Centre for Eye Health

Chair-side Reference: Screening Ocular Toxicity of Selected Drugs

Optometry
NEW SOUTH WALES
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Many systemic drugs have ocular side effects, some of which are potentially sight threatening. It is important to monitor and screen patients on these drugs as early detection and reporting to appropriate medical practitioners may be critical in preventing irreversible vision loss. This chairside reference describes the major potential ocular side effects related to selected systemic drugs, in particular those that with RPE/retinal implications.

Non-vision threatening toxicity such as vortex keratopathy from amiodarone is outside the scope of this reference. This reference provides recommendations on the workup and ongoing follow-up intervals in an optometric setting. It is not intended to cover the spectrum of all ocular side effects of systemic drugs (e.g. drugs that induce mydriasis, dry eyes, and steroids), nor is it designed to provide guidance on intervention or treatment.

Drug name	Use	Potential sight-threatening complication	Onset	Signs & Symptoms	Clinical examination recommendation*					Screening recommendation
					CV	VF	CFP	OCT	FAF	
Amiodarone (Cordarone)	Anti-arrhythmia	Optic neuropathy	Months	Insidious visual loss (mostly bilateral), colour vision abnormalities, variable field defect, disc oedema.	✓	✓ 30-2	✓	✓		Baseline evaluation before treatment, every 4, 8 and 12 months after treatment initiation, yearly thereafter or on an as-needed basis depending on clinical findings.
Fingolimod (Gilenya)	Anti-multiple sclerosis	Macular oedema	Months	Painless blurred vision, metamorphopsia, reduced VA.		✓ Amsler	✓	✓		Baseline evaluation before treatment, 3-4 months after treatment initiation. Advise patient to use Amsler grid self-monitoring. Patients with diabetes and uveitis are at a higher risk and may need to be screened more closely. Patients who undergo intraocular surgery also need pre and post-operative assessment.
Chloroquine (Nivaquine, Avlocor) Hydroxychloroquine (Plaquenil)	Anti-malarial, anti-rheumatologic	Bull's eye maculopathy	Years	Paracentral scotoma, nyctalopia, focal thinning of photoreceptors and RPE abnormality (early), vision loss and Bull's eye maculopathy (later).		✓ 10-2 for all, 30-2 (if FAF abnormal)	✓	✓		Baseline evaluation within the first year and yearly screenings begins after 5 years, sooner if risk factors (high dosage HCQ>5.0mg/kg real weight, CQ>2.3mg/kg real weight, long duration>5 years, renal disease, tamoxifen use, concomitant macula disease) are present.
Tamoxifen (Nolvadex)	Anti-neoplastic	Crystalline maculopathy; macular oedema	>1 year	Often asymptomatic. Bilateral fine deposits in perifoveal region, foveolar cyst; visual acuity loss if macula oedema or haemorrhages present.	✓		✓	✓		Baseline evaluation within first year and then 3-6 monthly if symptomatic. No continued screening is required if there is absence of signs and symptoms.
Interferon-alfa (Intron, Rebetron)	Anti-neoplastic	Ischaemic retinopathy; optic neuropathy	Months	Often asymptomatic, intraretinal haemorrhages and/or cotton wool spots (CWS).			✓	✓		Baseline evaluation before treatment and 3 monthly assessments thereafter.
Vigabatrin (Sabril)	Anti-epileptic	Irreversible field restriction	Months to years	Normal VA, bilateral, concentric or bi-nasal visual field defects, fundus is typically normal. May have disc pallor, arteriolar narrowing and/or abnormal macular reflexes.		✓ HVA full field screening or kinetic perimetry		✓		Initial visual field screening before treatment then every 6 months for 5 years. Yearly thereafter if no defects are present. If a visual field defect is noted, repeat within one month to confirm. Use threshold 30-2 to monitor progression. Electrophysiology is indicated if field testing is not viable.
Topiramate (Topamax)	Anti-epileptic	Angle closure glaucoma	Weeks	Blurred vision, ocular and/or periorbital pain, headache, increased IOP, myopic shift, angle closure, cilio-choroidal effusion.	✓ Gonio/ UBM					Baseline evaluation should include gonioscopy. Routine review is not recommended. Warn patients of side effects and symptoms and to seek urgent attention if they occur.
Thioridazine (Aldazine) Chlorpromazine (Thorazine)	Anti-psychotic	Pigmentary retinopathy	Months	Slightly reduced VA, nyctalopia, dyschromatopis, Salt-and-pepper pigmentary disturbance in mid-periphery and posterior pole, focal or diffuse loss of RPE and choriocapillaris.	✓		✓	✓	✓	Baseline evaluation followed by yearly review or sooner for high dose (>600mg per day)
Ethambutol (Myambutol)	Anti-tubercular	Optic neuropathy	Months	Sudden vision loss, colour vision abnormalities, central scotoma, normal or slightly swollen optic nerve.	✓	✓ 30-2	✓	✓		Baseline evaluation before treatment, followed by every 4 weeks if daily dose>15mg/kg, every 3-6 months for lower dose
Canthaxanthin	Anti-psoriasis	Crystalline maculopathy	Dose-dependent	Often asymptomatic, refractile, yellow-orange deposits form a ring-like pattern in perifoveal region.			✓	✓		Baseline evaluation followed by yearly review
Deferoxamine (Desferal, Desferrioxamine, deferasirox)	Iron chelator for transfusional haemosiderosis	Pigmentary retinopathy; optic neuropathy	Months	Decreased vision, nyctalopia, dyschromatopisa, field loss, multiple discrete hypo-pigmented lesions at posterior pole and mid-peripheral retina.	✓	✓	✓	✓	✓	Baseline evaluation followed by screening at 6-monthly intervals. Electrophysiology may be helpful in monitoring retinal dysfunction
Filler for intravenous narcotics	Talcum powder	Macular/retinal ischaemia; crystalline maculopathy	Unknown	Decreased vision, scotoma, bilateral hyper-reflective intraretinal small yellow deposits in macula, arterial occlusion, CWS, AV anastomosis, neovascularisation of the disc or in the periphery.			✓	✓		Baseline evaluation for current and past IV drug users For active IV drug users, monitor routinely for emboli and their ischemic sequelae
Methanol	Solvent, anti-freeze, recreational	Optic neuropathy	Within hours with high dose	Decreased central and/or peripheral vision, colour vision abnormalities, disc atrophy.	✓	✓ 30-2	✓	✓		Baseline evaluation should include a detailed history to identify other factors associated with toxic/nutritional optic neuropathy such as tobacco/alcohol abuse, vitamin deficiencies etc.

Visual field test program and pattern outlined are based on Humphrey Visual Field Analyser (HFA), equivalent tests are available in other perimeters

^ Onset may vary depending on dose and duration.

* In addition to comprehensive dilated fundus examination.

Key

CV: colour vision
VF: visual field
CFP: colour fundus photograph
FAF: fundus autofluorescence
UBM: ultrasonic biomicroscopy

A unique case:

Idiopathic, thyroid eye disease or myopia-associated esotropia syndrome?

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This original case report was submitted by fellow Optometry Australia member Laura Carson in response to our nation-wide call for papers.

A 23-year-old female myopic female presented with symptoms of intermittent diplopia, worse when wearing glasses than soft contact lenses (CLs). Visual acuity (VA) with her monthly replacement CLs were R 6/7.5 and L 6/6. Motilities and pupil reactions were normal.

Cover test while wearing CLs found esophoria at distance and near, with a magnitude of 9 prism dioptres (PD) and 19 PD, respectively. Spectacle refraction results were R -5.00/-1.25x100 VA 6/6- and L -5.00/-0.75x65 VA 6/6- with 6 base out (BO) PD split to neutralise intermittent esotropia. Stereopsis was 200 seconds of arc. Fundus examination was unremarkable (Figure 1).

She was diagnosed with transiently decompensating esophoria and a review for cycloplegic refraction was scheduled to determine if the underlying cause was accommodative. In the meantime, she was prescribed monthly replacement high add multifocal CLs, aiming to control the esophoria.

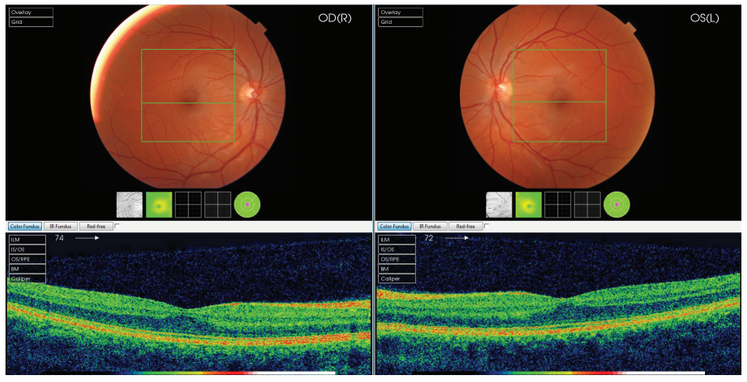

Figure 1. Macula OCT and fundus images

Review 1

The patient was reviewed two weeks later. She reported general improvement with the change to her CL prescription but was still closing one eye to eliminate occasional diplopia. Cycloplegic refraction results were consistent with previous findings and confirmed the need for prism correction. She was prescribed prescription glasses with 6 BO prism divided and a separate pair of plano glasses with fresnel prism (10 BO) for over the top of her CL's, to be used when driving. Thankfully this combination was satisfactory until she re-attended 12 months later for an update to her glasses and CL prescription, maintaining the prism corrections with both.

Review 2

Another 12 months later, the patient attended with symptoms of almost constant diplopia in her CL's and felt unable to wear them for long periods of time. Cover testing found a 18 PD esophoric deviation at distance when wearing CL's. Her existing 10 BO fresnel glasses only just controlled her diplopia. In glasses she was esotropic and exhibiting suppression at distance; cover test measured a total of 10 BO to neutralise the esotropia. Additionally, distance base in fusional reserves were limited with break at 2 PD, resolution at 1 PD. Aside from increasing the prism correction in her glasses, alternative management such as modifying her CLs and referral for an opinion on strabismus surgery was discussed.

Figure 2. Upgaze left and right abduction showing non commutative versions

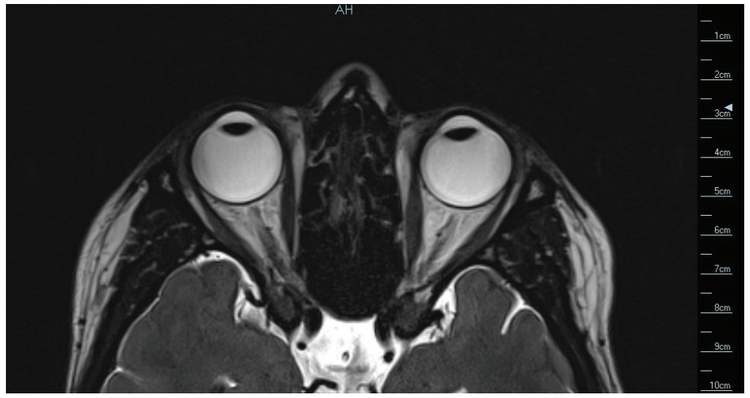

Figure 3. MRI of eye socket and slightly bulky extraocular muscles

Referral

After unsuccessful trials of alternative contact lens options, she was referred to a strabismus specialist. The ophthalmologist confirmed the measurements of her esophoria to decompensating esotropia and limited stereo acuity. Interestingly, considering her level of myopia, axial lengths were found to be R 24.11 and L 23.94 mm. She was also found to have R superior oblique underaction and associated non commutative versions (Figure 2) indicating possible abnormal lateral rectus muscle pulley anatomy. Differential diagnoses therefore became one of the myopia-associated esotropia syndromes, such as heavy eye syndrome or knobby eye syndrome.

She was sent for magnetic resonance imaging (MRI) to investigate further. The consultant radiologist reported that the MRI (Figure 3) showed 'somewhat prominent' extraocular muscles but still 'symmetrical in appearance and position.' They hypothesised Graves' disease, introducing a new differential diagnosis, however, blood tests did not confirm any active thyroid levels. The patient no longer wanted to be reliant on any level of prism correction so decided to proceed with surgical intervention–strabismus surgery.

One week post-surgery the findings were promising. VA's were R 6/7.6 and L 6/7.6 with glasses (a pair was made up without prism prior to surgery). She had near esotropia but distance orthophoria as well as an improvement in her stereopsis results, achieving 100 sec of arc.

Two weeks later, she attended with symptoms of worsening vision; VA with existing glasses was R 6/12+ and L 6/9.5= and refraction found a myopic shift of -0.75 in each eye, enabling a best corrected VA of R&L 6/6-. At her scheduled review with the ophthalmologist, her myopic shift was confirmed along with findings of improved stereoacuity of 70 sec of arc. She maintained distance orthophoria, albeit still with low fusional reserves. It was hypothesised that a change in corneal topography (Figure 4A, 4B) had caused the myopic shift, however, when her pre-and post-operative topography maps were compared (Table 1) this hypothesis was found to be unlikely.

Two months after surgery, the patient was found to have a stable prescription of R -7.00 VA 6/6- and L -6.25/-0.50x10 VA 6/6- which was prescribed in spectacles. Cover test found residual esophoria of 1 PD at distance and 4 PD at near. The patient is very pleased to be relieved of prismatic correction and has returned to wearing spherical monthly replacement CLs.

It has not been possible to ascertain a final diagnosis but this case highlights the management pathway and successful outcome of strabismus surgery in a unique case of progressive esophoria.

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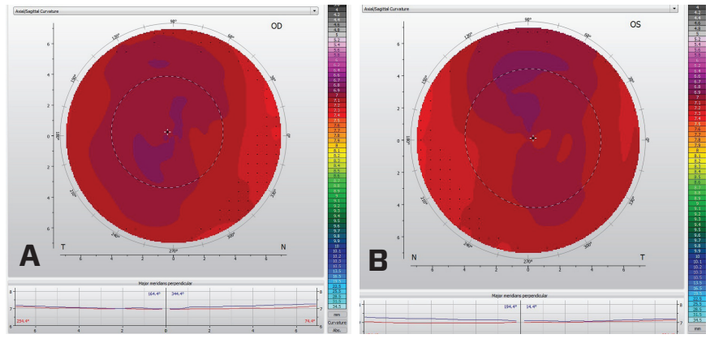

Figure 4. A: Right eye and B: left eye

	Right Eye (D)	Left Eye (D)
Pre-Surgical (IOL Master A scan)	47.60x142/48.28x52	47.54x21/48.56x111
Post-Surgical (Easygraph Topographer)	47.70x165/48.30x75	47.40x14/48.40x104

Table 1. Keratometry readings