

Controversies in neuro-ophthalmology: Steroid therapy for traumatic optic neuropathy

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Background: There is an increase in the incidence of traumatic optic neuropathy (TON) due to increasing urbanization and rapid spurt in the number of motor vehicles on the road. Despite early presentation and ease of diagnosis the visual outcomes in TON are still limited. There is also significant confusion about the timing, dose and efficacy of steroid treatment in its management. **Purpose:** To provide a clinical update of the pros and cons of steroid therapy for TON. **Design:** The paper is a retrospective review of the currently available literature in the English language indexed in PubMed. **Methods:** A PubMed search was conducted by the authors using the following terms: Traumatic optic neuropathy, megadose, steroids, methylprednisolone. Relevant original articles, review articles, and case reports related to the topic of discussion were evaluated and discussed in the paper. **Results:** There is no prospective randomized control trial evaluating the effect of steroids in TON. There are varying reports on the effect of steroid therapy from significant improvement to no difference compared to observation. **Conclusion:** The decision to give steroids to patients with TON has to be on an individual case to case basis and must involve informed consent from the patient. There are documented advantages and disadvantages of steroid therapy and a prospective, randomized, controlled trial is necessary comparing steroids, surgery and observation before definitive management can be evolved.

Key words: Megadose, methylprednisolone, steroids, traumatic optic neuropathy

Traumatic optic neuropathy (TON) refers to an acute injury of the optic nerve secondary to trauma. In the presence of history of nonpenetrating trauma to the forehead or malar region, subconjunctival hemorrhage, a relative afferent pupillary defect in unilateral cases and a normal fundus in the early posttraumatic period, the diagnosis can be made with relative ease. There may be associated injury to the orbital/facial bones but severe signs of blunt trauma to the eye are uncommon often only sign of injury being subconjunctival hemorrhage.^[1] It is most commonly seen in young adult males in the setting of a road traffic accident or an alleged assault.^[2] However, it is the management that is controversial. In this manuscript, we examine the factors that make therapeutic decision making in TON so difficult and focus on the controversies regarding use of steroids for treatment.

Anatomy and Pathophysiology

Currently two basic mechanisms for TON are understood. Direct mechanical injury to the optic nerve causing a tear or interruption of the nerve which has a worse prognosis. Indirect injury is a closed injury causing a reactionary edema in the nerve sheath which can compromise the vascular supply and neurotrophic supply of the ganglion cells by compressing the nerve in the tightly packed optic canal. In both these processes,

there is retrograde degeneration of the ganglion cells which are irreversibly lost.

The optic nerve is surrounded by pia, arachnoid, and dura mater which move along with the optic nerve during normal eye movements. At the entry to the optic canal, the optic nerve sheath fuses with the sphenoid periosteum and at the posterior foramen with an overlying falciform fold of dura. Therefore, the nerve and its sheath are tightly fixed to the bony canal within a confined space.

In indirect TON cases, optic nerve injury results from shearing forces to the fibers or to the vessels supplying the nerve. Cadaveric skull studies have demonstrated that if a force is given at the frontal bone or malar eminences they are concentrated and transferred to the optic canal. As the dural sheath is tightly adhered to the periosteum inside the optic canal this force is transferred to the nerve. Such injury leads to ischemic injury to the retinal ganglion cells within the optic canal followed by optic nerve swelling. This increases the intraluminal pressure of the canal further exacerbating retinal ganglion cell degeneration and compromises the vascular blood supply.

Treatment

Therapeutic options for TON revolve around minimizing the damage by stemming the above mechanisms.^[3] The basic concept is to decompress the nerve by either decreasing the edema by steroid therapy or creating more space by surgical decompression. The controversy in therapy of TON primarily stems from two facts. Firstly, literature lacks a well-executed randomized controlled clinical trial, due to both the relative difficulty in recruitment of adequate numbers and the highly heterogeneous presentation of such patients. The second reason is the unpredictable yet frequent incidence of spontaneous recovery.

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Steroid therapy in TON has been examined in multiple case series, mostly nonrandomized, unblinded and without controls.^[4,5] The doses used in these trials can be categorized as follows: Moderate dose (60–100 mg of oral prednisolone), high dose (1 g of intravenous [IV] methylprednisolone/day), or megadose (30 mg/kg loading dose of IV methylprednisolone, followed by 5.4 mg/kg/h for 24 h). The expected role of steroids has been in reducing inflammation and edema in the closed confines of the optic canal thereby preventing secondary compressive damage and providing neuroprotection by virtue of preventing free radical induced lipid peroxidation.

The initial concept of the role of steroids was derived from the National Acute Spinal Cord Injury Study 2.^[6] This was a multicenter clinical trial evaluating the role of steroids in patients with acute brain and spinal cord injury. The study evaluated the role of placebo, methylprednisolone, or naloxone in the outcome of these cases. The results showed that methylprednisolone (30 mg/kg loading dose, followed by 5.4 mg/kg/h for 24 h) started within 8 h of injury resulted in a significant improvement in neurological outcome compared with placebo. This fuelled an increasing role of IV steroids in the treatment of TON. Several studies though mostly retrospective have shown that patients with both conventional or megadose steroids have a greater likelihood of improvement in vision compared to natural recovery.^[7,8]

Subsequently the Corticosteroid Randomization After Significant Head injury trial was a large randomized placebo controlled study evaluating the role of megadose of steroids in traumatic brain injury compared to placebo.^[9] This study had to be stopped early due to the significantly increased risk of death in patients that received megadose steroids compared with the placebo group. The important difference with the previous study was the presence of significant head injury in these patients.

Due to the widely differing results of these two major studies and the histological differences between the spinal cord and optic nerve there are concerns about extrapolating data from spinal cord injury studies to TON.

The International Optic Nerve Trauma study was a comparative nonrandomized interventional study with concurrent treatment groups involving 133 enrolled patients.^[10] The study included patients who had an initial visual assessment within 3 days of injury and were willing for at least 1 month of follow-up. On the basis of treatment received within 7 days of injury, patients with unilateral injuries were categorized as being in one of three treatment groups: Untreated ($n = 9$), corticosteroid ($n = 85$), or optic canal decompression surgery ($n = 33$). The study found no difference between steroid therapy as against surgical or no intervention with 52% who received steroids showing visual improvement of three or more lines versus 57% in the observation group. The medical treatment included five levels of therapy ranging from low dose (<100 mg methylprednisolone/day), moderate dose (100–499 mg/day), high dose (500–1999 mg/day), very high dose (2000–5399 mg/day), and megadose (>5400 mg/day). The study concluded that neither the dosage nor the timing of steroid therapy had an effect on visual recovery. Several other authors have concurred with these results.^[11,12] While no animal study has demonstrated any beneficial effect of

steroid treatment, a dose dependent decrease in axons with increasing dose of steroids indicating negative impact of high doses of steroids on the injured optic nerve axon has been demonstrated.^[13,14] Moreover, megadose IV steroids are not without side effects including steroid psychosis, immunosuppression and impaired glucose metabolism.

Conclusion

There has been no large prospective placebo controlled trial evaluating the role of steroids for the treatment of TON and studies done till date show no convincing data that steroids provide additional benefit. While there is a relatively high rate of spontaneous visual recovery reported, anecdotal reports and case series have shown good outcomes with various doses of steroids. Current evidence definitely indicates that cases with concomitant brain injury may have poorer neurological outcomes with megadose steroids. Also in the presence of optic nerve transection or avulsion there is no advantage of treatment. Rationale of the use of lower doses of steroids for their anti-inflammatory effect is though unsubstantiated can be considered safe in cases with isolated TON. In these cases, presenting with significant visual loss, having a definite lucid interval, that is, time between injury and loss of vision and those presenting within 8 h of the injury, high dose steroids may be offered. Each case therefore needs to be assessed on an individual basis and proper informed consent is essential before initiating IV steroids in TON.

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