F_2a prostaglandins are not known to cause immune suppression, angiogenesis, or cancer. Further, these effects have certainly not been shown with latanoprost specifically. Latanoprost is the leading selling glaucoma medication worldwide and has 8 years of treatment experience. Case reports of series of tumours, immune problems, or angiogenesis have not been published. Further, such related side effects were not observed in well-controlled regulatory trials or in postapproval studies.

In addition, the clinical effect of a prostaglandin depends upon the available tissue levels. Two drops of latanoprost completely absorbed and dispersed into the total body water would have a peak plasma concentration of approximately 3×10^{-8} M (14 mg/l). Tissue studies show that it is very difficult to stimulate the FP receptor at this concentration. Further, the half-life of latanoprost in the plasma is probably 15 min. For this reason, latanoprost has not been shown conclusively to cause any systemic side effect.

Again, we agree with the authors in encouraging all ophthalmologists to be aware of side effects of glaucoma medicines. However, caution in the use of a glaucoma medicine must be based on rational knowledge of pharmacology and known side effects balanced with clinical efficacy and need of a medicine in the population to prevent blindness.

WC Stewart[1], AGP Konstas[2]

[1]Department of Ophthalmology
University of SC School of Medicine
Columbia, SC, USA

[2]Department of Ophthalmology
AHEPA Hospital Thessaloniki Greece

Correspondence: WC Stewart
Tel: +1 843 762 6500
Fax: +843 762 7444
E-mail: info@prnorb.com

Eye (2005) **19,** 805–806. doi:10.1038/sj.eye.6701639; published online 10 September 2004

Sir,

Ocular manifestations and MRI findings in a case of methanol poisoning

Methanol, which is usually used as an industrial solvent or automobile antifreeze, is a highly neurotoxic material. Accidental or intentional ingestion of methanol can produce severe metabolic acidosis, permanent neurological deficits, blindness, and death.[1] Toxic optic neuropathy caused by methanol intoxication is rarely reported. Here, we described a patient with methanol poisoning who developed profound vision loss and severe brain damage with characteristic bilateral haemorrhagic necrosis of the putamen shown on magnetic resonance imaging (MRI). The patient survived and significantly improved after intravenous steroids and osmotic diuretics treatment; but with optic atrophy.

Case report

This 49-year-old male was sent to a municipal hospital because of sudden loss of consciousness for 1 day. At the emergency room, he was unresponsive with shallow respiration. He was intubated immediately and put on mechanical ventilation. Blood gas and biochemical analyses revealed severe metabolic acidosis (pH 6.8, HCO_3 7 mEq/l), elevated liver enzymes and ammonia. Brain computed tomography images were unremarkable at that time. Initially, he was treated for metabolic acidosis. Under the impression of methanol intoxication, he underwent emergent haemodialysis. On the fourth day following exposure, blood methanol level was reported to be extremely high (811 mg/dl). The patient was transferred to our hospital for further management.

Information from the patient's family revealed that he had had headache, nausea, vomiting, general weakness, visual disturbance, and shortness of breath 1 day before his admission. All the above symptoms occurred several hours after drinking an unknown amount of home-made herbal wine, which he obtained from a friend.

He was successfully weaned from the respirator at our hospital. However, impaired consciousness, total blindness, and poor movement of his extremities were noted. An electroencephalogram showed diffuse cerebral dysfunction, compatible with the diagnosis of metabolic encephalopathy. The initial fundoscopic examination in both eyes showed moderately swollen, hyperaemic optic disc and dilated, unresponsive pupillary reflex. Visual-evoked potentials revealed marked suppression without identified waveform. Brain MRI performed on day 15 demonstrated multifocal necrosis in the bilateral putamen and frontal and occipital subcortical white matter regions, and marked perifocal vasogenic brain oedema (Figure 1). Intravenous corticosteroids were administered, initially with 300 mg hydrocortisone, and then 100 mg every 6 h. Intravenous osmotic diuretics were also used with 10% 300 ml glycerol every 8 h. Over the following 3–4 days, his consciousness gradually recovered, he became alert, and his motor function

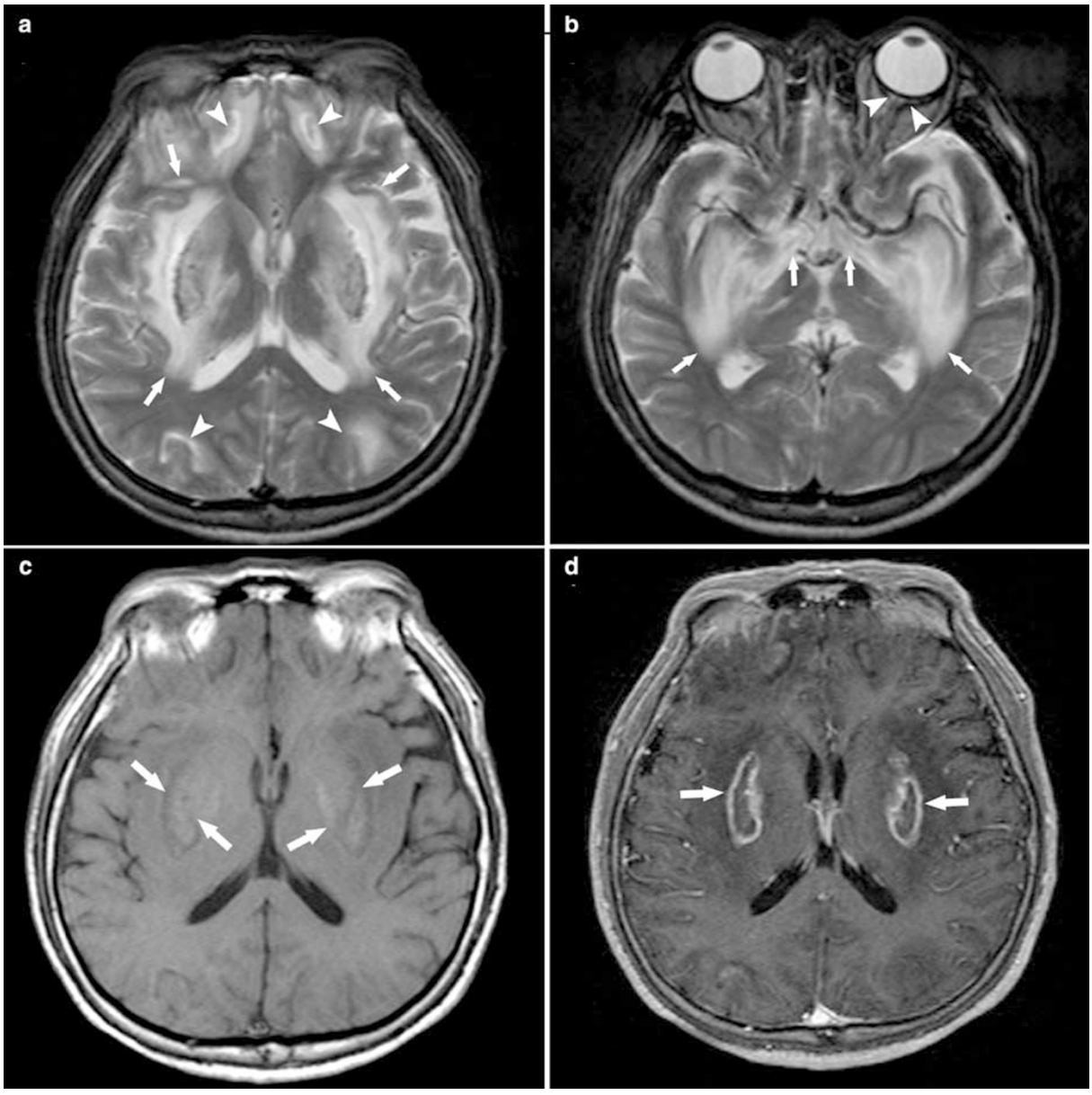

Figure 1 MRI on day 15 after methanol intoxication. (a) T2-weighted image showed high signal abnormalities in bilateral basal ganglia (arrows), frontal, and occipital subcortical white matter (arrowheads), consistent with oedematous change. (b) T2-weighted image showed oedematous change involving bilateral optic tracts and optic radiations (arrows). High signal oedematous change was also noted in the optic disc of left eye (arrowheads). (c) T1-weighted image showed slightly high signal component in bilateral basal ganglia, indicating the haemorrhage (arrows). (d) T1-weighted image with gadolinium administration showed marginal enhancement in bilateral putamen, indicating breakdown of the blood–brain barrier.

steadily improved. However, total blindness in both eyes persisted.

At 2 months after the accident, his visual acuity was still no light perception in either eye. His pupils measured 6 mm and were not reactive to light. Intraocular pressure was 13 mmHg OD and 15 mmHg OS. Fundoscopic examination showed bilateral optic atrophy and glaucomatous-like cupping of the optic disc with a narrow neuroretinal rim (Figure 2). Fluorescein angiography revealed hypoperfusion of the optic nerve head in both eyes, with an indiscernible neuroretinal rim. MRI on day 60 disclosed resolution of brain oedema. However, a residual putamen necrosis lesion was still noted.

Comment

Methanol (methyl alcohol) is an uncommon but life-threatening poison. Despite knowledge of its toxicity,

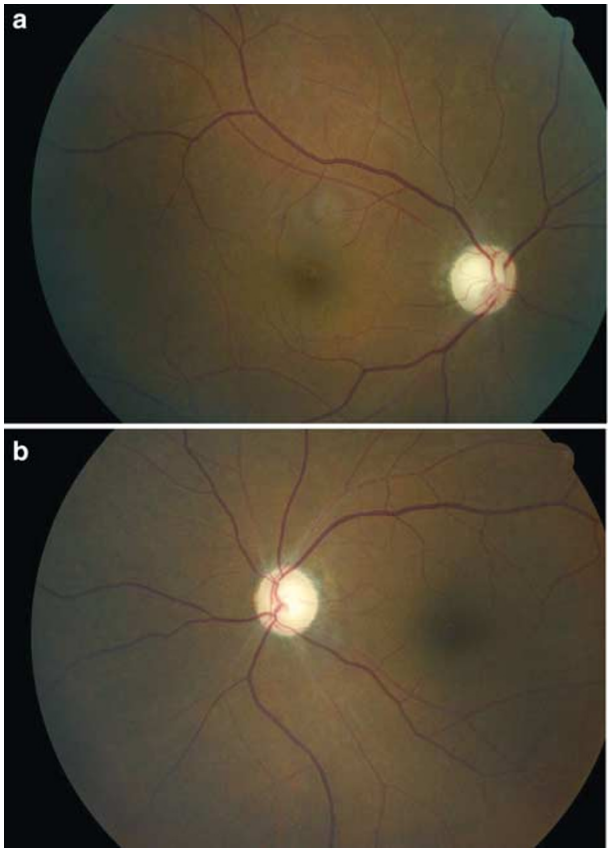

Figure 2 Fundus photography 2 months after methanol intoxication showed optic atrophy with glaucomatous-like cupping of the optic discs, and narrow neuroretinal rim with 0.9 cup in (a) right eye and 0.7 cup in (b) left eye. There was generalized narrowing of the retinal arteries.

methanol is rarely substituted for ethyl alcohol by unscrupulous wine makers. Methanol is primarily metabolized in the liver by hepatic alcohol dehydrogenase to formaldehyde. Formaldehyde is then converted by aldehyde dehydrogenase to formic acid. Although both formaldehyde and formic acid are extremely toxic, systemic metabolic acidosis caused by the accumulation of formic acid is thought to be the major toxic effect of methanol.[2] Besides the acidosis, the most important clinical features of methanol poisoning are damage to optic nerve and central nervous system. The onset of the symptoms of methanol poisoning is usually delayed for 12–24 h, and this latent period corresponds to the time required for methanol to be oxidized to its toxic metabolites.[2] Dizziness, headache, nausea, vomiting, weakness, abdominal pain, and blurring vision are the most common presenting symptoms. Dyspnoea, coma, convulsion, and blindness may subsequently occur in severe poisoning.

As methanol poisoning is potentially fatal, its prompt diagnosis and treatment is very important. However, in the emergency room, acute methanol poisoning might not be readily diagnosed, especially when we are facing an unconscious patient as in this case. Moreover, these toxicological facilities are not available in most hospitals. And, the laboratory results of methanol usually take more than 1 day to be complete. Wide serum anionic and osmotic gaps are auxiliary tools for its diagnosis, and fundoscopy might be another useful alternative. The management of acute methanol poisoning is gastric lavage, correction of the metabolic acidosis, competitive inhibition of methanol oxidation by ethanol or 4-methypyrazole, and the removal of both formate and methanol by haemodialysis.[3]

Our patient survived. However, he had permanent visual sequelae, which might be due to severe metabolic acidosis and treatment delay. Once the ocular toxicities occur, the probability of vision recovery after poisoning is poor. Optic atrophy is a common outcome,[4] although according to a recent report high doses of intravenous steroids may protect the vision of patients with methanol-induced optic neuropathy.[5] In our case, the neurological manifestations were significantly improved after treatment with steroids and diuretics. In spite of this, benefit to the visual system was not obvious. Therefore, treatments should be given as early as possible, before the irreversible optic neurological damage occurs. Generally, the prognosis of methanol-induced toxic optic neuropathy is determined by the methanol dose at exposure, the length of any treatment delay, and the pupillary response on presentation.

Methanol is particularly toxic to the optic nerve, leading to acute blindness. Based on a histopathological study,[1] the retrolaminar optic nerve myelin sheath seems to be selectively vulnerable to methanol poisoning due to its anatomical structure. In the acute phase, the hyperaemia and swelling of the optic disc has a papilloedema-like appearance.[4] The axoplasmic flow stasis at the nerve head and alteration of the myelin sheath in the retrolaminar nerve segment were demonstrated in experiments using rhesus monkeys.[6] The pathogenesis is presumed to be histotoxic anoxia in a vascular watershed area, which is the result of direct inhibition of cytochrome oxidase by formic acid.[7] Additionally, the increasing pressure following oedema in the visual pathway might further aggravate the deterioration due to ischaemic changes. Therefore, effective methods to treat the oedema might be important, such as the use of intravenous steroids and diuretics.[5] The mechanism of subsequent optic atrophy in patients with methanol poisoning is still unknown, it was suggested to be due to progressive demyelination.[8] The distinct glaucomatous-like cupping of the optic disc suggests extensive loss of retina ganglion cells, which has

been thought to result from retrograde degeneration of optic nerve axons.[8]

The bilateral haemorrhagic necrosis of the putamen and oedema in the deep white matter of our patient are the characteristic MRI findings of severe methanol intoxication.[9] Besides the optic disc oedema, the oedematous changes involving optic tracts and optic radiations shown on MRI might contribute to the profound vision loss in our case. The MRI in methanol poisoning not only demonstrates this specific pattern of brain damage but also provides good correlation among brain, visual pathway, and the evolution of the clinical course of the disorder.

In conclusion, methanol poisoning is a rare entity, and historically difficult to treat. Furthermore, it is worthwhile to study the administration of steroids, osmotic diuretics, antioxidants, vitamins, or other methods in protecting the optic nerve in acute or subacute phases of methanol poisoning in the future.

Acknowledgements

This study was supported by grants from National Science Council, Department of Health and Veterans General Hospital, Taiwan.

References

1 Sharpe JA, Hostovsky M, Bilbao JM, Rewcastle NB. Methanol optic neuropathy: a histopathological study. *Neurology* 1982; **32**: 1093–1100.
2 Mcmartin KE, Ambre JJ, Tephly TR. Methanol poisoning in human subjects: role of formic acid accumulation in metabolic acidosis. *Am J Med* 1980; **68**: 414–418.
3 Lushine KA, Harris CR, Holger JS. Methanol ingestion: prevention of toxic sequelae after massive ingestion. *J Emerg Med* 2003; **24**: 43–46.
4 Benton CD, Calhoun FP. The ocular side effects of methyl alcohol poisoning: report of a catastrophe involving 320 persons. *Trans Am Acad Ophthalmol Otolaryngol* 1952; **36**: 875–883.
5 Sodhi PK, Goyal JL, Mehta DK. Methanol-induced optic neuropathy: treatment with intravenous high dose steroids. *Int J Clin Pract* 2001; **55**: 599–602.
6 Baumbach GL, Cancilla PA, Martin-Amat G, Tephly TR, McMartin KE, Makar AB *et al*. Methyl alcohol poisoning IV: alterations of the morphological findings of the retina and optic nerve. *Arch Ophthalmol* 1977; **95**: 1859–1865.
7 Hayreh MS, Hayreh SS, Baumbach GL, Cancilla P, Martin-Amat G, Tephly TR *et al*. Methyl alcohol poisoning III: ocular toxicity. *Arch Ophthalmol* 1977; **95**: 1851–1855.
8 Sharma M, Volpe NJ, Dreyer EB. Methanol-induced optic nerve cupping. *Arch Ophthalmol* 1999; **17**: 286.
9 Kuteifan K, Oesterle H, Tajahmady, Gutbub AM, Laplatte G. Necrosis and hemorrhage of the putamen in methanol poisoning shown on MRI. *Neuroradiology* 1998; **40**: 158–160.

C-S Yang[1,2], W-J Tsai[2,3] and J-F Lirng[2,4]

[1]Department of Ophthalmology
Taipei Veterans General Hospital
Taipei, Taiwan, Republic of China

[2]National Yang-Ming University School of Medicine Taipei, Taiwan, Republic of China
[3]Division of Clinical Toxicology
Taipei Veterans General Hospital
Taipei, Taiwan, Republic of China

[4]Department of Radiology
Taipei Veterans General Hospital,
Taipei, Taiwan, Republic of China

Correspondence: C-S Yang
Tel: +886 2 28757325
Fax: +886 2 28761351
E-mail: csyang@vghtpe.gov.tw

Proprietary interest: none.

Eye (2005) **19,** 806–809. doi:10.1038/sj.eye.6701641; published online 24 September 2004

Sir,

Trypan blue vital staining of the anterior lens capsule in the management of cataract in true exfoliation of the lens capsule

True exfoliation or lamellar delamination of the lens capsule is a rare disorder characterised by thickening of the lens capsule with marked splitting of the superficial portion of the anterior lens capsule from the deeper layers, which then extends creating an unusual floating membrane structure in the anterior chamber.[1–3] There are no reports of patients with this condition undergoing modern phacoemulsification cataract surgery.

We describe a case in which completion of a continuous curvilinear capsulorhexis (CCC) was permitted by the use of trypan blue vital staining and uncomplicated phacoemulsification was completed.

Case report

A 65-year-old gentleman was referred to the eye clinic for consideration of cataract surgery. He complained of a gradual reduction in visual acuity over several months. There was no past ophthalmic history of note and no known systemic illness. He was taking no medication.

On examination, his visual acuities (VA) were 6/18 right and 6/12 left. Slit-lamp examination of the anterior segments demonstrated a striking floating membrane