Clinical Pharmacology & Toxicology Pearl of the Week

Amiodarone – Part 3 - Ophthalmologic Toxicity

The following is part of a series of reviews detailing specific organ toxicity of amiodarone, including basic information, diagnosis, and management.

Ocular adverse-effects:

- ✓ More than 90% of patients will develop corneal deposits (of unclear significance)
  - Deposited from lacrimal secretion
  - They can be associated with mild photophobia
  - Dubious reports of cataract development in a presbyopic population using antiarrhythmic agents
- ✓ < 5% of patients report visual changes, mostly halos (secondary to corneal deposits, as above)
- ✓ Rare case reports of purported amiodarone associated optic neuropathy (AAON), although this association has not born out in registry cohorts that include 10 000 person-years of follow up.
  - Two main (proposed) subtypes:
    - Sub-acute nonarteritic anterior ischemic optic neuropathy (NAION) – progressing over weeks to months
    - Acute NAION (sudden vision loss over days)

Optic Neuropathy Presentation: (Posterior eye disease)

- ✓ Progressive central vision loss
- ✓ Usually, bilateral involvement (Unlike traditional NAION) – although monocular vision complaints are observed
- ✓ Relative afferent pupillary defect is present
- ✓ Fundoscopy:
  - Hyperemic disc
  - Disc edema
- ✓ Pathology: Similar to peripheral neuropathy findings, accumulation of inclusion bodies along the axon. However, inclusion bodies occur in all tissue of patients receiving amiodarone

Risk Factors: (Amiodarone associated eye disease)

Anterior: (Corneal)

- ✓ Virtually all patients will have corneal depositions (evidence of amiodarone exposure, not toxicity)

Posterior: (Optic Neuropathy) – Weak purported association

- ✓ Men > Women (~70% of reported cases in men)
- ✓ Age > 50 years old (average age: 66-68)
- ✓ Amiodarone duration (before onset of subjective vision changes) - mean: ~ 1-3 years **(median: 6-9 months)**
- ✓ Speculation: Amiodarone serum steady-state concentration >2.5 mg/L
  Speculation: Other risk factors - Frailty, polypharmacy, digoxin co-administration

Management:

- ✓ Ophthalmic assessment at baseline – many will have pre-existing ophthalmic problems
  - Amiodarone is often a bystander and not the culprit for these conditions
- ✓ Visual halos or photophobia with higher doses:
  - Continued monitoring, but can continue with amiodarone
  - Annual ophthalmic exam
- ✓ Optic neuropathy:
  - Discontinuation of amiodarone was associated with an improvement in vision in about ~50-60% of patients
  - Vision will typically stabilize upon cessation of amiodarone
  - Disc edema and vision improvement (months) – Drug elimination takes up to a year given the prolonged half-life of amiodarone (~56 days) and longer for metabolites
- ✓ Discussion with cardiology on an amiodarone alternative

Take Home Points:

- ✓ Amiodarone will cause deposition on the cornea; this rarely causes symptoms and is simply evidence of amiodarone being present
- ✓ There is an unclear link between amiodarone and posterior eye involvement
- ✓ An ophthalmic assessment should be done as a baseline and whenever visual symptoms occur
- ✓ Vision problems are common in the population receiving amiodarone; it's not always the culprit! – Keep a broad differential
- ✓ Most vision changes with amiodarone are relatively benign
  - Halos or mild photophobia (benign corneal deposition)
  - Benign changes do not warrant cessation of amiodarone
- ✓ <0.5% of patients may develop more severe vision changes – NAION (optic neuropathy)
  - Progressive central vision loss
  - Median time to presentation: ~9 months
  - Management: Emergent ophthalmologic assessment and **cessation of amiodarone**
    - Consider alternative causes for vision loss
    - Cardiology assessment: amiodarone alternatives
    - Amiodarone ½ life is ~56 days, so if amiodarone is the driver, visual recovery is slow (months), if at all.

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA. Click HERE for more details.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

References:

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