Introduction

The effects that trauma to the head have on the optic nerve and the possibility of development of traumatic optic neuropathy (TON) have long been known and reported for nearly 70 years. Despite this, precise diagnosis of TON and determination of its prognosis are still often difficult to make. Both pathophysiology and prognosis are not fully understood and therefore management strategies remain controversial. Consequently, the term traumatic optic neuropathy has become a generic term, which is given to a spectrum of all injuries to the optic nerve which have resulted following trauma. It has become a diagnosis of exclusion, when no other cause for visual impairment can be found.

TON may be classified as either direct – where there is damage to the nerve directly (either by a crush injury, penetrating object, or from secondary local effects such as haemorrhage into the nerve itself), or indirect, where forces are transmitted to the optic nerve resulting in ganglionic cell death. Both of these may result in damage to the optic nerve, either within the optic foramen or along its pathway to the cortex.

Patients presenting with TON may present to many different specialties.
involved in the management of head and neck trauma\textsuperscript{4}. In the presence of co-existing and more serious injuries, or if the patient is unconscious, its presence may not be immediately apparent (or considered) and can be easily overlooked. Therefore an understanding of at-risk mechanisms, presenting features, diagnostic tests, investigations and management is important for us all and not just for the ophthalmology team.

**Epidemiology**

A recent study in the United Kingdom estimated the prevalence of TON to be approximately 1 per 1 million population\textsuperscript{4}. Whilst this gives a good estimation of the actual burden of TON across a population, there is little reported on the likelihood of developing TON following head injury. A large retrospective study found a significant association with nasoethmoid fractures, but no significant correlation with the presence of zygomatic or maxillary fractures\textsuperscript{5}. It has been proposed that in the absence of a fracture, kinetic energy is transmitted via the bony structures of the face and is transmitted to the optic foramen causing injury\textsuperscript{6}. If a fracture is present then a lot of the energy is absorbed at the site of the fracture. Interestingly, Hippocrates noted the association between blunt trauma to the forehead and loss of vision, in the absence of fracture\textsuperscript{7}, although the precise mechanism of this relationship was unknown. At present, there is no data on how medical risk factors, such as hypertension, impact the chance of developing TON.

One study in Canada showed that 0.4\% of patients admitted to a trauma centre following a traumatic injury had evidence of TON. In those patients presenting specifically with head trauma, the incidence was 2.3\%. All patients found to have TON had some evidence of head injury. Case series relating to traumatic head injuries report incidences in similar patients ranging between 0.7 and 2.5\%\textsuperscript{8,9}. Male patients make up the majority of those with TON and the most common mechanisms of injury are motor vehicle collisions (MVC), assaults in younger age groups and falls in the older age groups\textsuperscript{4}. Despite MVC’s being the most common cause of TON, falls are associated with a higher risk of its development (0.7\% vs. 0.4\%)\textsuperscript{5}.

**Pathophysiology**

Pathophysiology of TON includes primary and secondary mechanisms of injury:

1. Primary injuries to the optic nerve result in shearing of the nerve axons\textsuperscript{6}. At a cellular level, animal models have shown that the ganglion cell axons are the site of injury when there is
transection or a crush injury to the optic nerve\textsuperscript{10}.

2. Secondary injuries are thought to be due to swelling and vasospasm causing compression and ischaemia\textsuperscript{11}. Animal models demonstrating this have shown that following a primary injury there is delayed axonal loss, likely related to apoptosis\textsuperscript{12}.

Direct trauma to the optic nerve can cause a primary injury to the optic nerve as a result of crushing of the nerve, transection, or avulsion (where the nerve is forcibly separated from the globe). Direct trauma to the nerve can also cause a secondary injury. There may be haemorrhage within the damaged nerve or within the orbit. This can lead to Orbital Compartment Syndrome (OCS). OCS occurs where there is an increase in the contents of the orbit (usually blood or air) which exceeds the natural capacity of the orbit to compensate (via compression of the orbital fat and anterior movement of the globe). This subsequently causes a rise in pressure which exceeds the pressure of the blood within the peripapillary capillaries, preventing flow and leading to ischaemia of the optic nerve\textsuperscript{13}. Occasionally, pressure from air, leaked through a valve-like fracture of the paranasal sinuses can increase the intraorbital pressure and cause optic nerve damage via the same mechanism\textsuperscript{3}.

Significant swelling within the optic nerve as it passes through an intact foramen can also effectively result in a compartment syndrome type effect within the nerve.

In indirect TON, there is no primary injury to the optic nerve, but secondary injury is thought to occur as a result of forces transmitted to the optic canal, particularly following trauma to the frontal bone\textsuperscript{6}. Within the optic nerve pathway, there are thicker areas of bone, which encase and protect the nerve. However in high energy impacts these can fracture and injure the nerve. There are also thinner areas of bone such as the sphenoid, which deform and compress the optic nerve leading to damage to both the axons and vasculature\textsuperscript{6}.

**Clinical Features**

TON can only be diagnosed in the context of a recent history of trauma. It may be unilateral or bilateral. Clinical features can be difficult to assess in the acute period, because of the presence of other ocular or periorbital injuries. However, in the immediate period following injury the following can often be seen:

1. Impaired vision - the incidence of patients with TON presenting with no light perception (NLP) is between 36 and 78%. The majority of patients have
vision of 6/60 Snellen or worse\textsuperscript{4,14}. (See table 1)

2. A relative afferent pupillary defect (RAPD) unless both eyes are involved. Both pupils should respond equally to a bright light shone into either eye. If a pupil fails to constrict or dilates in response to light shone into either it or the fellow eye, this indicates the presence of an RAPD. This relies on their being a difference in the reactions of the two pupils so if both eyes are equally affected, an RAPD will not be present.

3. Impaired colour vision. Colour vision is an extremely sensitive test for damage to the optic nerve. It is often affected more severely than visual acuity. This is in contrast to macular or retinal pathologies in which colour vision is relatively preserved\textsuperscript{15}

4. Visual field deficits - these are variable and there is no characteristic pattern.

The following table (Table 1) demonstrates visual acuity measurements (poorest vision to best). This is measured in metres, i.e. a normal person can see the 6/60 letter at 60 meters away where as a person with 6/60 vision can only read that letter from a distance of 6 metres. (* = In the United Kingdom)

<table>
<thead>
<tr>
<th>No Light Perception (NLP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Perception (LP)</td>
</tr>
<tr>
<td>Hand Movements (HM)</td>
</tr>
<tr>
<td>Counting Fingers (CF)</td>
</tr>
<tr>
<td>6/60</td>
</tr>
<tr>
<td>6/36</td>
</tr>
<tr>
<td>6/24</td>
</tr>
<tr>
<td>6/18</td>
</tr>
<tr>
<td>6/12</td>
</tr>
<tr>
<td>Driving standard*</td>
</tr>
<tr>
<td>6/9</td>
</tr>
<tr>
<td>6/6</td>
</tr>
<tr>
<td>Normal visual acuity</td>
</tr>
<tr>
<td>6/5</td>
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</tbody>
</table>

Table 1

Fundoscopic examination of the optic nerve may reveal features which are consistent with the cause of the neuropathy e.g. avulsion or optic nerve haemorrhage.

Examination of the unconscious patient is difficult. The single most important finding for the diagnosis of TON in these patients is the presence of an RAPD. This can still be recognised in the unconscious patient. However care must be taken in those on opiate analgesics as these generally constrict the pupil (miosis) and can make identification difficult. Other relevant agents which can cause miosis include
some antiemetics such as domperidone, physostigmine and antipsychotics such as haloperidol. Fundus assessment can be performed on the unconscious patient with the use of mydriatic drops if required once the presence or absence of an RAPD has been elicited. Mydriatic agents should however be used with caution in patients with head injury as pupil reactions are an important component of neurological observations. Any agents used should be documented in the notes, including time of instillation and discussed with staff monitoring the patient. If fundus assessment is not critical to the patient, mydriatic agents can be delayed until the patient is neurologically stable. Investigations and imaging (see below) are likely to be of more value in such patients.

Following injury, there may be progressive changes in the visual acuity. These can worsen as a result of secondary injury as previously described. In principle, these changes are preventable and many therapeutic approaches are aimed at reducing oedema and swelling and maximising perfusion (analogous to the management of head injuries). If there is no reversible component of the TON, optic nerve atrophy finally occurs several weeks after the initial injury.

Whilst evaluation by an ophthalmologist is desirable, the presence or absence of the above features can be assessed by any physician involved in the care of patients with head trauma. The following checklist (Table 2) can be used to assist with this.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RAPD (Swing bright light from one eye across to the other and look for pupil constriction in response to light)</strong></td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>Visual Acuity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(use Snellen Chart or Mobile App Snellen Chart)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Colour Vision</strong></td>
<td></td>
<td></td>
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<tr>
<td>(Use Ishihara Test Plates)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Visual Field</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Test finger counting in all 4 quadrants-requires patient who can sit)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Optic Disc</strong></td>
<td></td>
<td></td>
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<tr>
<td>(direct ophthalmoscope)</td>
<td></td>
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</tbody>
</table>
Table 2: Checklist of features to assess for in determine whether a patient has evidence of TON.

Documentation of the above findings is important, to evaluate changes from the initial baseline and because facial injuries are often the subject of litigation. Damage to the optic nerve is a recognised complication of surgery following facial trauma\textsuperscript{16} and so documentation of its presence prior to intervention is also important.

TON does not always occur in isolation. It is therefore also important to look for other signs of injury within the orbit, such as ophthalmoplegia and proptosis. These may suggest treatable causes of optic nerve trauma (such as retrobulbar haemorrhage).

**Imaging and Investigations**

Computed Tomography (CT) scanning is the current primary imaging modality of choice in patients following head injury trauma or with neurological signs\textsuperscript{17}. CT scans are good at detecting bony injuries to the orbit which may be associated with TON, but they do not image the nerve itself very well.

A 2014 paper looked facial CT scans in patients following blunt facial trauma associated with traumatic optic neuropathy\textsuperscript{18}. Intracoronal haematoma, extracoronal haematoma, orbital canal fracture, intracoronal emphysema and haematoma along the posterior wall of the orbit were all found to be significantly correlated with the development of TON. These findings were proposed to be useful indicators in the development of a risk predictor, based on CT findings. It was suggested that a radiologist could report such findings and this would indicate that a patient was at risk of having had, or of developing TON. There was however no report on the correlation of these findings with patient outcome.

Magnetic Resonance Imaging (MRI) is performed less commonly in the acute setting, mostly due to limited availability. It should be used in caution in anyone with a suspected intraorbital or intraocular foreign body. MRI studies in TON have looked at two diffusion techniques, Diffusion Weighted Imaging MRI (DWI-MRI) and Diffusion Tensor Imaging MRI (DTI-MRI). In DWI-MRI, acutely ischaemic tissue appears more hyperintense (bright) due to reduced diffusion of water molecules and hyperintensity on DWI MRI has been shown in traumatic brain injury\textsuperscript{19}. DTI-MRI is a subset of DWI-MRI used in evaluation of the white matter tracts specifically. It looks at the regularity of water movement in the nerve fibres. Water normally moves in the direction of the axon in healthy nerve but moves more randomly in damaged nerves\textsuperscript{20}. A study looking at DWI-MRI in TON
shows hyperintensity of the optic nerve to be a specific but non-sensitive sign of TON. A study looking at DTI-MRI imaging in TON found reduced directional movement of water across the optic nerve affected by TON when compared to controls but this was a small sample and did not reach statistical significance.

Very few studies have looked at ultrasound in TON. Those that have been undertaken have looked at Doppler signals in the central retinal artery. Peak systolic and end diastolic bloodflow in the artery was significantly lower in eyes affected by TON than age and sex matched control eyes.

These measurements were however taken from patients on average 27 months post injury and so their relevance in the acute setting is unknown.

Visual Evoked Potentials (VEP) can also be of benefit, particularly in the unconscious patient and in patients with bilateral TON who therefore do not have an RAPD. VEP’s are recorded from electrodes placed on the scalp of a patient. Patients look at various visual targets (for example black and white gratings and flashing lights) and electrical activity produced as a response to these is recorded. Flash VEP testing (VEP’s recorded in response to a flashing target) has been shown to be correlated to visual acuity outcome in a small sample of TON patients. 11 patients with TON underwent flash VEP testing and those with higher amplitude VEP’s (closer to the normal eye) had better visual acuity measurements.

Whether flash VEP testing at presentation can predict final visual outcome has not yet been elicited. If VEP’s are unrecordable, the visual prognosis is likely to be poor.

Optical Coherence Tomography (OCT) scanning has also been evaluated in TON. This is a non-invasive method of viewing the retina in cross-section. Patients effectively have a cross sectional photograph taken of the retina with a camera using laser rather than visible spectrum light. OCT assesses the reflectivity of different layers of the retina (including the nerve fibre layer) to a specific wavelength of laser light. The nerve fibre layer is the outermost layer of the retina. Photoreceptors transmit electrical impulses via bipolar cells to the retinal ganglion cells. It is the axons of these which form the retinal nerve fibre layer (RNFL). Death of axons will cause thinning of the nerve fibre layer and this thinning gives rise to the pallor seen in the later stages of TON. A study assessing the thickness of the RNFL around the optic nerve head as a marker of TON showed that there was thinning of the nerve fibre layer in TON patients compared to controls. This reached
statistical significance at 2 weeks post injury in patients with vision better than NLP and at 4 weeks post injury in patients with NLP vision\textsuperscript{24}. However as there was no significant difference within the first 2 weeks following injury this may not help an initial diagnosis of TON.

Another study looking at retinal layer thickness showed thinning in the layers containing the bipolar and ganglion cells at the macula was significantly correlated with the presence of TON around 1.5 weeks after injury\textsuperscript{24}. The same study showed that there is significant thinning of the retina at the macula region in TON patients when compared to controls at 6 weeks post injury. These measurements were also significantly correlated with visual field deterioration in patients with TON\textsuperscript{25}.

Whilst imaging may have a role in the diagnosis and management of TON, it is important to remember that it is a clinical diagnosis. Radiological imaging in particular, does however play an important role in identifying associated ocular and orbital injuries.

**Prognosis**

Patients suffering from direct TON generally have severe irreversible visual loss and there are no interventions which have been shown to improve this\textsuperscript{26}. The exception to this is if there is a rapidly treated reversible cause to the optic nerve trauma, e.g. a bone fragment which can be removed\textsuperscript{27}. There are no large scale trials looking at visual recovery specifically in direct TON.

With indirect TON, there are several factors which have been associated with poorer outcomes. These include poorer initial VA, more marked RAPD and reduced amplitude and longer latency on flash visual evoked potential (VEP) testing\textsuperscript{28}. Those with blood in the posterior ethmoid cells, loss of consciousness at time of injury and age over 40 were also all significantly associated with poorer visual acuity in another study\textsuperscript{29}. The presence of an orbital fracture was not found to be associated with a poorer visual prognosis\textsuperscript{28}. Rates of visual improvement with differing active management methods are discussed below but the rate of 3 Snellen line or more visual improvement in patients with indirect traumatic optic neuropathy ranges from just 20-52\%\textsuperscript{4,30}.

**Management**

Four broad management categories for the treatment of TON have been investigated, i) no treatment, ii) high dose steroids iii) surgical managements, or iv) a combination of these. A Cochrane Review has been carried out comparing both steroids\textsuperscript{2} and surgery\textsuperscript{26} to conservative management in
traumatic optic neuropathy. The 2013 study into the use of steroids only found one randomised controlled trial which met their inclusion criteria. This showed no significant difference in visual acuity at final analysis at 3 months but there was improvement in both groups.

The largest study done to date looking at both steroids and surgery in TON was the International Optic Nerve Trauma Study (IONTS). This was a non-randomised study of 133 patients where patients were allocated to a conservative, high/megadose steroids (2g of intravenous methylprednisolone or more) or surgery group. They did not find any statistically significant difference in visual improvement across the three groups or any effect of intervention timing on visual outcome.

There is currently a prospective non-randomised trial recruiting looking at the effect of steroids or erythropoietin on TON. This is expected to report in 2017.

In addition to the potential benefit of steroids, potential side effects should be considered. There have been no studies specifically looking at side effects of intravenous steroids in TON and the trials mentioned above were not powered to detect differences in complication rates. The MRC CRASH study looked into the effects of steroids on death and disability following head trauma. They found a significant increase in the number of deaths in the group treated with steroids within 6 months.

A Cochrane review of surgery for TON has also been produced. This did not find any randomised controlled trials which compared surgery with other interventions for TON. A number of retrospective studies and case reports have been published. A study of 96 patients who underwent endonasal optic nerve compression showed an overall improvement rate of 40.6% following surgery. The IONTS study looked at 33 patients who underwent optic canal decompression surgery for TON and found that 32% of these patients achieved a 3 line or more improvement in visual acuity at baseline compared to 57% and 52% of patients receiving steroid or conservative treatment respectively. A study looking at transcranial optic nerve decompression on 39 patients with a clinical diagnosis and/or evidence of an optic canal fracture or haematoma showed that 54% of patients regained some degree of vision following surgery at 3 months post op. Most of the studies on surgery for TON are retrospective case series reviews with no randomisation of participants and no case matched comparison with conservative management. Surgery is
often reserved either for those for whom steroids are contraindicated or for more severe cases where a response is perhaps less likely.

Studies have also looked at a combination of steroids and surgical optic nerve decompression\textsuperscript{36,37}. A study of endonasal optic nerve decompression and steroids combined\textsuperscript{36} found no statistically significant difference between surgery and steroids and steroids alone. There was no conservative treatment arm. A further 2013 study of 42 patients\textsuperscript{37}, 21 of whom had been treated with various doses of steroids and 6 also had optic nerve decompression. Those who had received surgery alone had a 53\% rate of visual improvement whereas those who had both steroids and surgery had an improvement rate of only 29\%.

Along with erythropoetin, another agent which has been trialled in a small scale randomised, placebo controlled trial in patients with indirect TON was levodopa-carbidopa\textsuperscript{38}. This small scale study showed significant visual improvements in patients with better than HM vision at baseline given levodopa-carbidopa.

**Conclusion**

TON is a diagnosis which is present in a significant number of patients following a traumatic head injury. Despite this, it is something that many of the specialties involved in the initial assessment and management of patients with such injuries feel unconfident about. As illustrated above however, many of the diagnostic tests can be performed by any clinician and these alone will give a good indication as to the presence or absence of TON. Figure 1 provides an outline of the steps required for the diagnosis of TON which can be undertaken by anyone seeing a patient presenting with head trauma.

Despite several decades of research on TON, we still do not have a treatment strategy which has been shown to be effective in a large number of patients. It is however vitally important to identify patients who are at risk of TON, diagnose those who have evidence of it and liaise with appropriate specialists for further assessment. This will allow us to give patients accurate information on their condition and reduce the chance of retrospective claims against the treating clinicians.

Due to the difficulty in recruiting for a prospective randomised trial\textsuperscript{30} we cannot rely on being able to obtain best quality evidence on the optimum management for TON in the near future. However, new trials are currently recruiting\textsuperscript{32} and hopefully this will change. At present, patients should be given a realistic expectation of their
prognosis with or without treatment and treatment strategies should be guided by an MDT decision based on the presenting patient’s features and local expertise in management.

**Learning points**

1. TON is a rare complication of head injury but its presence should be assessed in all at risk patients

2. Examinations to establish a provisional diagnosis of TON can be carried out by all clinicians involved in the care of head injured patients

3. Whilst TON is a clinical diagnosis, radiological and other investigations can be of use, particularly identifying those at risk.

4. No treatment has shown to significantly improve the outcome in TON over any other.

5. Assessment and management of TON should be carried out as part of an MDT assessment.
Figure 1: Algorithm for the assessment of a patient with suspected TON

References


5. Pirouzmand F: Epidemiological trends of traumatic optic nerve injuries in the largest Canadian adult trauma center: J Craniofac Surg. 2012: 23(2) 516-20


17. NICE Guidelines CG176: www.nice.org.uk


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