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STUDY OF VISUAL PROGNOSIS IN PATIENTS WITH TRAUMATIC OPTIC NEUROPATHY TREATED WITH TRAUMATIC OPTIC NEUROPATHY TREATMENT TRIAL (T-ONTT)

Ophthalmology

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ABSTRACT

AIM: The aim of the study was to emphasize the importance of T-ONTT (Traumatic Optic Neuropathy Treatment Trial) in the management of traumatic optic neuropathy and assessment of visual outcome at the end of treatment.

BACKGROUND: Optic neuropathy is a potentially blinding complication of head or orbital trauma. In this study, we tried to emphasize the importance of TONTT (traumatic optic neuropathy treatment trial) in patients with traumatic optic neuropathy.

MATERIALS AND METHODS: This hospital-based prospective study was conducted for a period of 1 year in Government Stanley medical college hospital. All patients admitted with history of facial or head injury in trauma ward with RAPD (RELATIVE AFFERENT PUPILLARY DEFECT) on examination were included and they underwent complete ocular examination including visual acuity testing, grading of RAPD by swinging flash light test, colour desaturation, visual fields, flash VEP and detailed fundus evaluation along with CT scan of orbit with optic nerve cuts. Patients were treated according to T-ONTT (Traumatic Optic Neuropathy Treatment Trial) and their visual prognosis were analysed at the end.

RESULTS: A total of 20 eyes of 20 patients, with the age group of 17-48 years were examined and included in the TONTT trial. The correlation between RAPD and vision, VEP changes and vision were made. Out of 20 patients, the most common RAPD grading was found to be grade 2+. It was found that RAPD grading and VEP changes well correlated with visual acuity. All patients received treatment according to TONTT (Traumatic Optic Neuropathy Treatment Trial). Out of 20 patients, 90% patients showed improvement in terms of visual acuity by 2 snellen's line at the end of treatment.

CONCLUSION: The effectiveness of methyl prednisolone in traumatic optic neuropathy was found to be effective if instituted early as possible irrespective of the presenting visual acuity.

KEYWORDS

Traumatic optic neuropathy, T-ONTT, RAPD, VEP changes, Intravenous methyl prednisolone.

BACKGROUND: Optic neuropathy is a potentially blinding complication of head or orbital trauma. [1.] The incidence of traumatic optic neuropathy in the setting of closed head trauma is 0.5-5% with a male predilection and mean age of 34 years. In this study, we tried to emphasize the importance of TONTT (traumatic optic neuropathy treatment trial) in patients with traumatic optic neuropathy.

AIMS AND OBJECTIVES: The purpose of this study was to evaluate and emphasize the importance of TONTT (Traumatic Optic Neuropathy Treatment Trial) in the management of traumatic optic neuropathy and to analyse the visual outcome at the end of treatment.

MATERIALS & METHODS: All patients admitted in trauma ward in Government Stanley Medical College Hospital with history of face or head injury with RAPD (Relative Afferent Pupillary Defect) on examination were included in the study. All patients underwent complete ocular examination including visual acuity testing by snellen's chart, grading of RAPD by swinging flash light test, colour desaturation, visual fields testing by Automated perimetry, flash VEP (Visual Evoked Potential) response and detailed fundus evaluation along with CT scan of orbit with optic nerve cuts. The data recorded include age, sex, baseline visual acuity, RAPD grading, VEP changes, and final visual acuity following treatment according to T-ONTT.

STUDY DESIGN: Prospective hospital-based observational study

DURATION OF STUDY: 1 year

INCLUSION CRITERIA: All patients with history of trauma to head or face with RAPD on examination.

EXCLUSION CRITERIA:

1) Patients with RAPD due to causes other than trauma and
2) Patients with pre-existing pupillary abnormalities.

INTRODUCTION: Traumatic optic neuropathy can take many forms; direct & indirect. Direct injuries are caused by projectile or penetrating objects that enter the orbit, indirect injuries are caused by forces that are transmitted to the optic canal from globe and orbit.

[2.] Optic nerve injury is classified into primary and secondary, depending on the nature of pathology. Primary damage occurs when there is an immediate disruption (direct trauma) or shearing (indirect trauma) of retinal ganglion cells, whereas secondary damage is due to inflammation and vascular dysfunction. Though the pathophysiologies of both mechanisms differ greatly, patients often have elements of both. The most common site is the intra canalicular part (due to tight adherence of dural sheath of the nerve to the periosteum) followed by intracranial part (due to close proximity of the falciform dural fold to the optic nerve).

RAPD: [3.]A relative afferent pupillary defect is necessary for the diagnosis in cases of suspected unilateral traumatic optic neuropathy. The only available simple test is swinging flash light test.

COLOUR DESATURATION: [4.]Red desaturation assesses the integrity of the optic nerve by testing the ocular sensitivity to the red colour. The test is used clinically for the detection of asymmetric optic nerve function. A positive response would be that the red colour looks faded pink or washed out.

FUNDUS APPEARANCE: [5.]Optic disc appearance depends on the anatomical site and timing of injury. With injuries to optic nerve anterior to entry of central retinal vessels, there is optic disc swelling with associated hemorrhages, in posterior injuries which are more common, the fundus looks normal. Optic disc pallor usually develops about 6 weeks following initial injury.

FVEP RESPONSE: [6.]Visual evoked potential (VEP) are electrical potential differences recorded from scalp in response to visual stimuli. Visual system can produce abnormal VEP's if there is disturbance anywhere in the visual pathway. On giving a pattern or visual stimulus, there is increased metabolism not only in primary visual area (area 17) but also in visual association areas (area18 &19). The most commonly

studied wave forms typically contains an initial negative peak (N1), followed by a positive (P1, also known as P100 for its usual location at 100 millisecond); second negative (N2) and second positive (P2) peaks follow. The latency of onset of a peak after light stimulus and (to a lesser degree) the amplitude of the peak is the most useful features analysed.

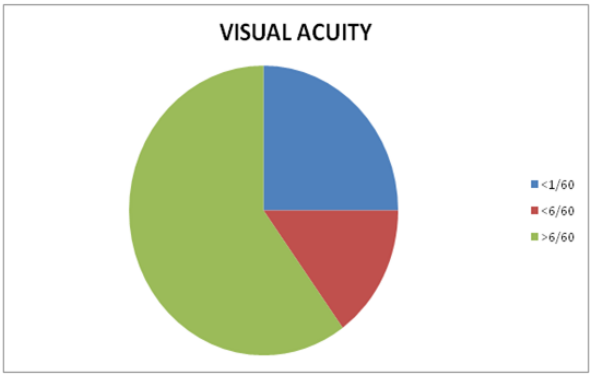
PATHOGENESIS: [7.] In acute injury, cell membrane **lipid peroxidation** is the key mechanism demonstrated which is post-traumatically initiated by highly reactive oxygen species, which damages both micro vascular and parenchymal cell membranes. Lipid peroxidation is a consequence of post-traumatic glutamate release, activation of arachidonic acid cascade, and production of prostaglandins, resulting in vasoconstriction and micro embolism and the formation of oxygen radicals which further initiate lipid peroxidation. Iron is a powerful catalyst that accelerates the propagation of lipid peroxidation reaction. Iron is derived from haemoglobin of petechial hemorrhages. In addition, anaerobically derived lactate promotes lipid peroxidation by stimulating the release of iron from storage sites, apart from which dysfunctional mitochondria appear to be an important source of reactive oxygen species. Lipid peroxidation occurs in neurons and blood vessels, directly impairing neuronal and axonal membrane function and causing micro vascular damage and secondary ischemia that indirectly contributes to the secondary injury to neurons and axons. This mechanism prompted the development of glucocorticoids in antagonizing the oxygen free radical induced lipid peroxidation in a safe and effective manner.

METHYL PREDNISOLONE SODIUM SUCCINATE:
Glucocorticoid steroids are effective inhibitors of post-traumatic lipid peroxidation, based on their high lipid solubility and known ability to intercalate into artificial membranes between hydrophobic polyunsaturated fatty acids and thereby limit propagation of lipid peroxidation chain reactions. Other uses were in attenuating post-traumatic oedema. Methyl prednisolone can prevent the loss of spinal cord neuro filament proteins, facilitate neuronal excitability and impulse conduction, improve blood flow, enhance Na+K+ ATPase activity and decrease lipid peroxidation and prevent ischemia induced damage. This helps to improve impulse conduction and recovery of function in injured spinal cord. Thus Methyl prednisolone has a combined vaso- and neuro- protective effect.

TREATMENT: The main options in current use are systemic steroids, surgical decompression of optic nerve sheath with a combination of steroids, surgery or observation alone.

RESULTS: A total 20 eyes of 20 patients were examined and included in the TONTT trial. All patients were males.

CHART: 1

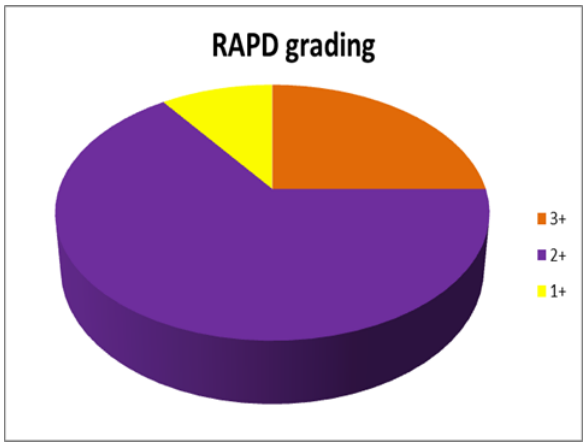


After data analysis, the enrolled 20 patients were divided into 3 groups based on visual acuity as <1/60 - 5 patients, <6/60 - 3 patients and >6/60 - 12 patients **(Table 1).**

TABLE: 1

VISUAL ACUITY	NO. OF PATIENTS
<1/60	5
<6/60	3
>6/60	12

CHART: 2

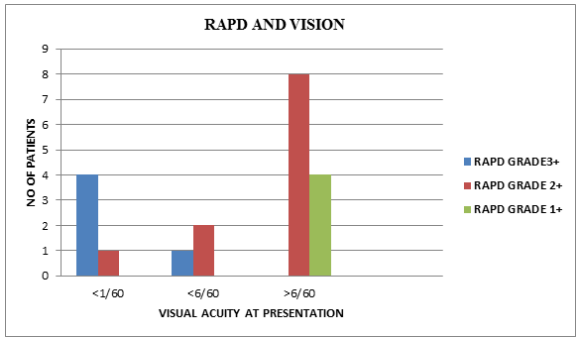


The RAPD grading was grade 3+ in 5 patients, grade 2+ in 11 patients; grade 1+ in 4 patients. In group 1 comprising of 5 patients with V/A <1/60; grade 3+ in 4 patients and grade 2+ in 1 patient. In group 2 comprising of 3 patients with V/A <6/60; grade 3+ in 1 patient and grade 2+ in 2 patients, whereas in group 3 comprising of 12 patients with V/A >6/60; grade2+ in 8 patients & grade1+ in 4 patients **(Table2).**

TABLE: 2

VISUAL ACUITY		NO. OF PATIENTS	RAPD GRADING		
			3+	2+	1+
GROUP 1	<1/60	5	4	1	NIL
GROUP 2	<6/60	3	1	2	NIL
GROUP 3	>6/60	12	NIL	8	4

CHART: 3



In all our patients, the degree of visual loss (visual acuity in log MAR) was well correlated with the grading of RAPD **(Chart 3).**

CHART: 4

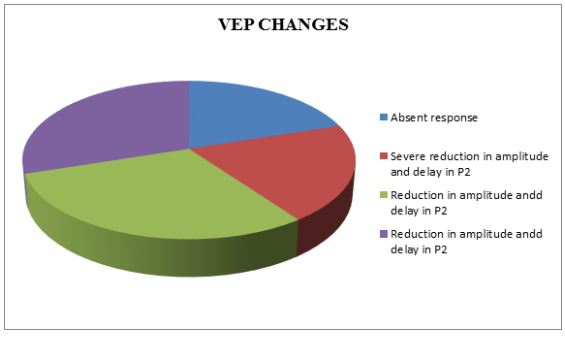
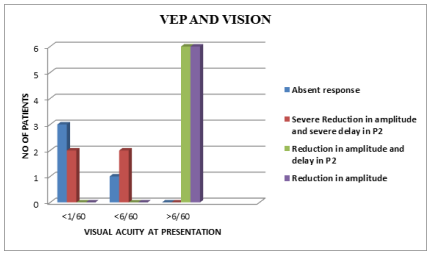


TABLE: 3

VEP CHANGES	NO. OF PATIENTS
Absent response	4
Severe reduction in amplitude and delay in P2	4
Reduction in amplitude and delay in P2	6
Reduction in amplitude	6

CHART: 4



The F-VEP (Flash- Visual Evoked Potential) response is elicited by a 100 milliseconds diffuse light flash presented at 2 Hertz. The response obtained in **group 1** patients was an absent response in 3 patients and severe reduction in amplitude and delay in P2 in 2 patients. In **group 2** patients, there was an absent response in only 1 patient, reduction in amplitude and severe delay in P2 in remaining 2 patients. In the **group 3** there was a reduction in amplitude alone in 6 patients and reduction in amplitude and delay in P2 in 6 patients **(Chart 4).**

TABLE: 4

Visual Acuity		No. Of Patients	Flash Vep Response			
			Absent Response	Severe reduction in Amplitude and delay in P2	Reduction in Amplitude and delay in P2	Reduction in Amplitude
Group 1	<1/60	5	3	2	NIL	NIL
Group 2	<6/60	3	1	2	NIL	NIL
Group 3	>6/60	12	NIL	NIL	6	6

In **group 1** comprising of 5 patients; 1 patient had a fracture of lamina papyracea, 2 patients had comminuted fracture of roof, medial wall and floor of orbit and remaining 2 patients had fracture of medial wall and floor of orbit alone. In **group 2** comprising of 3 patients; 1 had no bony injury and remaining 2 had fracture of lateral wall and floor. In **group 3** comprising of 12 patients; 8 had no bony injury, the remaining 4 had fracture of one wall alone. All our patients had a red desaturation range of 25%- 90%. In 4 out of 20 patients the field changes observed were centrocaecal scotoma.

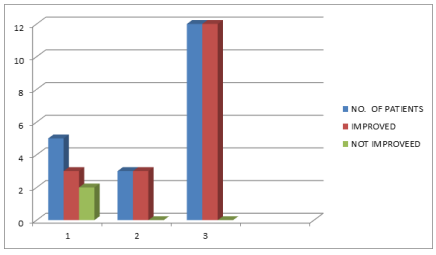
The commonest RAPD grading observed was grade 2+ **(Chart 2).** The Flash-VEP response was well correlated with the degree of visual acuity **(Chart 4)** and the grading of RAPD with the degree of visual acuity **(Chart 3).** In all patients diagnosed with TON, orbital computed tomography revealed grievous injury in 13 patients and remaining 7 patients it was simple injury. All the 20 patients received Intravenous methyl prednisolone 1 gram once a day in 100ml of DNS within 12 hours of trauma for initial 3 days, followed by extended oral prednisolone acetate 1 mg/kg/day for 11 days in tapering dose. Blood sugar and blood pressure monitoring was done in all patients. All the patients were compliant to the drugs. 2 out of 20 patients underwent surgical decompression of optic nerve sheath.

In all patients diagnosed with TON, orbital computed tomography revealed grievous injury in 13 patients and remaining 7 patients it was simple injury.

TABLE: 5

GROUP	NO. OF PATIENTS	IMPROVED	NOT IMPROVED
1	5	3	2
2	3	3	NIL
3	12	12	NIL

CHART: 5 VISUAL OUTCOME AFTER TREATMENT



Analysis with difference between final and baseline visual acuity as dependent was done. Recovery of vision was defined as improvement of at least two Snellen's line at the end of treatment. In order to provide a common scale of visual acuity for analysis, all data were converted into decimal fraction of Snellen's visual acuity. Out of 20 patients, 18 patients showed improvement and 2 patients showed no improvement whose final visual acuity was hand movements **(Table 5).**

DISCUSSION: The results of this study showed that the most common mode of trauma was road traffic accidents with all patients being males.

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS NOTED	
Age(years)	**17 to 48**
Sex	
Male	**20**
Female	**nil**
Baseline visual acuity	
<1/60	**5**
<6/60	**3**
>6/60	**12**
RAPD grading	
3+	**5**
2+	**11**
1+	**4**
VEP change	
Absent response	**4**
Reduction in amplitude and delay in P2	**6**
Severe reduction in amplitude and delay in P2	**4**
Reduction in amplitude	**6**

The commonest RAPD grading observed was grade 2+ **(Chart 2).** When possible, patients were investigated with VEP in order to confirm optic nerve involvement. The Flash-VEP response also was well correlated with the degree of visual acuity and grading of RAPD **(Table 4)**. In all patients diagnosed with TON, orbital computed tomography revealed grievous injury in 13 patients and remaining 7 patients it was simple injury. In group 1 comprising 5 patients; of the 2patients, one patient had a fracture of lamina papyracea and remaining one patient had a comminuted fracture involving medial wall, floor and roof, (none of the patients had a fracture of the optic canal or bony impingement). All patients diagnosed with TON had been admitted in hospital and hence high dose steroids were started in all patients within 12 hours of trauma according to the protocol used in ONTT trial **(Table 6)**. As there are no controlled guidelines for management of patients affected by TON, correct management for TON remain a clinical dilemma. Analysis with difference between final and baseline visual acuity as dependent was done. Recovery of vision was defined as improvement of at least two Snellen's line at the end of treatment. In order to provide a common scale of visual acuity for analysis, all data were converted into decimal fraction of Snellen's visual acuity.

TABLE: 6

Initial visual acuity (log mar)	No of patients	No of patients given steroid	No of patients improved after steroids	Final visual acuity	No of patients underg one decomp ression surgery	No of patients improved after surgery	Final visual acuity
<1/60 (+1.3)	5	5	3	<6/60 (<+1.0)	2	Nil	Hm
<6/60 (<+1.0)	3	3	3	5/60(-6/ 36(+0.8)	-	-	-
>6/60 (>+1.0)	12	12	12	6/36(+0. 8)-6/9 (+0.2)	-	-	-

In group 1 (v/a <1/60), 3 out of 5 patients showed improvement, whereas remaining 2 patients showed no improvement those of which underwent combined steroids and optic nerve decompression. The VEP response in 3 out of 5 patients in group1 patients was only an absent response which strongly correlates with the severe degree of optic nerve involvement. [8] **Mahapatra and Tandon** 1993, in his study showed no improvement with surgery. [9] **Chuenkongkaew and**

Chirapapaisan 2002 also showed no improvement. [10.] **Ragniganth et al.,** 2003 in a study of 44 patients, 70% showed improvement in vision within days of surgery and 24% after 7 days.[11.] **Chen et al.,** 2007 showed 50% improvement with surgery. Surgical intervention for traumatic optic neuropathy was shown not to be beneficial in the International optic nerve trauma study. In the [12.] **IONTS** study, visual acuity improvement of > 3 lines was seen in 57% of the untreated group, 52% of the group that received steroids alone, 32% of the group that underwent surgery. Thus the comparative data from (**IONTS**) group showed that neither corticosteroid therapy nor optic nerve decompression is the gold standards for treatment of traumatic optic neuropathy. According to

[13.] **A. Agarwal et al**, IJO, a retrospective analysis of PubMed article concluded that there has been no large prospective placebo trial evaluating the role of steroids for the treatment of traumatic optic neuropathy and studies done till date showed no convincing data that steroids provide additional benefit. According to[5.] **Cochrane collaboration study** there is a relatively high rate of spontaneous visual recovery in traumatic optic neuropathy and there is no convincing data that steroids provide additional visual benefit over observation alone.

In group 2 (v/a ,<6/60) comprising of 3 patients, one patient with grade 3+ RAPD and absent response in VEP showed only minimal visual improvement, whereas other 2 patients with grade 2+ RAPD and VEP response of reduction in amplitude and severe delay in P2 showed optimal visual improvement. [14.] **Cook et al**., in a meta-analysis, reported that recovery of vision in patients treated with mega dose steroids or surgical decompression of optic canal was significantly better than those receiving no treatment**.** [15.] **Entezari et al.,** 2007 in a study which included 31 patients, 16 showed vision improvement with steroids and 15 showed improvement conservatively. At present, there is no proven form of treatment for this condition and there is controversy over its optimal management.

In group 3 (v/a, > 6/60), comprising a total of 12 patients, 8 patients had RAPD gr1+ and 12 patients had RAPD gr2+, the VEP response was either reduction in amplitude and delay in P2 or a reduction in amplitude alone. All the 12 patients showed improvement in vision**.** [16.] **Joseph et al.,** 1990 showed 78.5% improvement with corticosteroids. [17.] **Entezari et al.,** 2007 showed 68.8% improvement with steroids. [18.] **Chen et al.,** 1998 and Seiff 1990 both showed improvement of vision by 62%.[19.] **Matsuzaki et al.,** 1982 showed 58.8% improvement with steroids. [20.] **Chou et al.,** 1996 showed 57% improvement with steroids.[21.] **Levin et al.,** 1999 showed 52% improvement in visual acuity. In our study there was 90% improvement in visual acuity after high dose steroids instituted within 12 hours of trauma. [22.] **Sundeep et al.,** showed IV methyl prednisolone to be effective for treatment of traumatic optic neuropathy provided the pre-treatment visual acuity is not less than counting fingers.

CONCLUSION:

In our study 18 (90%) of 20 patients had good visual improvement following T-ONTT. The study emphasizes that T-ONTT, if started within 12 hours of trauma, irrespective of the presenting visual acuity, has good visual prognosis and that patients with indirect form of optic nerve injury benefit with good visual recovery following T-ONTT than other forms of injury. Thus in conclusion, ONTT trial for optic neuritis can be effective method of treatment for traumatic optic neuropathy.

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