My Vision is Blurry: Could it be from any of the medications that I am taking?

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Mark Dunbar: Disclosure
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“I am having blurry vision – could this be from any of the medications that I am taking?”

Systemic Interactions
• At least 76 classes of systemic drugs have been associated with ocular side effects
• Drug can interact with and disrupt any step of the biochemical process resulting in deleterious effects to the ocular tissues
• Drugs may incite an exaggerated immune response within the eye
  – Uveitis or retinitis
• Penetration by certain systemic meds may cause deposition of the solidified form of the molecule

Systemic Interactions
• Medications may cause alteration of the pigment
  – Plaquenil -> Bull’s eye maculopathy
• Pharmacologic toxicity can occur leading to cell death and loss of function
  – Can affect the optic nerve
• Patient variability may influence and cause unexpected effects
  – Pharmaceutical studies provide statistical evidence supporting appropriate dosage for meds, however individual variation can result in unexpected results

What are your/our obligations in deciding if certain medications that a patient is taking are affecting the patients vision?
How About This One…

- 37 y/o Hispanic female presented with a recent onset of blurred vision OU x 1 mo – 3 episodes
- Currently taking Rifampin, Ethambutol, Clarithromycin 5 mo prior for MAC (TB)
  – PCP recommended eye exam when starting meds
- VA: 20/20 RE; 20/25 – corrects to 20/20 LE
  – Very low hyperopic correction (+0.25)
- CVF: FTFC OU, Pupils: Normal
- Normal fundus exam

Ethambutol Toxic Neuropathy

- 1st described by Leibold in the 1960’s
- Dose dependent
- Risk is 6-18% for pts with dose > 30 mg/kg/day (18% at 35 mg/kg/day)
- Develops in 1-3% at dose 15-25 mg/kg/day

Ethambutol

- TB regimens begin at either 50 mg/kg/day (maximum 4 grams) for 2 weeks or 25-30 mg/kg/day (maximum 2 grams) for 3 weeks, and then maintained at 15-20 mg/kg/day (max 2 grams)
- For MAC regimens the maintenance dose is 15 mg/kg/day (maximum 2.5 grams).
  – Depending on the species of mycobacteria pts, may be treated with a loading dose of 25 mg/kg/day for the first two months of therapy (Mandell et al., 2005; Micromedex 2007).

Ocular side effects:
- Optic neuritis/neuropathy and blindness.
- Change tears, sweat, saliva, urine, feces and contact lenses a red-orange color.

Anti-tuberculosis drugs

- Ethambutol HCL (Myambutol), Isoniazid (Laniazid), Rifampin (Rimactane)
- Chelates copper, so the decreased levels impair mitochondrial activity of axonal transport in optic nerve leading to optic neuropathy

51 y/o White Female

- 1st presented to OD practice 11/24/09 with blurred vision distance and near
  – Also typical dry eye symptoms
- Was noted to be on plaquenil 100 mg bid
- BCVA: 20/40 each eye with myopic correction (~ -2.50)
- Color Vision: 3/5
- CVF: FTFC OU – screening perimetry done
- Fundus: Normal, screening photo done
  – Patient refused dilation

Anti-tuberculosis drugs

- Ophthalmic examinations are recommended by the PDR every month for doses of ethambutol greater than 15mg/kg/day.
- No official standard of care exists in dosages less than 15 mg/kg/day.
- Optic neuropathy can occur at any dose despite regular ophthalmic exams: vision loss can be severe and irreversible.
- Obtain a baseline exam to include a visual field test, color vision test, dilated fundus and optic nerve exam, and visual acuity.
- If any visual symptoms occur, patients should discontinue the medication and see an ophthalmologist.
6/14/2012: 16 mo later

- “Blurred vision, at all ranges, night blindness or difficulty.”
- Entering VA: 20/40
- BCVA: 20/30 OU
- Fields: full, pupils normal
- Color: 3/5
- Fundus: seen with 90D, pupil dilation not ordered
  - Macula normal

11 mo later: 5/23/2013

- See’s other OD in community
  - VA: 20/30 OU
- Orders VF for the next week – 6/10/2013
  - Pt returns as directed

What are your obligations for managing a patient on plaquenil?

- What is the risk of having ocular problems from plaquenil?
- What testing is necessary?
- How often do you need to follow her?

Plaquenil (Hydroxychloroquine)

- Prescribed in 200 mg tablets
  - Dose is 200mg or 400mg daily
- Risks for macular damage include
  - Cumulative dose of 1000g
  - 5-7 years or more of use
  - 1% risk after 1000g total dose (7 years)
  - Renal or hepatic dysfunction (both)
  - Pre-existing macular pathology
  - Short stature / obesity

Plaquenil Screening: Traditionally

- Baseline macula photos
- Color vision testing
- Amsler grid
- 10-2 Visual fields
- Yearly exams

Revised Recommendations on Screening for Plaquenil Toxicity

- Amsler grid testing removed as an acceptable screening technique
  - NOT equivalent to threshold VF testing
- Strongly advised that 10-2 VF screening be supplemented with sensitive objective tests such as:
  - Multifocal ERG
  - Spectral domain OCT
  - Fundus autofluorescence

Ophth Feb 2011
Revised Recommendations on Screening for Plaquenil Toxicity

Tests **Not Recommended** for Screening:
- Fundus photography
- Time domain OCT
- Fluorescein angiography
- Full-field ERG
- Amsler grid
- Color vision screening
- EOG

Revised Recommendations on Screening for Plaquenil Toxicity

- Parafoveal loss of visual sensitivity may appear before changes are seen on fundus evaluation
- Many instances where retinopathy was unrecognized for years as field changes were dismissed as “non-specific” until the damage was severe
  - 10-2 VF should always be repeated promptly when central or parafoveal changes are observed to determine if they are repeatable

Revised Recommendations on Screening for Plaquenil Toxicity

- Older literature focused on daily dose/kg
- Newer literature emphasizes cumulative dose as the most critical factor
- Initial baseline
  - Within 1 year of beginning medication
  - Then screening for toxicity should be initiated no later than 5 years after starting the medication

Revised recommendations on screening for retinopathy

65 y/o Hispanic Female
History of Metastatic Beast Ca
On Chemo: Abraxane, Gemzar
Blurred VA OU X 2 mo
Impression

• Severe Non-Staining CME
• No Pertinent Ocular History to Explain
• Let's look at the literature:

Abraxane (Paclitaxel)

• Member of the “taxane family” of microtubule stabilizing agents that has demonstrated clinical efficacy in multiple human malignancies
• Toxic effects to bone marrow is the predominant adverse effect
• Ophthalmic adverse effects include: decreased vision, scintillating scotomas, and abnormal VEP’s.
• Non-staining CME was 1st reported in 2007 and other cases have since been reported.

Follow Up

• Informed oncologist and medications stopped
  – Different medications started
• CME Resolved and Vision Returned to 20/25 OU

Patient History

57 y/o White Female

• Presented on 2/29/08 with decreased vision, near > distance
• 2o CC: can my medicine affect my eyes
  – Meds
    • Pegasys
    • Copegus
    • Visine prn

LEE: 1970’s

Ocular Hx

• Punched in her eyes
• Penetration of tree bark into eye socket
• Metal fragments in eyes
• No glasses

Medical Hx

• Hepatitis C (2006)
• ADHD
• MVA (2000) resulting in positional vertigo
• Basal cell carcinoma X 3 (arm, chest)
Clinical Exam

- BCVA: 20/20 OD (+1.25 DS), +2.00 add
  20/20 OS (+1.25 DS)
- Confrontation: FTFC OU
- EOM: full
- External: unremarkable
- Pupils: 3 mm OU, PERRL, (-) APD
- BP: 133/79 mmHg @ 3:00p

Interferons (Intron A/Avonex/Pegasys)

- Interferons
  - Delayed type hypersensitivity reaction.
  - In many infectious and systemic diseases, the deposition of immune complexes with subsequent complement activation is a major pathogenic mechanism for the development of uveitis

Ocular Side Effects:
- Cotton wool spots
- Optic neuritis
- Ocular pain
- Conjunctivitis
- Pronounced dry eye
- Dilated eye exam prior to treatment and 2-4 weeks after treatments

Antiarrhythmics

Amiodarone (Cordarone)

Photosensitizer, tendency towards lipid storage in the cornea and lens
Dose and duration dependent, usually reversible

Ocular side effects
- Vortex Keratopathy
  - Nearly 100% pts treated greater than 6 months
  - <10% bothered by blurred vision or haloes
- Anterior and posterior subcapsular lens changes
- Optic neuropathy

Digoxin (Digitek)

Inhibition of Na+K+ ATPase which plays a vital role in maintaining normal cone receptor function and ciliary epithelium responsible for active transport of sodium necessary for aqueous secretion

Ocular Side Effects
- Affects cone receptor function
- 11-25% of patients red-green color defects
- Yellow tinged vision (xanthopsia)
- Snowy, hazy, or dimming vision
- Flickering or flashes of light, and colored spots
- Reduces aqueous secretion and IOP

Ever wonder why there is a predominance of the color yellow in most of Van Gogh’s works?

- In the 19th century, Digitalis was widely used; often to treat epilepsy, mania, asthma, and among others.
- Vincent van Gogh was diagnosed as having Epilepsy and Mania
- He was said to have been prescribed Digitalis by his attending physician, who was interestingly enough, painted by Van Gogh beside a Foxglove plant, where Digitalis is derived
- Digitalis was widely used and plasma level controls were non-existent. One can, therefore imagine how easy it was to prescribe an overdose of digitalis at the time.
- Van Gogh suffered from Xanthopsia, a distortion in color vision, in which objects appear more yellow than they truly are; a usual sign of Digitalis Toxicity.

What drug is prescribed for breast cancer and reducing the incidence of breast cancer among high-risk women
Tamoxifen citrate

- Tamoxifen competitively binds to estrogen receptors on tumor cells and other tissue targets, producing a nuclear complex that decreases DNA synthesis and inhibits estrogen effects.

Ocular Side Effects:
- Crystalline retinopathy
- Treatment involves withdrawal of the drug as it is reversible
- Ocular complications are rare (0.6%)

Corticosteroids

Prednisone
- To treat inflammatory and allergic conditions.
- They are very effective for acute disease states as well as chronic conditions

Ocular Side Effects
- Posterior subcapsular cataract
- Elevated intraocular pressure
- Papilledema
- Exacerbation of herpetic keratitis

Corticosteroids
- Cataracts resulting from steroid use are well known and occur with topical, systemic, and nasal administration.
- The development of cataract is related to the cumulative dose of prednisone; 25% of patients who use 15 mg/day for 1 year or more will get cataracts that interfere enough with vision to require surgical removal
- The etiology is unknown, the drug may react with amino groups of crystalline lens fibers causing protein complexes to aggregate

ERECTILE DYSFUNCTION

- Viagra (sildenafil citrate)
- Cialis (tadalafil)
- Levitra (vardenafil)
- Staxyn (vardenafil HCl)
- Stendra (avanafil)

Viagra inhibits phosphodiesterase-5 (PDE-5) which results in vasodilation of smooth muscle.

Ocular Side Effects
- Objects have color tinges—usually blue or blue-green, may be pink or yellow
- 11% of patients on 100mg perceive a blue haze up to four hours
- Dark colors appear darker
- Visual disturbances
- NAION

A man reports discoloration of vision after taking a medication from his pill box last night?
ERECTILE DYSFUNCTION

- Ocular side effects are dose-dependent with all three drugs.
- For sildenafil side effects occur at the following incidences:
  - 50mg 3%
  - 100mg 10%
  - 200mg 40-50%
- The side effects based on dosage with sildenafil start 15-30 minutes after ingestion of the drug, and usually peak 60 minutes after ingestion.

Patients who should not take phosphodiesterase type 5 inhibitors are those who have previously suffered ischemic optic neuropathy (NAION) in one eye or anyone who experiences transitory visual loss while on these medications.
- These patients may be more prone to developing NAION in the same or fellow eye if sildenafil or other medicines in this class are ingested.

What is the OD’s Responsibility in Determining if Meds are Causing Ocular Side-effects?
- It’s impossible to be aware of every class of meds and their possible side-effects!
- If a patient specifically asks (or is sent by physician) it is your responsibility/obligation to find out the answer
  – Just because the eye exam seems normal doesn’t mean that it is….
- Don’t be afraid to admit that you don’t know
  – “Let’s look it up…”