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Traumatic Optic Neuropathy: A Review

Authors
Dr Prabha Gupta MS[1], Dr Abha Shukla MS[2], Dr Rashmi Kujur[3]
[1]Senior Resident, Dept of Ophthalmology, Gajra Raja Medical College Gwalior, Madhya Pradesh, India
[2,3]Assistant Professor, Dept of Ophthalmology, Gajra Raja Medical College Gwalior, Madhya Pradesh, India
Corresponding Author
Dr Prabha Gupta
Senior Resident Dept of Ophthalmology, Gajra Raja Medical College Gwalior, Madhya Pradesh, India
Email: *drprabhagupta@gmail.com*

Abstract
Traumatic optic neuropathy (TON) is acute optic nerve injury secondary to ocular or head trauma which can lead to variable amount of visual loss. An effective management for traumatic optic neuropathy is still a challenge for an ophthalmologist. In majority of cases with poor prognostic factors, the visual outcomes may not be good once the diagnosis of TON has been made. There were several trials in past which were able to generate some evidence which guided the use of steroids, surgery or observation in TON. Though surgery, corticosteroids and conservative supportive management forms the mainstay of treatment for TON but there is inadequate evidence from clinical trials to support any specific treatment. Recent evidence also suggests a possible detrimental effect of steroids in TON. Each case therefore needs to be assessed on an individual basis and patient should be counselled before embarking on any mode of treatment.
Key Words: *Traumatic optic neuropathy, ocular trauma, optic neuropathy.*

Background

Traumatic optic neuropathy (TON) is acute optic nerve injury secondary to ocular or head trauma which can lead to variable amount of visual loss. Though the visual loss caused by traumatic optic neuropathy is quite variable and a significant number of patients are left with "light perception" or "no light perception" making it a significant cause of permanent visual loss.

Direct TON result from an anatomical disruption of optic nerve fibres by penetrating orbital trauma, compression of optic nerve secondary to orbital and optic canal fracture or hematoma of nerve sheath. In contrast the indirect TON results from transmission of shearing forces to the optic nerve, concentrated at the optic canal without disruption of anatomical structures around the optic nerve. Initially there is compression of the superior orbital rim, which is transferred to the orbital roof and then to the optic canal where the optic nerve is fixed and is more vulnerable to damage. The shearing injury to the axons and microvasculature leads to TON[1].

Incidence

The incidence of TON varies between 0.5 – 5% in settings of closed traumatic head injury[2,3]. There is male preponderance (85%) with mean age of presentation being 34 years.

Aetiology

Below mentioned are the common causes of TON:

1. Road traffic accidents involving Motor and bicycle accidents are the most frequent causes.
2. Other causes with frontal bone impact by assault, stab wounds, gun shot, skateboar-ding, bottle-cork injuries, seemingly trivial injuries, and endoscopic sinus surgery.
3. Self-inflicted avulsion of the optic nerve or Oedipism

Indirect optic nerve injury within the optic canal is referred to as intracanalicular injury which is the most common site for TON. The intracranial optic nerve is the next most common site of injury, followed by injuries that also involve the chiasm.[4]

Pathogenesis

Optic nerve injury results in both mechanical and ischemic insult. Laser interferometry studies suggest forces applied to the frontal bone are transferred and concentrated in the optic canal. Deceleration forces loaded into the facial bones, over milliseconds elastically deform the sphenoid bone, causing direct transfer of force into the intracanalicular region of optic nerve, where optic nerve is tightly bound, causing contusion necrosis of the nerve by disrupting axons and vasculature resulting in TON. The intracranial course of optic nerve can also be injured against the falciformdural fold at the moment of impact.

Injury mechanisms are classified into primary and secondary mechanism.

Primary Mechanisms: Permanent injury to the optic nerve occur at the moment of impact

Primary injury occur from mechanical shearing of optic nerve axons and vasculature causing damage to the micro-circulation.

Secondary mechanisms: Injury to the optic nerve occur subsequent to the force of impact

Secondary injury occur due to disturbances of cellular homeostasis adjacent to areas of irreversible optic nerve damage, diverse and interrelated mechanisms operate which lead to loss of axons which had survived the original insult. Intervention has potential to salvage the axons that survived the initial insult.[5,6]

The proposed mechanisms of injury are:

1. Ischemia and reperfusion injury – Partial ischemia followed by reperfusion of these transiently ischemic regions leads to peroxidation of cell membrane lipids leading to generation of oxygen free radicals which cause tissue damage.
2. Bradykinin: Bradykinin activation following trauma causes release of arachidonic acid from nerve cells. The prostaglandins derived from arachidonic acid metabolism along with free radicals and lipid peroxide leads to optic canal edema which may further aggravates the ischemia at the cellular level
3. Calcium ions: Calcium ions enter intracellular compartment following optic nerve ischemia which then acts as a metabolic toxin and leads to cell death.
4. Cell mediated mechanisms: Following trauma, Polymorphonuclear cells predominate in the initial 48hrs, which are then replaced by macrophages in 5-7 days. Macrophages leads to delayed tissue damage, demyelination and gliosis.[5]

Presentation

Clinical presentation of TON is quite variable with varying degree of severity.

- Ocular Involvement can be unilateral or bilateral
- Variable loss of visual acuity- Varies mainly between 20/200 to no light perception. Recent reports suggests even milder vision loss in TON.[7]
- Color vision impairment;
- Relative afferent papillary defect
- In patients who retain adequate visual acuity, there could be variable visual field defects. Goldmannperimetry or with

confrontational visual field testing can be used for patients with poor visual acuity (worse than 20/200) .Though no visual field loss pattern is pathognomonic, a dense central scotoma is characteristic for traumatic optic neuropathy (TON). Serial visual field testing can be used to document any recovery in optic nerve function.

- An optic disc appearance that will depend on the anatomical site of injury. Fundus may vary according to the site of insult in relation to the origin of central retinal vessels, at presentation fundus may appear normal. Posterior injuries may lead to disc edema due tohemorrhagesin nerve sheath whereas anterior injuries lead to venous obstruction and traumatic AION. Findings like commotio retinae and choroidal rupture may also be present.
- Development of optic atrophy- Disc pallor usually takes about 3-4 weeks to develop and may not be the initial presentation.

Neuroimaging studies

Computed Tomography or magnetic resonance imaging are important tools to evaluate a case of suspected TON. Computed Tomography is the preferred modality to look for fracture in optic canal, impingement of displaced bony fragment upon the optic nerve, hematoma of optic nerve sheath, orbital emphysema in the post trauma setting. Cranial and an orbital MRI may be useful in delineating the extent of hemorrhage involving the neurovascular structures at the orbital apex or to rule out inflammatory or infiltrative causes for an optic neuropathy.

Visual evoked potentials (VEP) can be helpful to document the presence of TON in unresponsive patients or in cases with concomitant ocular injuries, though in few it may not be possible to shift the patients to electrophysiological labs in case of polytrauma. Serial VEP examinations on follow-ups can be useful in documenting recovery of function when clinical parameters are equivocal. A flash VEP amplitude ratio (affected side/normal side) greater than 0.5 is predictive of a favourable, long-term visual outcome in unilateral cases of TON. Visual recovery is considered unlikely when VEP amplitudes are not recordable.[8]

Poor prognostic factors in patients with TON

- No light perception at presentation
- Loss of consciousness
- Lack of visual recovery after 48 hours
- Presence of an optic canal fracture and intracanalicular hematoma
- RAPD more than 2.1 log units when measured with neutral density filters[7]
- Absent responses on VEP. (flash VEP amplitude ratio > 0.5 has favourable outcome)[8]

Management-

Patients with TON may require a multi-disciplinary management approach. Patients with head injury requires trauma physician, head and neck surgeon, ophthalmologists and neurosur-geons. An effective management for traumatic optic neuropathy is still a challenge for an ophthalmologist. In majority of cases with poor prognostic factors, the visual outcomes may not be good once the diagnosis of TON has been made.

Treatment options for indirect traumatic optic neuropathy

Steroids, Optic canal decompression and sometimes observation alone may be the mainstay of treatment in cases of indirect traumatic optic neuropathy. There are multiple school of thoughts with respect to best treatment options for a patient but there is not much evidence to prove or disapprove the same.

In 1982, Anderson popularised the use of corticosteroids for TON based on reports that high doses of intravenous corticosteroids [intravenous methylprednisolone (IVMP) 15-30 mg/kg] improves microcirculation, energy metabolism, post-injury histology and functional outcomes in

animal models of spinal cord injury[9-11]. Post this; it became handy for ophthalmologist to offer corticosteroids for their patients without much evidence of benefit.

The possible mechanism of action by which the corticosteroids may be helpful in case of CNS injuries are membrane stabilization (reduction of extracellular edema), anti-inflammatory, antiox-idant and proposed neuroprotective mechanisms. The dose of steroid used is quitevariable in previous studies: moderate dose (60-100mg of oral prednisolone), high dose (1 gram of intravenous methylprednisolone/day), or mega dose (30 mg/kg loading dose of intravenous methylprednisolone, followed by 5.4 mg/kg/h for 24 hours). [4]

There were several trials in past which were able to generate some evidence which guided the use of steroids, surgery or observation in TON. In 1990, Bracken and colleagues published their findings of Multicentre, prospective, National Acute Spinal Cord Injury Study 2 (NASCIS 2) randomized trial where the use of mega dose corticosteroid therapy (4200mg/day) administered during the 1st 8 hours after injury, resulted in improved long term function both motor and sensory(motor>sensory) when compared to placebo. However patients treated with steroids more than 8 hours after injury had a worse neurological outcome (both sensory and motor). The findings of the NASCIS trials significantly influenced clinical practice and led to an increased use of steroids in treating TON. However, the clinical improvement was modest in these studies, and concern existed that the clinical benefit demonstrated for those patients treated in the first eight hours with mega dose steroids was the result of a statistical bias.[12]

In 2005 multicentric, randomized, placebo-controlled, The Corticosteroid Randomization After Significant Head Injury (CRASH trial) [13] raised concerns regarding the use of mega dose steroids (high-dose methylprednisolone (30 mg/kg loading followed by an infusion of 5.4 mg/kg per hour) for 48 hours within 8 hours of trauma) in traumatic brain injury because of higher risk of death in patients that received mega dose of steroid, and no motor or sensory improvement was noted in the patients who survived at their 6-month follow-up when compared with the placebo group.

The contradictory results of the above two studies were ascribed to important histologic distinctions between the spinal cord and optic nerve. Optic nerve consists of axons which are structurally similar to the white matter and thus more comparable to cerebral tissue whereas Spinal cord contains both grey (motor) and white matter (sensory). Hence there is a significant biologic differences exist between the repair mechanisms of the optic nerve axons and spinal cordaons. NASCIS trials also showed more improvement in the motor as compared to the sensory counterpart which was not seen in the CRASH trial.

In 1999, the International Optic Nerve Trauma Study (IONTS)[14] assessed the benefit for visual outcome of corticosteroid treatment (n=85) or optic canal decompression surgery (n=33) versus observation (n=9) in patients with TON within 7 days of traumatic event in a nonrandomized intervention including 133 study subjects. Follow-up results could not demonstrated any benefit with corticosteroid therapy or surgical decompression when compared to observation alone

In an experimental trial in which rats were treated with various regimes of methylprednisolone compared with sham controls following an optic nerve crush injury showed axonal loss and a significant dose-dependent decline in axonal counts with increasing doses of steroids, concluding that steroids can exert a negative effect on ganglion cell survival, especially at higher, mega dose levels, by suppressing endogenous neuroprotective pathways.[15,16]

Cochrane review [4] suggested relatively high rate of spontaneous visual recovery in traumatic optic neuropathy and there is no convincing evidence that steroids provide any additional benefit over conservative management.

Thus each case needs to be assessed on an individual basis and the patient needs to be counselled regarding the theoretical risks suggested by recent studies, and the risk of serious adverse reaction to steroids. It is unclear from the current evidence, whether additional RCTs looking at a very high dose or mega dose steroids would be ethical.

Surgical treatment

Based on the presumption that optic nerve swelling following trauma would compromise the blood supply to the optic nerve and further aggravate the ischaemic damage to the nerve, optic canal decompression surgery was suggested by few as treatment of TON. Surgical decompression of optic nerve at the site of injury, which is often the intracanalicular segment is thought to help reduce optic nerve compression and subsequent vascular compromise that may occur as a result of the indirect injury. Surgery has also been done to remove bone fragments that may be impinging on the optic nerve within the optic canal. Fukado et al in the largest series of 400 cases had suggested good results in optic canal decompressive surgery[17]. Optic nerve decompression remains useful as a salvage procedure in conventional dose steroid failed cases of TON. However, no randomized, controlled studies have been performed to evaluate the role of surgery in TON. As mentioned earlier, IONTS has not shown any convincing evidence that surgical decompression of the optic canal in TON is superior to observation or corticosteroid therapy.

Additionally, in cases in which bony fragments are impinging on the optic nerve within the canal, the prognosis of visual recovery is extremely poor because the bony fragments are more likely to have anatomically disrupted the optic nerve axons, leading to irreversible visual loss and the risk of possible surgical complications such as cerebrospinal fluid leak or postoperative bleeding cannot be ignored.[18]

Observation alone

The rate of reported spontaneous visual improvement for untreated cases of TON has ranged from 0% to 67%, with baseline visual acuity being the most important predictor of final outcome[19,20]. But the natural history of untreated TON and the rate of spontaneous visual recovery is a matter of concern. There is a relatively high rate of spontaneous visual recovery in TON and there is no convincing data that steroids provide any additional visual benefit over observation alone.

In summary

Though surgery, corticosteroids and conservative supportive management forms the mainstay of treatment for TON but there is inadequate evidence from clinical trials to support any specific treatment. Recent evidence also suggests a possible detrimental effect of steroids in TON. Each case therefore needs to be assessed on an individual basis and patient should be counselled before initiating on any mode of treatment. The families of such patients should be taken into confidence and the role and efficacy of each treatment modality should be discussed with them.

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