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Anatomic and Functional Effects of Systemic Corticosteroids for Treating Toxic Optic Neuropathy Due to Methanol Intoxication

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ABSTRACT

Introduction: The aim of this study was to examine the anatomical and functional effects of high-dose intravenous steroids for toxic optic neuropathy due to methanol intoxication.

Methods: In this retrospective study, we demonstrated six cases of toxic optic neuropathy due to acute methanol poisoning. Medical charts were evaluated for demographic characteristics of patients, best corrected visual acuity (BCVA), fundus examination, optical coherence tomography, visually evoked potential (VEP) before and after the high-dose intravenous steroid treatment in the first week and the first month.

Results: Ten eyes were involved. All patients were male and the mean age was 49.5±10.59 years. The duration of initiating the therapy was 4.5±1.3 days (3-6 days). BCVA values detected in the first week and the first month after the treatment were compared with those before the treatment, a statistically significant increase was found. In the total retinal nerve fiber layer (RNFL) and Ganglion cell complex (GCC) in the first week, an increased thickness, which was not detected statistically significant, but in the first month, a statistically significant thinning was found. No significant difference was found in the VEP values after the treatment.

Conclusion: For treating toxic optic neuropathy due to methanol, although an increase in visual acuity was observed at the end of the first month, optic nerve values such as RNFL and GCC continue to decrease.

Keywords: Methanol intoxication, retinal nerve fiber layer, toxic optic neuropathy

Introduction

The formaldehyde and formic acid that are formed when methyl alcohol is metabolized by the body have high toxicity to the central nervous system, gastrointestinal system and eyes. In patients who survive the acute phase of intoxication, permanent blindness and pathologies of the central nervous system may be observed (1-4).

Six-thirty hours after the ingestion of methyl alcohol (longer if ingested alongside ethyl alcohol), symptoms such as blurred vision, changes in color vision, diplopia are observed either alone or together with symptoms such as headache, dizziness, nausea, vomiting, abdominal pain. Papilledema, hyperemia, or atrophy can be detected in the fundus examination (1,5-9).

Treatment involves ethanol, gastric lavage, fomepizole, hemodialysis, alkalinization and folic acid (10,11). The aim of this study is to demonstrate six cases, who presented to our hospital during a period of sudden increase in the rate of methanol intoxication in Istanbul and were treated with hemodialysis, Folic Acid and high dose methylprednisolone. In this study, the cases were analyzed retrospectively in terms of the efficiency of systemic steroids on anatomic and functional symptoms together with the pre- and post-treatment.

Methods

Among the patients who presented to the Emergency Service of İstanbul Training and Research Hospital due to fake alcohol consumed at the same venue and diagnosed with methanol intoxication, those who had visual symptoms were referred to the Opthalmology Service of İstanbul Training and Research Hospital.

This retrospective study was conducted with the approval of the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (1183, date: 23.02.2018), in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients and/or relatives before the treatment. The files of the patients whose treatments were regulated and who met the inclusion criteria were analyzed.

The inclusion criteria were; administration of systemic steroid treatment, visual acuity on the seventh day and the first month before and after the treatment, and the completion of biomicroscopy fundus tests, spectral domain optical coherence tomography (OCT) and visual evoked potentials (VEP) measurements.

Patients who had accompanying factors that can cause optic neuropathy, patients who have chorio-retinopathy or amblyopia that can affect visual

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acuity, patients who have uncontrolled systemic and ocular infection, patients who discontinued the steroid use were excluded from the study.

The diagnosis of methanol intoxication was diagnosed based on the fact that the subject attracted interest, all patients had a history of purchasing and ingesting fake alcohol at the same venue, clinical, systemic and ophthalmologic examination, increased anion and osmolar gap.

As treatment, all patients underwent hemodialysis with nephrology consultation. The nephrologists also helped in correcting the metabolic disturbance and sodium bicarbonate dosage. Three doses of folic acid (1 mg/kg) were administered intravenously every other day. The maintenance dose was administered at a dose of 10 mg/day for 2 weeks of oral intake. The patients received 1 g/day of intravenous methylprednisolone every other day for 5 days and continued oral prednisolone at 1 mg/kg for 10 days (12-18). The time of starting the treatment, and demographic characteristics of the patients were recorded.

Patients best corrected visual acuity (BCVA) testing with the logarithm of the minimum angle of resolution (logMAR) measurements were recorded. Anterior segment examination using biomicroscopy, and dilated fundus examination using an indirect ophthalmoscope were performed. VEP (The Neuro-MEP-Micro EMG system, Neurosoft Ltd., 5 Voronin Street, Ivanovo, Russia) and OCT [(Optovue OCT (V 5.1, RTVue 100-2, Optovue, Fremont, CA, USA)] measurements were performed. The patients' cranial magnetic resonance imaging (MRIs) were obtained.

In OCT measurements, the mean central macular thickness (CMT) of both eyes, macular ellipsoid zone integrity, choroidal thickness (CT), total retinal nerve fiber layer (RNFL) thickness, disk topography values (disc area, cup area, rim area, cup volume, rim volume) Ganglion cell complex (GCC) measurements (GCC-RNFL, GCC +, GCC ++) were recorded. BCVA (logMAR), CMT, RNFL, CT, and GCC measurements were compared statistically on the seventh day and the first month before and after the treatment.

Latency (N75, P100, N145) and amplitude (N75-P100, P100-N145) were measured in the pattern VEP measurements. The results were divided into three groups: unable to record data, low latency amplitude detected, and normal latency and amplitude detected.

In the fundus examination, the presence of optic nerve edema and atrophy of the optic disc 1 month before and after the treatment were examined.

Statistical Analysis

For statistical analysis, SPSS 15.0 for the Windows program was used. Descriptive statistics were number and percentage for categorical variables, mean, standard deviation, minimum and maximum for numeric variables. Paired samples t-test, Wilcoxon signed-ranks test, and Friedman test were used in the evaluation of the data. $P<0.05$ was considered significant.

Results

Two patients had right eye involvement and 4 patients had both eyes involved. All patients were male and the mean age was 49.5±10.59 years (34-61 years). The duration of initiating the therapy was 4.5±1.3 days (3-6 days).

BCVA values detected in the first week and the first month after the treatment were compared with those before the treatment, a statistically significant increase was detected (using Wilcoxon Signed-Ranks test; p=0.026 and p=0.042 for the right eye, p=0.038 and p=0.047 for the left eye) (Figure 1). In 80% of patients, an increase in BCVA was detected.

RNFL, in the first week, an increased thickness, which was not statistically significant (right p=0.893, left p=0.854; Wilcoxon signed-ranks test) was detected, in and in the first month, a statistically significant thinning (right p=0.028, left: 0.046; Wilcoxon signed-ranks test) was detected (Figure 2). In disc topography values, no significant difference was detected between the two eyes in the first week and the first month of the treatment (p>0.05 Wilcoxon signed-ranks test and Friedman test).

A statistically insignificant increase in GCC thickness was detected in the first week for the right eye (right p=0.109, left p=0.715; Wilcoxon signed-ranks test) and statistically significant GCC thinning was detected in the first month for both eyes (right p=0.028, left p=0.046; Wilcoxon signed-ranks test) (Figure 3).

No significant difference was found in VEP values in all controls (p>0.05, Wilcoxon signed-ranks test).

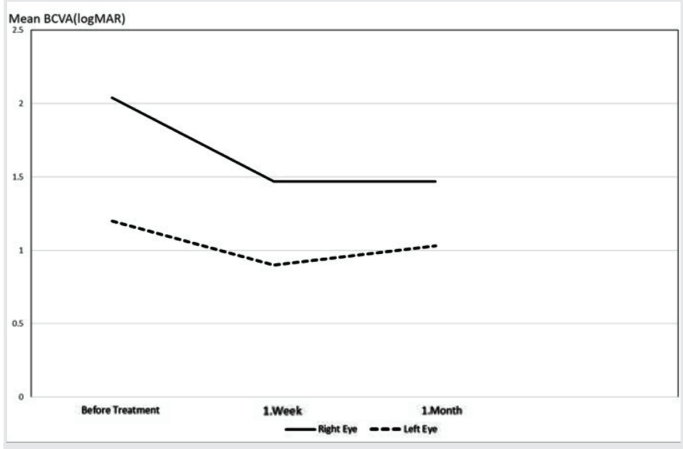

Figure 1. Mean best-corrected visual acuity (LogMAR) changes before treatment, first week and 1st month after the treatment

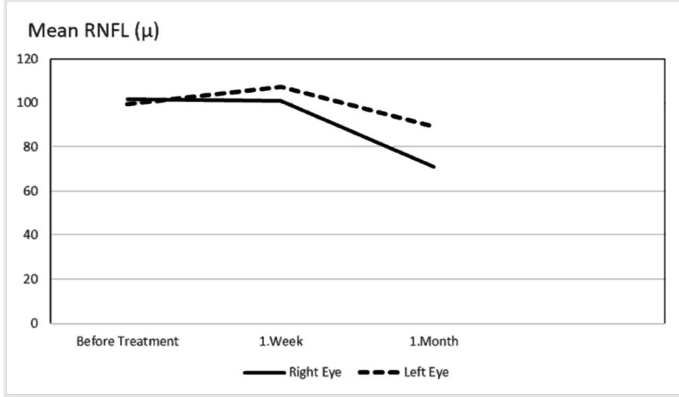

Figure 2. Mean RNFL (μ) changes before treatment, first week and 1st month after the treatment
RNFL: Retinal nerve fiber layer

No significant difference was found in CT, CMT (p>0.05, Wilcoxon signed-ranks test, and Friedman test). Ellipsoid zone was preserved before and after the treatment in all patients.

The mean ± SD of BCVA, RNFL, GCC++, CMT, and p-values (paired sample t-test) of 10 eyes before and after treatment are summarized in Table 1.

Optic nerve edema was detected in both the involved eyes of a patient. Optic nerve edema was not detected in the other involved eyes. At the end of the first month, all the involved eyes had optic disc atrophy.

No systemic corticosteroid-dependent side effects were observed. In the cranial MRI of all patients, brain stem, cerebellum, basal ganglia and cerebral cortices were normal.

Discussion

Formic acid formed upon methanol intoxication causes cellular damage at the mitochondrial level and demyelination of the optic nerve due to its myelinoclastic effect, thus affecting the optic nerve and retrolaminar area and leading to optic nerve edema, necrosis, myelin sheath and axon damages. Formaldehyde inhibits retinal hexokinases and causes retinal pigment epithelium, photoreceptor inner segment and optic nerve damages, as shown in an animal model (19-21).

The main objectives of the treatment are to eliminate methanol and the toxic products, treat metabolic acidosis, and to prevent the metabolization of methanol.

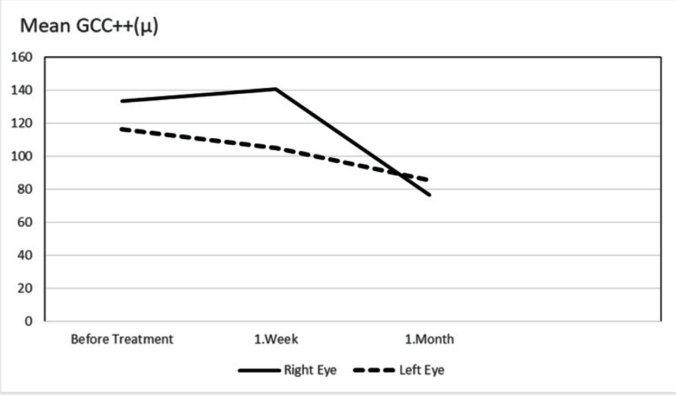

Figure 3. Mean GCC (μ) changes before treatment, first week and 1st month after the treatment
GCC: Ganglion cell complex

Antidotes (fomepizole or ethanol) are used to prevent the conversion of methanol into toxic products. In the early phase, methanol can be removed via gastric lavage. Methanol and its toxic products can be rapidly eliminated by hemodialysis. Folic acid accelerates the conversion of formic acid to carbon dioxide and water (12).

Theoretically, it is considered that optic nerve edema and axon compression in the lamina cribrosa will decrease when systemic steroids are used. The studies on the effect of high dose systemic steroid for treating methanol induce toxic optic neuropathy are mostly case series and there are studies in which increased BCVA is detected.

In the literature, the number of patients varies between 1 and 17, and the duration of starting the steroid treatment varies between 1 and 45 days. The steroid protocol used is 1 mg/kg oral prednisolone for 10-14 days, following 3 doses of 500 mg-1 g/day intravenous methylprednisolone every day or every other day. Shukla et al. (17) Discontinued steroids after 6 weeks by gradually decreasing the dose after 14 days. Our steroid protocol is in accordance with the literature (16,22-25).

In this study, at the end of the first month, an increase was detected in BCVA in 80% of the patients. Sharma et al. (16) have detected increased BCVA in 87.5% of the patients at the end of the first year, and Shukla et al. (17) detected an increased BCVA in 88% of the patients at the end of the first month. A statistically significant increase in BCVA was detected at the end of the first month, and there are studies in the literature, which detected increased BCVA after systemic steroid treatment (22,23,25).

In our study, no difference was detected between the first week and the first month before and after treatment with respect to CT and CMT. Abrishami et al. (22) Found no differences in terms of CMT, but did not specify the CMT values.

After treatment, a slight increase in RNFL was observed in the first week, but it was not statistically significant. However, at the end of the first month, a statistically significant decrease was detected. Fujihara et al. (23) Started treatment in a single case 6 days after methanol intoxication and found an increase in BCVA. This study also found that RNFL initially increased and then decreased.

In this study, differently from the other studies in the literature, GCC parameters were observed and it was found that there was been a thinning in the GCC at the first month, just like RNFL. Moreover,

Table 1. Mean best corrected visual acuity (LogMAR), retinal nerve fiber layer, Ganglion cell complex, central macular thickness values, and p-values before and after treatment of 10 eyes are shown

Parameters	Before treatment	The first week after treatment	The first month after treatment	p^1 p^2
BCVA (logMAR)	1.94±0.52	1.43±0.69	1.27±0.83	**$p=0.002^1$** **$p=0.01^2$**
RNFL	100.1±29.0	104.3±21.1	81.1±19.1	$p=0.54^1$ **$p=0.02^2$**
GCC^{++}	128.4±69.3	136.4±64.8	77.3±20.65	$p=0.06^1$ **$p=0.02^2$**
CMT	251.7±39.1	248.1±31.8	261±27.7	$p=0.19^1$ $p=0.48^2$

BCVA: Best corrected visual acuity, logMAR: Logarithm of the minimum angle of resolution, RNFL: Retinal nerve fiber layer (μ), GCC^{++}: Ganglion cell complex (μ), CMT: Central macular thickness (μ), p^1: p-values (Paired sample t-test) first week after treatment, p^2: p-values (Paired sample t-test) first month after treatment

no statistically significant difference was detected between the disc topography values identified using OCT.

We found structural and functional changes, especially in BCVA, RNFL, and GCC in the first week and month after methanol intoxication. Therefore, monitoring patients during this period may be important. Because OCT is used for monitoring many optic nerve head diseases, it may also be used for toxic optic neuropathy due to methanol intoxication. Further studies are needed on this subject.

Study Limitations

The limitations of our study are the small number of patients, retrospective structure, lack of a control group and lack of randomization. However, in our study, in addition to BCVA, OCT parameters were also included. Considering the side effects of high dose systemic steroids, more studies are required on this subject.

Conclusion

In conclusion, for treating toxic optic neuropathy due to methanol, although an increase in BCVA is observed at the end of the first month, optic nerve values such as RNFL and GCC continue to decrease.

ETHICS

Ethics Committee Approval: This retrospective study was conducted with the approval of the University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethics Committee (1183, date: 23.02.2018), in accordance with the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all patients and/or relatives before the treatment.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: P.S., H.G., F.Ç.; Design: P.S., H.G., F.Ç.; Data Collection and/or Processing: P.S., H.G., F.Ç.; Analysis and/or Interpretation: P.S., H.G., F.Ç.; Literature Search: P.S., H.G., F.Ç.; Writing: P.S., H.G., F.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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