Eyeball Control: The *Other* Potential Side Effects of Atropine for Myopia

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“So, what % Atropine do you start with?”

This is a question that I get asked by colleagues who assume that because I see a lot of children, I must do a lot of work with Atropine

My typical response is simply, “I don’t” and then try to change the subject

Rather than trying to escape the conversation, I decided to really investigate why the concept of Atropine use bugs me so much

…so here it is!

Myopia Today and Tomorrow

- It is estimated that by the start of this year, **2.5 Billion** people will be myopic
- By 2050, that number is expected to balloon to **6.0 Billion**
- To put that into perspective, the current population of Earth is approximately **7.6 Billion!**
- There is no safe or insignificant amount of myopia; even as little as -0.75D more than doubles the odds of ocular disease related to myopic etiologies
  - D.I. Flitcroft / Progress in Retinal and Eye Research 31 (2012) 622e660

Myopia – a Structural Look

- Fibroblasts (which secrete collagen) are the only cell type found in the sclera. The activity of fibroblasts is affected by many factors, including local release of growth-modifying factors, retinal activity, signals from the matrix and iris-ciliary body, and systemic factors such as hormones, steroids, and cytokines. *The finding that proliferation of fibroblasts in the sclera declines during development of myopia but increases during recovery raises hopes for an intervention* (Choo, Vivien, "A look at slowing progression of myopia", The Lancet, Volume 361, Number 9369, May 2003)
- During development of myopia, collagen degradation in the sclera is accelerated and collagen synthesis is reduced (*J Biol Chem* 2003; **278**: 16587–94)
- The eye enlargement is accompanied by scleral thinning, which occurs early in the development of myopia and which is due not to passive stretching but to tissue remodeling. A later feature is a reduction in the diameter of the scleral collagen fibrils, which further weakens the sclera (Choo, Vivien, "A look at slowing progression of myopia", The Lancet, Volume 361, Number 9369, May 2003)

Atropine use for Myopia Progression

- The use of Atropine for the control of myopia progression has been very “en vogue” for the past few years
- Atropine is a non-selective muscarinic antagonist
- Its exact method of action in regards to myopia progression is largely unknown. A non-selective antimuscarinic effect on scleral fibroblasts is a possibility, as are blocking of accommodation, suppression of retinal signals that control eye growth, and suppression of growth hormone secretion (Choo, Vivien, “A look at slowing progression of myopia”, The Lancet, Volume 361, Number 9369, May 2003)

Documented Success with Atropine for Myopia Progression

- A meta-analysis of 19 studies that included 3137 children found atropine to be effective in slowing progression of myopia
  - Average documented progression 0.50D compared to average 1.00D control patients
- No difference in efficacy was identified between different doses of atropine within this (0.01%-1.0%) range. Higher doses of atropine were associated with more adverse effects. This supports the use of 0.01% dosage of atropine to minimize SEs.

Efficacy and Adverse Effects of Atropine in Childhood Myopia - A Meta-analysis; Qianwen Gong, MD et al; JAMA Ophthalmol. 2017 Jun; 135(6): 624–630. Published online 2017 Jun 8.

Documented Side Effects

- Photophobia (6-43% depending on atropine dose)
- Poor Near VA (2-12% depending on atropine dose)
- Allergy (3%)
- “Other” (1%)
  - Headaches
  - Chalazia
  - Systemic Effects

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‘Undocumented” Side Effects

- This is what interested me more
- Our patients are NOT walking myopia-holders – they are people!

- What are we REALLY subjecting them to when we prescribe atropine?

COVD 2019

- I had the opportunity to meet and speak with Tiong Peng Yap, Optometrist (Singapore) who did an oral presentation on the use of Atropine in clinical practice.
- His presentation reported the use of atropine in a number of cases and showed the amount of myopia progression in each case.
- What struck me about these cases were the other symptoms the patients reported which are not on the list of documented side effects

- The following are a summary of some of those cases (used with permission)

Summary from TP Yap:

- Atropine is used widely by ophthalmologists (optometrists cannot Rx therapeutics)
- Typically, 0.01% is the starting Rx, but it will be increased if the patient continues to have myopia progression
- He includes a retrospective look at his patients who have been on Atropine for more than one year between 2012-2015
- These patients subjectively list symptoms as starting after the initiation of Atropine use

Patient TYM, Age 9, Atropine Dose: 2 yrs @0.01%, 1 yr @0.1%, 1 month @1%

- Start of Tx:
  - OD -2.25, OS -2.50-0.50x060
- New Rx Given:
  - OD -2.25, OS -2.50-0.50x060, add +2.00
- Symptoms:
  - Blurred Vision
  - Photophobia
  - Squinting
  - Mydriasis
  - Abnormal Head Posture*
  - Slants sideways when watching TV*

Patient LJK, Age 9, Atropine Dose: 2yrs @1%

- Starting Rx:
  - OD -0.75-1.00x005, OS -4.00-0.75x180
- New Rx given:
  - OD -1.75-1.00x005, OS -4.00-0.75x180, add +2.00
- Symptoms:
  - Photophobia
  - Mydriasis
  - Anisocoria
  - Removes glasses and turns head to read*

Patient JN, Age 10, Atropine Dose: 1 yr @0.1%, 2 yrs @1%

- Starting Rx:
  - OD -7.75-2.00x180, OS -8.00-3.25x180, add +3.00 (no change)
- Current Diagnoses:
  - Learning Disability
  - Dyslexia
- Symptoms:
  - Photophobia
  - Blurred Vision
  - Words moving*
  - Diplopia*
- Testing
  - NPC 40cm*
  - Stereo 100”*
  - Amps 4D OU

Patient BC, Age 10, Atropine Dose: 3 yrs@ 0.1%, 1 yr @1%

- Starting Rx:
  - OD -5.25-1.50x180, OS -4.25-1.25x160, add +2.50
- Current Diagnoses:
  - Intermittent XT@N
  - Irlen Syndrome
- Symptoms:
  - HAs x 5 yrs*
  - Blurred Vision
  - Skips words*
  - Head turn*
  - Diplopia when reading*
  - Bumps into things*
  - Mydriasis
- Testing:
  - IXT @N*
  - NPC 40/50cm*
  - Equil: BO -/8/0, BI -/25/20

Patient BC Continued:

- **Decided to STOP Atropine due to perceived SEs**
- Testing Post Atropine (4 Months):
  - NPC 15/30cm
  - Int suppression
- **4 Months of VT**
  - NPC 10cm
  - Equil: BO 18/20/18, BI -/18/16
  - Stereo 32”
  - No suppression
  - OD -6.50-2.25x005, OS -6.00-2.25x160

My Patient – CS, Gr 3 – Dec 23, 2019

- Recently moved to Canada from Chicago, wants a refill Rx for Atropine gtts
- History:
  - Had an eye exam age 4 by an OD – no problems, 20/20 OU
  - Had an eye exam one year later after failing a school screening in Kindergarten by an ophthalmologist and was told -2.00 OU. He was given specs to wear FT.
  - Age 6: pt wearing -3.00 OU and prescribed Atropine 0.025% starting dose (Oct 2018). Pt was told to take 1 gtt OU qhs for 2 years. Since that time, he has progressed another 0.25D. Pt now wearing -3.25 OU. Mom very pleased. No SEs noted
  - Plays iPad 30 min in the morning and evening, reads 20 min/day (forced, not enjoyed). Likes math, hates reading, doesn't enjoy any sports or playing outside
  - Born FT, (-) complications, passed newborn hearing test
  - Crawled on all fours starting 8 months, walked 10 months, mild speech delay
  - No hx frequent ear/UR infections
- Observations:
  - Low-tone, slumped in chair
  - Wears his specs low on his nose and reads over them (near card)

CS - Exam

- UVA: 20/200 OD, 20/100 OS
- AVA: 20/20-1 OU, OS, OU
- NAVA: 0.4/0.4M OD, OS, OU – skipped 2 words and one line of text (unnoticed)
- NUVA: 0.4/0.4M OD, OS, OU – slow, arduous
- Cover Test (cRx): N/S, ortho @D, N/S 4XP @N
- NSUCO Pursuits: 3/3/4, can't resolve CP, but can with touch
- Stereo: 20"
- W4D: fused, w/ +/-2.00 fused
- Stress Ret: +2.75 over Hab (-3.25)
- **Dynamic Ret: OD -2.00 (20/20), OS -1.50-0.25x180 (20/20)**
- Subjective: OD -2.00, OS -1.50 *W/-1.00 OU: 20/25-2
- Equil: BO -/30/8, BI -/18/4
- Phoria: Vert – ortho, Hori – 1XP

CS – Exam (Near Testing)

- Phoria (with sub): 4XP
- Equil: BO -/-/-, BI -/14/2
- FCC: +0.50
- NRA/PRA: +3.00/-3.00 (A)
- Phoria (with sub+FCC): 6XP
- DEM: Vert 40th, Hori <1st
- Readalyser: Pt refused (almost cried)

CS - Thoughts

- Frank oculo-motor concerns
- Dealing with visual problems by avoidance of near activities
- Over-minused by PO
  - Mom thrilled that Atropine is “making him better”
- My recommendations:
  - Rx: OU-1.00 w/ +0.50 add
  - VT, recheck q8weeks and adjust specs prn
  - D/C Atropine
- Mom doesn’t like any of these recommendations. Wants to continue the remainder of the 2 years as outlined by the PO in Chicago and re-visit these options at that time. Doesn’t want CS to be at all “under-corrected”.
- Final Rx: OD -2.00, OS -1.50 (SV), Rx given of Atropine 0.025%, recheck 6 mo
- Mom made fully aware of all options (including the above). She is willing to consider VT and BF in Oct 2020 when the 2 years is up.

Holes in my own Theories

- In neither my own patient nor in Tiong's, do I (or he) have the optometric data from before and during/after atropine therapy, so I really don't know how many of these symptoms are truly "side effects" of atropine use or if they were already present to a lesser/sub-clinical extent

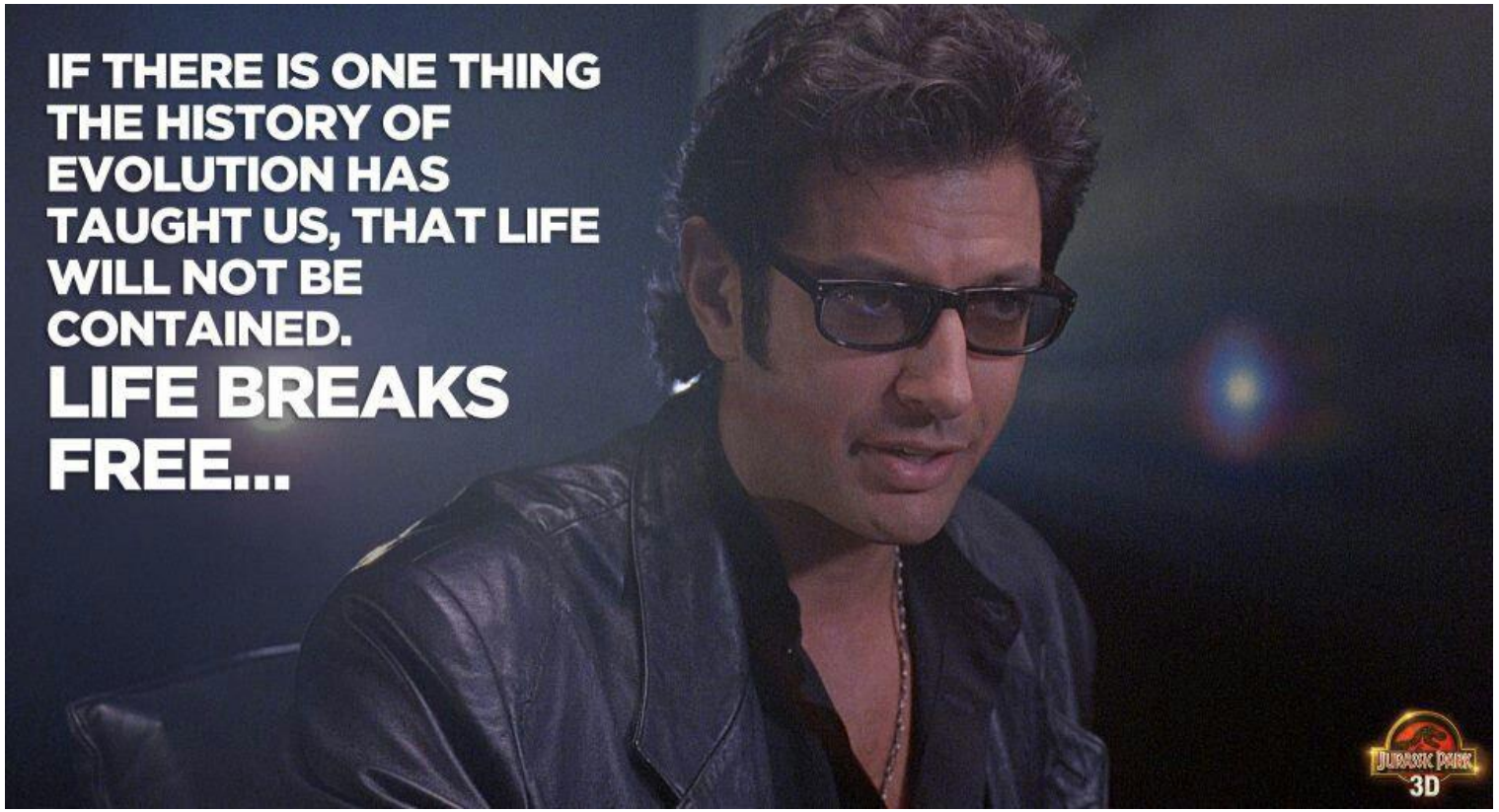
- My own patient did not appear to suffer from any postural asymmetries as many of the Asian patients did. This may be due to the fact that many of the Asian patients listed were on a much higher dose of Atropine than my patient was

- **My suspicion is that these symptoms are the result of the patients' vision systems attempting to cope with the vision problems they already possess while not able to use the coping strategy that nature pre-disposed them to (myopia)**

So Why do we Care?

- Myopia is the symptom, not the problem!
- Trying to halt myopia by preventing the eyeball from elongating can be thought of as akin to trying to stop weight-gain by wearing a corset
- Myopia remains a problem with roots both in “nature” and in “nurture”
- By using *only* Atropine for the treatment of myopia-progression, we are addressing the “nature” but not the “nurture”
- Visual hygiene counselling, VT, and/or appropriate prescribing should always be included in the therapeutic options

In Other Words:



“So, what % Atropine do you start with?”

I don’t

…so how about this weather?

Your Thoughts?

Special thanks to Tiong Peng Yap, Optometrist