• Clinical Research •

Newly onset indirect traumatic optic neuropathy-surgical treatment first versus steroid treatment first

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Abstract

● **AIM:** To investigate the efficacy and safety of the treatment of endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) with combination of steroid in patients with newly onset indirect traumatic optic neuropathy (ITON) and compare the outcome between immediate ETOCD treatment and ETOCD with preoperative steroid treatment.

● **METHODS:** Patients presented as newly onset ITON (suffered trauma within 3d) at a tertiary medical center between Mar 1st, 2016 and Mar 1st, 2018 were enrolled in this study. All patients were equally and randomly divided into 2 groups. Cases in group A were performed ETOCD immediately after admition while cases in group B were prescribed by methylprednisolone (20 mg/kg·d) for 3d before ETOCD. Methylprednisolone (20 mg/kg·d) was used after surgery for 6d in group A and 3d in group B. Follow-up was up to 3mo in all cases. Visual acuity (VA) before and after treatment between the two groups were taken into comparison.

● **RESULTS:** Complete postoperative data were acquired from 34 patients in group A and from 32 patients in group B. Group A had significantly higher effective rate in VA than group B (χ^2 =4.905, *P*=0.027).

● **CONCLUSION:** For patients with newly onset ITON, combination treatment of ETOCD with high-dose steroid is an effective and safe way. Immediate surgery will lead to better prognosis for these cases.

● **KEYWORDS:** indirect traumatic optic neuropathy; endoscopic trans-ethmosphenoid optic canal decompression; steroid; visual acuity; newly onset

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INTRODUCTION

Traumatic optic neuropathy (TON) is a rare and potentially vision-threatening condition caused by ocular or head trauma with the incidence rate of 0.5%-5%[1-3].

TON may result from either direct or indirect injury. Direct optic nerve injury is usually caused by optic nerve laceration or avulsion, or by direct fracture of the optic canal. Thus, it could always lead to poor prognosis. Indirect optic injury is usually due to increased intracanalicular pressure after an injury. A secondary disorders would happen due to the a cascade of molecular and chemical mediators, initiated by this increased intracanalicular pressure[4]. Therefore, indirect injuries may derive benefit from treatment[4-5].

Time between the trauma and first treatment is considered as a strong predictor of indirect traumatic optic neuropathy (ITON). Early treatment always leads to better prognosis[6-7].

The treatment of ITON, especially for newly on-set cases, is still controversial. High-dose steroid is recommended as the primary treatment for ITON by previous studies[8-9]. Endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) was brought out by some ENTs as a new therapy for ITON[10]. Treatment of ETOCD with combination of steroid was then used as another treatment of ITON which was considered as a more effective way of treating ITON[1,6,11]. However, when to perform ETOCD, immediate after admition or after several days steroid treatment, hasn't reached agreement. Yang *et al*[12] suggested that high dose intravenous steroid therapy should be the primary treatment for ITON, and ETOCD can be performed as an adjuvant to steroid therapy in cases where steroids failed. However, Song *et al*[13] found that no differences in the outcomes between cases who received surgery with pre-operative steroid therapy and those underwent surgery alone. He believed that it was not necessary to wait for the effect of steroid before surgery[13].

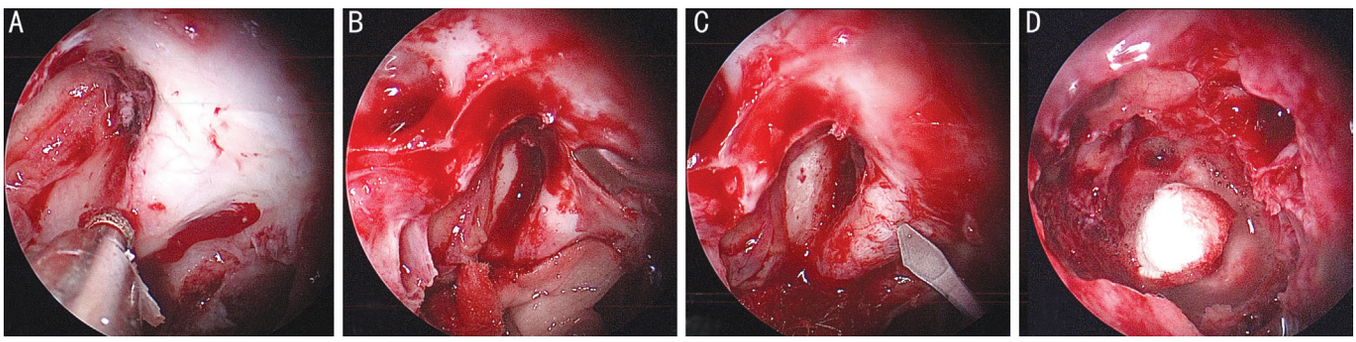

Figure 1 The surgical procedures of endoscopic trans-ETOCD A: A microdrill was used to thin the middle wall of optic canal; B: The thinned medial wall was removed by a microcurrette; C: A sharp 9# MVR knife was used to incised the optic nerve sheath; D: The opened sphenoid sinus was covered by a piece of sponge that was immersed in mouse-derived neuron growth factor and dexamethasone.

Our study aimed to investigate the efficacy and safety of the treatment of ETOCD with combination of steroid in patients with newly on-set ITON and compare the outcome between immediate ETOCD treatment and ETOCD with preoperative steroid treatment.

SUBJECTS AND METHODS

Ethical Approval The study was approved by the local Ethical Research Committee (KYK[2016]18) and was authorized by the Eye Hospital of Wenzhou Medical University, informed consent was obtained from all the patients. Patients presented as newly on-set ITON (suffered trauma within 3d) in Department of Orbital & Oculoplastic Surgery, Eye Hospital of Wenzhou Medical University between Mar 1st, 2016 and Mar 1st, 2018 were enrolled in this study.

All patients in this series had loss of vision after trauma with an afferent pupillary defect in the involved eye. High resolution brain and orbital computed tomography scans were performed in all patients. Optical coherence tomography scan and fundus photo were performed as well.

Patients with bilateral ITON were excluded in our study. Patients had previous treatment or with a history of consciousness impairment were also excluded in our study. Cases who refused surgery were excluded in this study as well. Then the rest patients were randomly equally divided into 2 groups, group A and group B. Cases in group A were performed ETOCD immediately after admition while cases in group B were prescribed by methylprednisolone (20 mg/kg·d) for 3d before ETOCD. Methylprednisolone (20 mg/kg·d) was used after surgery for 6d in group A and 3d in group B. Patients were followed up to 3mo after surgery. Written content was signed by all cases before surgery. We recorded the demographic characteristics of the patients, including visual acuity (VA) before and 3mo after surgery, time to medical treatment, other accompanied conditions, including hemorrhage within sphenoid sinus and/or the post-ethmoid, optic canal fracture and orbital fracture. VA improvement is defined as 1) VA improved ≥2 lines on the Snellen visual chart; 2) VA improved from no light perception (NLP) to light perception (LP) or better; 3) VA improved from LP to hand motion (HM) or better; 4) VA improved from HM to finger counting (FC) or better; 5) VA improved from FC to 0.01 or better[5-6].

Surgical Procedure All of the procedures were performed by the same surgeon (Wu WC). The surgical procedure was detailed describe in our previous studies[2,11]. During the surgery, a routine endoscopic sphenoethmoidectomy was performed using the Messerklinger technique. After sphenoethmoidectomy and optic nerve canal locating, the optic canal was thinned with a microdrill and removed with a microcurrette. Then, the periorbita of the orbital apex, annulus of Zinn and the optic nerve sheath were incised with a sharp 9# microvitreoretinal (MVR) knife. Finally, a piece of sterile gelatine sponge that was immersed in mouse-derived nerve growth factor (30 mg/mL; Staidson, Biopharmaceuticals Co., Beijing) and dexamethasone (5 mg/2 mL) was used in the operating field of the optic canal at the end of the surgery. Postoperative care included administering methylprednisolone (20 mg/kg·d) for 6d in group A and 3d in group B, ceftriaxone (2.0 g/d) for 5d (Figure 1).

Statistical Analysis Statistical analyses were performed with SPSS version 17.0 in this study. NLP rate was defined as the number of patients with NLP vision before surgery divided by overall number of patients in each group. Effective rate was defined as the number of patients with improve VA after ETOCD divided by overall number of patients enrolled in our study. Independent-samples *t*-test was used to compare patients' age between group A and group B. χ^2 test was used to compare the NLP rate before treatment, the rate of hemorrhage within the sphenoid sinus and/or post-ethmoid, the rate of orbital fracture and the rate of optic canal facture (OCF) between group A and group B. The effective rate between group A and group B was used by χ^2 test as well. Results were considered significant at $P<0.05$.

RESULTS

Totally, 82 cases were enrolled in this study (41 cases in

each group). Of 34 cases in group A finished the follow-up while 32 cases in group B finished the follow-up. The clinical characteristic of them were list in Table 1.

There were no statistically significant differences in patients age (t=0.396, P=0.693), NLP rate before treatment (χ^2=0.324, P=0.569), the rate of hemorrhage within the post-ethmoid and/or sphenoid sinus (χ^2=0.504, P=0.478), orbital fracture (χ^2=0.655, P=0.418) and OCF (χ^2=0.324, P=0.569) between group A and group B.

VA in 25 out of 34 patients in group A was improved, with an effective rate of 73.5%. These patients had pre-treatment NLP in 20 eyes, LP in 5 eyes, HM in 2 eyes, FC in 2 eyes and better than FC in 5 eyes. Twelve of 20 cases with NLP pre-treatment had improved post-treatment vision, including LP in 3 eyes, HM in 1 eye, FC in 3 eyes and better than FC in 5 eyes. All 5 patients with LP pre-treatment had improved in vision after treatment, including HM in 2 eyes and better than FC in 3 eyes. Both 2 cases with HM before treatment had improved to FC in vision after treatment. Both 2 cases with FC pre-treatment had improved to 20/200 after treatment. Four of 5 cases with better than FC pre-treatment had improved in vision after treatment, including 1 from 20/200 to 20/60, 1 from 20/200 to 20/50, 1 from 20/100 to 20/20 and 1 from 20/40 to 20/20 (Table 2).

VA was improved in 15 out of 32 patients in group B, with an effective rate of 46.9%. These patients had pre-treatment NLP in 21 eyes, LP in 1 eye, HM in 3 eyes, FC in 5 eyes and better than FC in 2 eyes. Nine of 21 cases with NLP pre-treatment had improved in vision after treatment, including LP in 1 eyes, HM in 1 eye, FC in 5 eyes and better than FC in 2 eyes. Patient with LP pre-treatment had improved to FC vision after treatment. Two of 3 cases with HM before treatment had improved in vision after treatment, including FC in 1 eye and 20/200 in 1 eye. Two of 5 cases with FC pre-treatment had improved in vision after treatment, including 20/400 in 1 eye and 20/100 in 1 eye. One of 2 cases with better than FC pre-treatment had improved in vision, who improved from 20/40 to 20/25 (Table 3). Group A had significantly higher effective rate than group B (χ^2=4.905, P<0.05).

During the surgery, cerebrospinal fluid rhinorrhea was happened in 4 patients. All of them were repaired by mucosal flap transplantation uneventfully during surgery and totally recovered from strict bed rest in a 30 degree of head-up position for a week. No other severe complications were observed.

Table 1 Clinical characteristics of patients *n* (%)

Characteristics	Case in group A	Case in group B
Injury type		
Fall	6 (17.6)	12 (37.5)
Car accident	19 (55.9)	12 (37.5)
Assault	9 (26.5)	6 (18.75)
Explode	0 (0）	2 (6.25)
Age, y	33.74±11.53	32.72±9.80
Orbital bone fracture		
Yes	15 (44.1)	11 (34.4)
No	19 (55.9)	21 (65.6)
Hemorrhage within the sphenoid sinus and/or post-ethmoid		
Yes	13 (38.2)	15(46.9)
No	21 (61.8)	17(53.1)
Optic canal fracture		
Yes	20 (58.8)	21(65.6)
No	14 (41.2)	11(34.4)
The time to medical treatment		
Within 1d	11 (32.3)	9 (28.1)
1 to 2d	15 (44.1)	13 (40.6)
2 to 3d	8 (23.5)	10 (31.3)
VA before surgery		
NLP	20 (58.8)	21 (65.6)
Non-NLP	14 (41.2)	11 (34.4)

VA: Visual acuity; NLP: No light perception; Non-NLP: Visual acuity better than no light perception.

Table 2 The VA before and after treatment of cases in group A

VA pre-treatment (*n*)	VA post-treatment				
	NLP	LP	HM	FC	Better than FC
NLP (20)	8	3	1	3	5
LP (5)	0	0	2	0	3
HM (2)	0	0	0	2	0
FC (2)	0	0	0	0	2
Better than FC (5)	0	0	0	0	5[a]

VA: Visual acuity; NLP: No light perception; LP: Light perception; HM: Hand motion; FC: Finger count. [a]Four of 5 cases with better than FC pre-treatment had improved in vision after treatment, including 1 from 20/200 to 20/60, 1 from 20/200 to 20/50, 1 from 20/100 to 20/20 and 1 from 20/40 to 20/20.

Table 3 The VA before and after treatment of cases in group B

VA pre-treatment (*n*)	VA post-treatment				
	NLP	LP	HM	FC	Better than FC
NLP (21)	12	1	1	5	2
LP (1)	0	0	0	1	0
HM (3)	0	0	1	1	1
FC (5)	0	0	0	3	2
Better than FC (2)	0	0	0	0	2[a]

VA: Visual acuity; NLP: No light perception; LP: Light perception; HM: Hand motion; FC: Finger count. [a]One cases with better than FC pre-treatment had improved in vision , who improved from 20/40 to 20/25.

DISCUSSION

ITON is a serious complication of head trauma which could have serious outcomes. Most of patients suffer ITON in their early 30's. Motorbike is the most common cause of ITON, followed by bicycle accident, falls and assaults[14]. We enrolled 66 patients in our study, aging from 18 to 59 years old, among which 56 patients (84.84%) were 20 to 49 years old. The

most common cause of ITON in our study was car accident, followed by falls, assaults and explore.

Indirect optic nerve injury is caused by increased intracanalicular pressure after injury[4-5]. Though this disease has been known for over for many years, the precise pathogenesis of ITON is still unclear. However, various studies trying to explain the mechanism of optic nerve damaging in ITON were conducted. Some studies suggested that when forces applied to the frontal bone, it would be transferred and concentrated in the optic canal region. It would result in optic nerve damaging[15]. Others demonstrated that patients with indirect injury to optic nerve had been consistent with localization of the lesion to this area which may cause damaging in optic nerve[16]. Increased intracanalicular pressure after injury may initiate a cascade of molecular and chemical mediators. A secondary disorders such as intraneural oedema, haematoma, altered microvasculature or cerebrospinal fluid circulation, and interruption of direct axoplasmic transport, would happen due to the a cascade of molecular and chemical mediators, initiated by this increased intracanalicular pressure[4].

Treatment for ITON remains controversy. Although observation alone showed improvement in VA in some cases[17-18], most ophthalmologists do not think it is enough for ITON especially for newly on-set ones. High-dose steroid is recommended as the primary treatment for ITON by previous studies[8-9]. Optic canal decompression (OCD) was raised up these years by some authors. OCD physically decompresses the optic nerve within the canal, which could create space for the nerve to swell, thus to decrease the damaging effect[13]. Different approaches have been advocated for OCD, including transcranial, transantral, intranasal microscopic and endoscopic approaches[10,13,19-21]. There are many advantages with endoscopic approach, such as less morbidity, good cosmetic results without external scarring, preservation of olfaction, and a shorter recovery time. In addition, the endoscopic approach provides an excellent view of the orbital apex[22]. Thus, endoscopic approach of OCD was chosen in our study.

Treatment of OCD with combination of steroid and surgery was found to be more effective than steroid only. According to previous researches, the VA improvement rate of high-dose steroid treatment alone was 4.3%-44%, and high-dose steroid combined with OCD was 60.9%-71.1%[11,22-23]. According to the retrospective study we made before, the effective rate of combination treatment was higher than it of using steroid only[11]. Therefore, this combination therapy was used in our study as well.

When to perform ETOCD is still controversial. Song *et al*'s[13] believed that it was not necessary to wait the effect of steroid before surgery[13]. We found that cases who received immediate ETOCD had better prognosis than those underwent steroid therapy before ETOCD. This may because that ETOCD has better effect of OCD than steroid. We found the subsiding of optic nerve edema at the second day after ETOCD while it remained the same at the second day after steroid treatment. What's more, ETOCD can relieve the compression of optic nerve caused by optic canal fracture.

Whether to split the nerve sheath is another controversial issue[23]. Thakar *et al*[24] believed that the annulus of Zinn at the anterior end of the fibrous sheath may related to edema. However, sheath splitting could increase the risk of cerebrospinal fluid leakage, the happening of ophthalmic artery injury and injury to the optic nerve. In order to improve the effectiveness and safety of surgery, several modified surgical methods were made in our surgical procedure: 1) Punctuated optic nerve sheath splitting was made in this study. This procedure is different from the traditional way, which is associated with complications like cerebrospinal fluid leakage, ophthalmic artery injury and optic nerve injury. In our surgery, 5 to 6 small punctuated incision about 1 mm was made to the sheath to release the pressure with little risk of complications. 2) Decompressed the orbit apex by opening the periorbital of the orbital apex and annulus of Zinn in this study in order to further decrease intracanal pressure. 3) At the end of surgery, a piece of sterile gelatine sponge that was immersed in dexamethasone and mouse-derived neuron growth factor was inserted to cover the operating field of the optic canal[2]. This procedure may benefit the recovery of function of optic nerve.

For patients with newly on-set ITON, combination treatment of ETOCD with high-dose steroid is an effect and safety way. Immediate surgery will lead to better prognosis for these cases.

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