120 patients underwent treatment with EPO, methylprednisolone, or observation.[59] The final visual acuity and colour vision was significantly improved in the EPO group, suggesting that EPO may be a safe and effective treatment for TON.[62,63] Although the chances of complications arising from steroid and EPO treatment are low, it is still unclear whether these drugs provide any advantages in improving VA among individuals with TON since there is no conclusive evidence to support this assertion. Based on EPO studies, it has been reported that temporary hypotension can pose a risk to patients who are unstable and have multiple traumas.[62]

Experimental Treatment Modalities

New approaches for the treatment of traumatic optic neuropathy were investigated in a study. The study explored whether inhibiting TNFá and therapeutic hypothermia could help to retain retinal ganglion cells (RGCs) in an optic nerve crush (ONC) model and a novel animal model for TON.[64]

Glutamate binds to NMDA receptors and is responsible for excitatory signaling in the nervous system. Experimental mouse models of TON suggest that blocking NMDA receptors[65] with memantine, phenytoin, and dizocilpine (MK801) can protect RGCs.[66,67] Dexanabinol (HU-211), a cannabinoid and NMDA receptor antagonist, has shown potential clinical implications by reducing degeneration and promoting regeneration in rat optic nerves.[68] Traxoprodil reduced mortality by 7% compared to placebo ($p = 0.08$) in a randomized study.[69]

Crystallin is an anti-inflammatory and anti-shock protein. In mice, á-crystallin treatment suppresses expression of TNF-á and iNOS induced by optic nerve injury.[70] Additionally, it promotes axonal regeneration.[71]

Mito therapy, which involves transplanting external mitochondria, has shown promise in mitigating neurological disease progression. Studies have found that it can improve oxidative metabolism and electrical activity in the retina one day after transplantation, increase axonal extension of injured neurons after 28 days, and enhance RGC survival after 14 days.[72,73]

Naringenin, a bioflavonoid in citrus fruits, inhibits JUN phosphorylation in cultured cells and increases RGC survival after TON in mice with optic nerve crush injury.[74,75]

Surgery

Surgery is an alternative to observation and high-dose corticosteroid therapy for TON. It involves removing structures around the optic nerve to relieve compression and alleviate ischemia. Surgery is typically performed by an otolaryngologist or neurosurgeon, using either an intranasal endoscopic or transcranial approach. Results could be better if performed more than two weeks after the injury.[43] Surgery is not proven to be a better option for indirect TON and was not beneficial for TON in The International Optic Nerve Trauma Study.[1]Patients with vision loss and a bone fragment on the optic nerve are ideal for surgery.A study reported that children with indirect TON and residual vision had better improvement rates following endoscopic trans-ethmo-sphenoid optic canal decompression (ETOCD), with rates of 69.7% compared to 37.9% for those with no light perception.Direct optic nerve injuries usually don't improve.[6]Complications that can occur after decompression surgery for TON include infection (such as meningitis), CSF leaks, and worsening of

traumatic optic neuropathy. In addition, if high or "mega" dose steroids are used, there is a risk of wound infection, a range of systemic adverse effects (such as GI bleeding), and an increased risk of death.[1]Observation alone is just as effective as surgery in improving the prognosis, and to date, surgery has not been proven to provide any additional benefits.

Prognosis

According to the International Optic Nerve Trauma Study, the prognosis for optic nerve injury highly depends on the damage's extent.[1] Patients with no light perception (NLP) vision had a lower chance of improvement than those with better vision. The study showed that visual acuity improvement of >3 lines on the Snellen chart was seen in 57% of the untreated observation group, 52% of the corticosteroid steroid group, and 32% of the surgery group. However, studies showed that up to 50% of patients with TON can have some improvement in vision, with or without treatment, although most of the time, improvement is minimal.[1,9,31,54,55]Research has found that concomitant orbital fractures in TON cases can lead to more significant visual impairment. A specific study found that up to 85% of patients (29 out of 34) with an orbital fracture presented with NLP.[76,77] An orbital fracture can injure the optic nerve more severely due to increased force transmission to the optic canal.[76] Good visual acuity is the most significant factor in predicting recovery among patients with traumatic optic neuropathy (TON). It is crucial to ensure that patients with TON receive timely and appropriate treatment to optimize visual outcomes.[78]

Conclusion

Traumatic optic neuropathy (TON) can result in permanent vision loss especially in young male patients who have suffered from ocular or head trauma. Neuroimaging must be done if the condition is suspected when an afferent pupillary defect is detected despite an intact globe and clear media. Poor initial visual acuity and intracranial injuries are predicting poor final visual outcomes. However, if intracranial injury is ruled out, high-dose intravenous steroid treatment can improve the final visual outcome in patients with traumatic optic neuropathy. Erythropoietin (EPO) may be effective in some cases; surgical decompression is also not a recommended treatment option in TON. It is important to discuss treatment options for potential benefits and risks with the patient and their family to make an informed decision.

Declaration of interest

The authors disclose no conflicts of interest and take full responsibility for the content and writing of this article.

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