Visual outcome of methanol toxic optic neuropathy after erythropoietin treatment in Riyadh, Saudi Arabia

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Abstract:

PURPOSE: The purpose of this study is to evaluate the visual response of methanol-induced optic neuropathy to management with erythropoietin (EPO) along with conventional therapy.

METHODS: This retrospective case series examines the ophthalmological data of patients diagnosed with methanol-induced optic neuropathy between 2020 and 2021 at two centers, Riyadh, Saudi Arabia. Patients' characteristics and the results of initial and final ophthalmological examinations were documented and compared between patients who received EPO in addition to conventional management and those who received only conventional management.

RESULTS: A total of nine cases were reviewed, of which eight (88.9%) were males and one was female (11.1%). The mean age was 37.7 years. At presentation, funduscopic examination revealed optic disc edema in four eyes (two patients), and 14 eyes had normal appearance (seven patients). Among the nine patients who received conventional management, 5 (55.6%) additionally received intravenous EPO during the treatment course. There was no clinically or statistically significant difference in terms of visual outcome between the two groups. The mean visual acuity at the final presentation was 1.32 ± 0.79 logarithm of the minimum angle of resolution (LogMAR) in the EPO group and 1.36 ± 0.85 LogMAR in the non-EPO group. Optical coherence tomography indicated that the EPO group had an average retinal nerve fiber layer thickness of 48.13μm (±6.2), at the final assessment.

CONCLUSION: Managing the visual impairments in individuals with methanol-induced optic neuropathy using intravenous EPO resulted in similar final visual outcomes compared to conventional management.

Keywords:

Erythropoietin, methanol, optic neuropathy, toxicity

Introduction

Methanol intoxication is a dangerous condition that can lead to serious sequela with significant morbidity and mortality rates. Commercially, it is a common constituent of solvents which present in detergents, perfumes, copy-machine fluids, and antifreeze formulations such as windshield-washer fluid. Methanol exposure is unusual but may occur accidentally among children due to exploratory behavior, as well as in adults from methanol-contaminated ethanol (homemade ethanol). Less commonly, it occurs intentionally in suicide attempts. It is sometimes used in illegal spirit drinks as a cheap substitute for ethanol.[1] Multiple outbreaks of methanol poisoning have been reported in different regions with visual disturbance as one of the most commonly reported presentations.[2,3]

The management of methanol intoxication mainly includes ethanol or fomepizole as antidotes, bicarbonate, folate, and, when indicated, extracorporeal elimination (mostly hemodialysis). Ethanol and fomepizole prevent further toxin formations by interfering with the metabolism of methanol to formic acid, while bicarbonate, serves to buffer acidosis. Folate facilitates the metabolism of formic acid into carbon dioxide and water; and extracorporeal elimination removes methanol and its toxic metabolites.[1]

Erythropoietin (EPO) is a known hematopoietic glycoprotein that increases erythrocyte mass by

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inhibiting the apoptosis of red blood cell progenitors. Other than the hematopoietic effect, as demonstrated by multiple experimental studies, it has been suggested that EPO has anti-inflammatory,[4] antiapoptotic,[5] and neuroprotective characteristics.[6,7] EPO research conducted on different ophthalmological conditions such as ischemic retinal disease,[8] retinal ganglion cell protection,[9] and optic neuropathy[7-9] have shown promising therapeutic potential.[10] In a retrospective study assessing the visual outcome of late-stage optic neuropathy, intravitreal EPO showed no clinical differences.[11] A prospective noncomparative study of 16 cases with methanol-induced optic neuropathy reported a significant increase in visual acuity after EPO administration.[12] However, the inconsistency in the findings of previous comparisons necessitates further studies. Therefore, the aim of this study is to assess the visual outcome of methanol-induced optic neuropathy managed with EPO in addition to conventional management.

Methods

This is a retrospective case series that examined nine patients seen at two large centers in Riyadh, Saudi Arabia. The computer databases of all centers were searched for all patients who had a diagnosis of methanol-induced optic neuropathy between March 2020 and October 2021. We report ophthalmological data that were documented in medical records of patients who survived and had vision loss within 2 weeks of methanol ingestion. Patients with visual disturbances attributed to any other ocular, neurological, or systemic diseases were excluded from the study.

All of the included patients were identified as cases of methanol intoxication by experienced emergency medicine specialists and a neuro-ophthalmologist. Methanol-induced optic neuropathy was defined as a painless progressive reduction of vision with evidence of recent methanol ingestion in the absence of other ocular causes. The data collected included patient characteristics such as age at diagnosis and gender; details about the acute phase of intoxication including the onset of symptoms, the time from ingestion to presentation at the emergency department (ED); ophthalmological examination results, the volume of the ingested methanol reported by the patients; and arterial blood-gas tests (pH, PCO_2, HCO_3, base excess, and anion gap) were collected. Data about therapies were also obtained, including fomepizole, ethanol, bicarbonate, folic acid, Vitamin B1, corticosteroid, and hemodialysis treatments.

The initial and final ophthalmological examinations consisted of the best-corrected visual acuity (BCVA), color vision test, visual field, pupillary reaction, anterior segment and funduscopic examination, and retinal nerve fiber layer (RNFL) thickness according to optical coherence tomography (OCT). Some of the patients admitted (5, 55.6%) additionally received 20,000 IU of intravenous EPO (human recombinant) for 3 consecutive days as a daily infusion over 45 min. Those patients were considered as the EPO group, and their outcomes were compared to the patients who did not receive EPO.

Patient data were collected and analyzed by means of descriptive statistics. For the purpose of comparison, the Snellen chart acuity was converted to the logarithm of the minimum angle of resolution (LogMAR) with the values of 1.9, 2.3, 2.7, and 3.0 considered for visual analog scale of counting fingers (CF), hand motion (HM), light perception (LP), and no LP (NLP), respectively. The study was conducted after obtaining approval from the institutional review boards of the research ethics committees of the two centers. All data were maintained confidential without using identifiers, and subjects' privacy and confidentiality were assured.

Results

There were a total of nine cases (18 eyes), of which eight patients were males, and one was female. The mean age was 37.67 years (±16.86). Visual symptoms started within 24 h after methanol ingestion in six cases, while in the remaining three cases, symptoms appeared within 48 h or beyond. The mean amount of ingested methanol was 621 ± 16.86 ml. Five patients had results for arterial blood gases, which showed metabolic acidosis with a high anion gap. The patient characteristics on presentation and the treatment given are shown in Table 1.

At the initial presentation, bilateral visual involvement was noted in eight patients (88.89%). Pupils had a sluggish reaction in two patients (22.22%), and five patients (55.56%) had a

Table 1: Patient's characteristics and management

Case number	Age/sex	Time of presentation	Onset of symptoms (within) (h)	Treatment regimen
1	72/male	1st day	24	IV ethanol + folic acid + hemodialysis
2	26/male	2nd day	24	Fomepizole + bicarbonate + folic acid + Vitamin B1 + hemodialysis
3	42/male	3rd day	48	IV ethanol + Vitamin B1 + hemodialysis + oral corticosteroids
4	24/male	1st day	24	Fomepizole + bicarbonate + folic acid + Vitamin B1 + hemodialysis
5	33/male	7th day	After 48	Folic acid + Vitamin B12 + IV corticosteroids + IV EPO
6	31/female	1st day	2	Bicarbonate + Vitamin B1 + IV corticosteroids + IV EPO
7	58/male	3rd day	After 48	Vitamin B12 + hemodialysis + inhaled corticosteroids + IV EPO
8	23/male	1st day	24	Fomepizole + bicarbonate + folic acid + Vitamin B1 + hemodialysis + IV EPO
9	30/male	1st day	24	Folic acid + Vitamin B12 + hemodialysis + IV corticosteroids + IV EPO

EPO: Erythropoietin, IV: Intravenous

relative afferent pupillary defect. Visual field assessment was possible in four eyes, which showed a full visual field in three eyes (16.67%) and inferior nasal defect in one eye (5.56%). However, in the remaining eyes, the visual field could not be assessed due to poor vision or lack of cooperation. Funduscopic examinations showed optic disc edema in four eyes (22.22%), and 14 eyes (77.78%) had normal appearance, as shown in Table 2.

For all nine included patients, the median follow-up time was 84 days, and there were no reported adverse events. There was a documented improvement of vision in seven eyes (38.89%), among which three improved from NLP, LP, and HM to CF; one eye improved from CF to 20/100; and one eye improved from 20/30 to 20/20. In two eyes from the EPO group, there was a dramatic improvement from CF to 20/20 at the initial phase of the treatment, which was later followed by visual deterioration to 20/400 in both eyes.

The mean visual acuity in the EPO patients at the final visit was 1.32 ± 0.79 LogMAR. In comparison, 1.75 ± 0.72 LogMAR was obtained in the initial assessments (−0.43). In the non-EPO group, the final mean visual acuity was 1.36 ± 0.85 LogMAR compared to 1.46 ± 0.99 LogMAR at the initial assessment (−0.1). There was no marked improvement between the initial and final assessments in terms of color vision and pupillary reaction in both groups. The fundus examination revealed optic-disc pallor in the final examination in all eyes, and optic-disc edema resolved. The systemic and visual findings based on the management received are summarized in Table 3.

OCT was initially performed on seven eyes, which had total thicknesses of RNFL of 124, 102, 139, 141, 69, 154, and 155 μm (126.3 ± 31.22 μm). The final OCT readings of RNFL of the same eyes after receiving EPO were 45, 42, 59, 49, 53, 43, and 42 μm, respectively. In one eye, there was disc swelling, and the final OCT measurements showed an RNFL of 52 μm. The average thickness of the RNFL at the final assessment was 48.13 μm (±6.20), with a mean difference from the baseline readings of 78.71 μm (±33.37). Unfortunately, no initial or final OCT readings were available for the non-EPO group.

In addition, the vertical cup-to-disc ratio (CDR) was assessed among the EPO group using the OCT measurements. In three eyes, the initial vertical CDRs were 0.61, 0.38, and 0.17, which progressed to 0.89, 0.71, and 0.87, respectively. Two eyes had an initially healthy-looking disc, and the vertical CDRs were measured as 0.79 and 0.97 at the final assessment. In another two eyes, only the final vertical CDRs were available (0.91 and 0.94).

Discussion

In the past 2 years, there seems to have been an increase in the incidence of methanol toxicity reports. As spirits and other alcoholic drinks are prohibited in Saudi Arabia, the increase in the number of patients is attributed to the lockdown and travel ban that occurred as a consequence of the COVID-19 pandemic. This could have led to increased consumption of unbranded and homemade alcohol. The present study evaluated nine patients admitted to two major centers in Saudi Arabia as cases of visual loss induced by methanol toxicity. All of the included patients were males except for one, and the majority were young or middle aged. All of them sought ophthalmological assessment for serious visual loss at least 3 days following methanol poisoning. Among all patients, the mean visual acuity at the initial assessment was equivalent to 20/800, while at the final assessment, it was 20/400. All nine patients received conventional systematic management, and 5 of them additionally received IV EPO.

Methanol is metabolized mainly in the liver by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase into formic acid. Formic acid is highly toxic and is responsible for metabolic acidosis, which occurs through the inhibition of aerobic metabolism by blocking the activity of

Table 2: Initial and final ophthalmologic findings of the cases

Case number	Time from encounter to ophthalmological examination (day)	Initial			Final		
		BCVA (OD/OS)	Pupil	Fundoscopy	BCVA (OD/OS)	Pupil	Fundoscopy
1	1st day	HM/CF@2 FT	RAPD (OS)	Normal	CF/CF	RAPD (OU)	Optic disc pallor (OU)
2	2nd day	20/20	RRR	Normal	22.5/20	RRR	Optic disc pallor (OU)
3	7th day	CF@ 6 FT/ CF@4 FT	Sluggish	Normal	CF@4 FT/ CFNF	RAPD (OS)	Temporal disc pallor (OU)
4	4th day	400/LP	RAPD (OS)	Normal	400/CF	RAPD (OU)	Temporal disc pallor (OU)
5	14th day	CFNF/CFNF	RRR	Optic disc edema (OU)	HM/CFNF	RAPD (OU)	Optic disc pallor (OU)
6	16th day	CFNF/CFNF	Sluggish	Normal	400/400	RRR	Optic disc pallor (OU)
7	4th day	30/200	RAPD (OS)	Normal	20/CFNF	RAPD (OS)	Optic disc pallor (OU)
8	6th day	CF@1 FT/ CFNF	RAPD (OS)	Normal	CF@5 FT/ CF@1 FT	Sluggish	Optic disc pallor (OU)
9	10th day	CF/NLP	RAPD (OS)	Optic disc edema (OU)	100/CF @3 FT	RRR	Optic disc pallor (OU)

OD: Right eye, OS: Left eye, OU: Both eyes, BCVA: Best-corrected visual acuity, RRR: Round in shape, regular, and reacting to light, RAPD: Relative afferent pupillary defect, CF: Counting finger, HM: Hand motion, LP: Light perception, NLP: No LP, CFNF: CF near the face

Table 3: The systemic and visual findings based on the management

	EPO group (*n*=5 patients, 10 eyes)	Control group (*n*=4 patients, 8 eyes)	Total (*n*=9 patients, 18 eyes)
Age (years), mean±SD (minimum–maximum)	35±13.40 (23–58)	41±22.18 (24–72)	37.67±16.86 (23–72)
Level of ingested methanol (mL), mean±SD (minimum–maximum)	450±251.66 100–700)	850±132.29 (750–1000)	612.43±288.47 (100–1000)
Laboratory test, mean±SD			
pH	6.39±0.55	7.07±0.26	6.80±0.50
HCO_3	8.33±3.21	9.33±2.08	8.83±2.48
Initial ophthalmologic examination			
Visual acuity, mean±SD (LogMar)	1.75±0.72	1.46±0.99	1.62±0.84
Color vision, *n* (%)			
Normal	1 (10)	4 (50)	5 (27.78)
Abnormal	1 (10)	2 (25)	3 (16.67)
Pupillary reaction, number of patients (%)*			
RRR	1 (20)	1 (25)	2 (22.22)
Sluggish	1 (20)	1 (25)	2 (22.22)
RAPD	3 (60)	2 (50)	5 (55.56)
Fundus examination, *n* (%)			
Normal optic disc	6 (60)	8 (100)	14 (77.78)
Optic disc pallor	0	0	0
Optic disc edema	4 (40)	0	4 (22.22)
Final ophthalmologic examination			
Visual acuity, mean±SD (LogMar)	1.32±0.79	1.36±0.85	1.34±0.80
Color vision, *n* (%)			
Normal	1 (10)	4 (50)	5 (27.78)
Abnormal	3 (30)	2 (25)	5 (27.78)
Pupillary reaction, number of patients (%)*			
Normal	2 (40)	1 (25)	3 (33.33)
Sluggish	1 (20)	0	1 (11.11)
RAPD	2 (40)	3 (75)	5 (55.56)
Fundus examination, *n* (%)			
Normal optic disc	0	0	0
Optic disc pallor	10 (100)	8 (100)	18 (100)
Optic disc edema	0	0	0

*Pupillary reaction: Presented as number of patients (%). Data are presented as number of eyes (%) unless otherwise stated. RRR: Round in shape, regular and reacting to light, RAPD: Relative afferent pupillary defect, EPO: Erythropoietin, SD: Standard deviation, LogMar: Logarithm of the minimum angle of resolution

intra-mitochondrial cytochrome C oxidase.[1] Martin-Amat *et al*. confirmed the effect of methanol on cytochrome C oxidase in animal studies, in which the enzyme's inhibition was found to be prominent in retrolaminar and laminar regions of the optic nerve.[13] In addition, acidosis seems to augment formic-acid diffusion and mitochondrial damage through the production of hydroxyl radicals and reactive oxygen species.[14,15] Formic acid is converted to CO_2 and H_2O slowly through processes requiring folate, which is normally present in small amounts in the human liver. Because it is not easily eliminated, formic acid accumulation, through its effect on mitochondrial oxidative respiration, leads to retinal toxicity, optic neuropathy, necrosis of basal ganglia, and end-organ damage.[1,16]

The vulnerability of optic-nerve regions might be explained by the higher energy requirements and cytochrome C oxidase activity, which is supported by the findings of Barron *et al*.[17] In methanol-induced optic neuropathy, when unbound formic acid targets the optic nerve, it causes axonal injury and myelin-sheath destruction. The consequent myelin-sheath swelling and edema result in axonal trauma through compression-type injury to optic nerve fibers. This condition is further escalated by concomitant acidosis and leads to retrograde ganglion-cell degeneration and conduction deficit.[14,18] Patients can have different ophthalmological presentations ranging from snowfield or blurred vision to total blindness. This could be attributed to variations in ingested methanol concentration, rate of metabolism, and the degree of metabolic acidosis among the patients involved. As reported by Sanaei-Zadeh *et al*., snowfield and blurred vision are transient, and some patients experience some recovery from blindness but never normalize.[19] In this study, the bilateral decrease of vision was the initial complaint in 88.89% of the patients. The majority had visual symptoms starting within 24–48 h from methanol exposure, which is consistent with the interval reported in multiple previous studies.[20,21] This latent period probably represents the slow degradation of methanol into its metabolites and the time for formic acid to accumulate and diffuse intracellularly.

The management of methanol poisoning focuses on inhibiting further formic acid formation by ADH enzyme

blockers (ethanol or fomepizole), correction of acidosis with bicarbonate, and folinic/folic acid, and immediate extracorporeal elimination of toxic metabolite by hemodialysis, if indicated.[22-24] Nonetheless, success rates in restoring visual function are limited among survivors and serious visual deficit may persist.[19] In general, the documented outcomes of methanol-induced optic neuropathy are poor with eventual unsatisfactory visual function.

With the administration of IV EPO, the cytoprotective function is attributable to not only the increase of erythrocyte supply, but EPO may also have a direct cellular antioxidative effect that occurs by recruiting intracellular mechanisms such as glutathione and heme oxygenase-1. In addition, it seems to indirectly stimulate iron depletion with consequent inhibition of iron-dependent oxidative insult.[25]

Two previous studies reported some improvement in the vision of patients who received IV EPO. According to Pakdel *et al*., the median visual acuity significantly increased posttreatment from LP to 1.00 LogMAR, and rapid improvement was noted when EPO injections were administered within 3 weeks from methanol exposure.[21] Pakravan and Sanjari found improvement in vision in both the control group and the EPO group, but BCVA was significantly better in the latter ($P = 0.012$).[12] In the present study, no remarkable difference was found between the two groups in terms of final visual improvement, despite the fact that the same dosage of EPO injection of 20,000 IU daily for 3 consecutive days was standardized as in the previously reported studies. It is noteworthy that one patient from the EPO group showed a dramatic increase in visual acuity from CF near the face to 20/20 in both eyes. This could indicate a transient effect of EPO on vision, as reported by Zamani *et al*., who examined three patients who had similar visual deterioration after their early improvement when they were followed up with a mean interval of 2 months.[26] In the present study, the patient with the transient improvement completed a follow-up period with the longest interval among the involved patients (more than 1 year). This might indicate a progressive nature of the disease with a latent visual disturbance that could only be detected with a sufficient follow-up period. In this regard, it is clear that a larger sample size and longer follow-up duration are needed.

As supported by Fujihara, the axons of papillomacular bundles that are abundant in mitochondria are disproportionately altered in methanol-induced optic neuropathy. Therefore, acute swelling of the peripapillary nerve fiber layer and chronic diffuse retinal thinning are direct consequences of methanol's toxic effects.[27] In this study, the final average RNFL thickness of patients treated with EPO was 48.13 μm (−78.71 μm), which indicates greater thinning compared to the findings of the EPO group in a previous study. The RNFL thickness in patients treated with EPO reported by Pakravan and Sanjari showed an average of 77 μm with a difference of −53.64 μm from baseline.[12] The less-affected RNFL in the previous study could be explained by the shorter follow-up interval for the EPO group.

This study is subject to multiple limitations due to the small number of patients and the absence of randomization. The retrospective nature of the study might also have resulted in selection bias. Furthermore, we could not conclude that EPO is effective in managing visual defects nor can we decline the hypothesis. This could be the result of patients being treated in various stages of intoxication, with different timing, and with different management modalities. Some confounding factors could not be standardized. The levels of ingested methanol were lower and more patients received IV corticosteroid in the EPO group compared to the non-EPO group. Additional variables, including visual field defect and color vision, could not be analyzed due to significantly insufficient data. Future prospective studies with a large number of patients are needed to validate the magnitude of EPO in treating methanol-induced optic neuropathy, alone and in conjugation with systemic therapy.

Conclusion

The use of IV EPO in the management of visual disturbances in patients diagnosed with methanol-induced optic neuropathy showed a major but transient improvement in one patient, and no adverse events were reported. However, these findings cannot be generalized, and prospective comparisons with sufficient control and a larger sample size are required. Furthermore, studies addressing the optimal effective dose of EPO and intervention interval are recommended. Methanol toxicity leads to significant visual impairment, and promoting public education could potentially minimize its morbid effects.

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Conflicts of interest

There are no conflicts of interest.

References

1. Jacobsen D, McMartin KE. Methanol and ethylene glycol poisonings. Mechanism of toxicity, clinical course, diagnosis and treatment. Med Toxicol 1986;1:309-34.
2. Rostrup M, Edwards JK, Abukalish M, Ezzabi M, Some D, Ritter H, *et al.* The methanol poisoning outbreaks in Libya 2013 and Kenya 2014. PLoS One 2016;11:e0152676.
3. Gulen M, Satar S, Avci A, Acehan S, Orhan U, Nazik H. Methanol poisoning in Turkey: Two outbreaks, a single Center experience. Alcohol 2020;88:83-90.
4. Feng Q. Beyond erythropoiesis: The anti-inflammatory effects of erythropoietin. Cardiovasc Res 2006;71:615-7.
5. Weishaupt JH, Rohde G, Pölking E, Siren AL, Ehrenreich H, Bähr M. Effect of erythropoietin axotomy-induced apoptosis in rat retinal ganglion cells. Invest Ophthalmol Vis Sci 2004;45:1514-22.
6. Mammis A, McIntosh TK, Maniker AH. Erythropoietin as a neuroprotective agent in traumatic brain injury Review. Surg Neurol 2009;71:527-31.
7. Kucuk B, Cevik Y, Acar U, Sobaci G. Therapeutic potential of erythropoietin in retinal and optic nerve diseases. CNS Neurol Disord Drug Targets 2015;14:1225-34.
8. Jehle T, Meschede W, Dersch R, Feltgen N, Bach M, Lagrèze WA. Erythropoietin protects retinal ganglion cells and visual function after ocular ischemia and optic nerve compression. Ophthalmologe

2010;107:347-53.
9. King CE, Rodger J, Bartlett C, Esmaili T, Dunlop SA, Beazley LD. Erythropoietin is both neuroprotective and neuroregenerative following optic nerve transection. Exp Neurol 2007;205:48-55.
10. Abri Aghdam K, Soltan Sanjari M, Ghasemi Falavarjani K. Erythropoietin in ophthalmology: A literature review. J Curr Ophthalmol 2016;28:5-11.
11. Acar U, Kucuk B, Sevinc MK, Aykas S, Erdurmus M, Sobaci G. Intravitreal erythropoietin injection in late-stage optic neuropathy: A safety study on human. Int Ophthalmol 2018;38:1021-5.
12. Pakravan M, Sanjari N. Erythropoietin treatment for methanol optic neuropathy. J Neuroophthalmol 2012;32:325-8.
13. Martin-Amat G, Tephly TR, McMartin KE, Makar AB, Hayreh MS, Hayreh SS, *et al.* Methyl alcohol poisoning. II. Development of a model for ocular toxicity in methyl alcohol poisoning using the rhesus monkey. Arch Ophthalmol 1977;95:1847-50.
14. Sharpe JA, Hostovsky M, Bilbao JM, Rewcastle NB. Methanol optic neuropathy: A histopathological study. Neurology 1982;32:1093-100.
15. Skrzydlewska E. Toxicological and metabolic consequences of methanol poisoning. Toxicol Mech Methods 2003;13:277-93.
16. Zakharov S, Nurieva O, Kotikova K, Urban P, Navratil T, Pelclova D. Factors predicting optic nerve axonal degeneration after methanol-induced acute optic neuropathy: A 2-year prospective study in 54 patients. Monatsh Chem 2015;147:251-61.
17. Barron MJ, Griffiths P, Turnbull DM, Bates D, Nichols P. The distributions of mitochondria and sodium channels reflect the specific energy requirements and conduction properties of the human optic nerve head. Br J Ophthalmol 2004;88:286-90.
18. McMartin KE, Ambre JJ, Tephly TR. Methanol poisoning in human subjects. Role for formic acid accumulation in the metabolic acidosis. Am J Med 1980;68:414-8.
19. Sanaei-Zadeh H, Zamani N, Shadnia S. Outcomes of visual disturbances after methanol poisoning. Clin Toxicol (Phila) 2011;49:102-7.
20. Sharma R, Marasini S, Sharma AK, Shrestha JK, Nepal BP. Methanol poisoning: Ocular and neurological manifestations. Optom Vis Sci 2012;89:178-82.
21. Pakdel F, Sanjari MS, Naderi A, Pirmarzdashti N, Haghighi A, Kashkouli MB. Erythropoietin in treatment of methanol optic neuropathy. J Neuroophthalmol 2018;38:167-71.
22. Zakharov S, Pelclova D, Navratil T, Belacek J, Komarc M, Eddleston M, *et al.* Fomepizole versus ethanol in the treatment of acute methanol poisoning: Comparison of clinical effectiveness in a mass poisoning outbreak. Clin Toxicol (Phila) 2015;53:797-806.
23. Zakharov S, Nurieva O, Navratil T, Diblik P, Kuthan P, Pelclova D. Acute methanol poisonings: Folates administration and visual sequelae. J Appl Biomed 2014;12:309-16.
24. Roberts DM, Yates C, Megarbane B, Winchester JF, Maclaren R, Gosselin S, *et al.* Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: A systematic review and consensus statement. Crit Care Med 2015;43:461-72.
25. Katavetin P, Tungsanga K, Eiam-Ong S, Nangaku M. Antioxidative effects of erythropoietin. Kidney Int Suppl 2007;27:S10-5.
26. Zamani N, Hassanian-Moghaddam H, Shojaei M, Rahimian S. Evaluation of the effect of erythropoietin+corticosteroid versus corticosteroid alone in methanol-induced optic nerve neuropathy. Cutan Ocul Toxicol 2018;37:186-90.
27. Fujihara M, Kikuchi M, Kurimoto Y. Methanol-induced retinal toxicity patient examined by optical coherence tomography. Jpn J Ophthalmol 2006;50:239-41.