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Myopia: What would be your treatment of choice?

Myopia control soft contact lenses

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DISCLOSURE

- I have received funding from the following bodies for lectures, key opinion leader/product feedback, and research:
  - Alcon, American Academy of Optometry (UK), Association of Optometrists, Birmingham Focus on Blindness, Black & Lizars, the Central Fund, Cerium Visual Technologies, College of Optometrists, Coopervision, ESRC, Essilor, General Optical Council, Hadassah College, Hoya, Institute of Optometry, Iris Fund for Prevention of Blindness, Johnson & Johnson, Leightons, MRC, NIOS, Norville, Optos, Paul Hamlyn Trust, Perceptive, Scrivens, Specsavers, Thomas Pocklington Trust.
- Lecture content always my own
- I am not a myopia researcher, but a clinician with an interest in helping my myopic patients

Visual problems

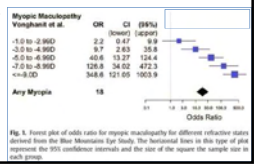
- What is the commonest cause of visual impairment?

Pie chart figures approximate, based on data on WHO website

- Myopia is the most common vision disorder and the leading cause of visual impairment worldwide (Tkatchenko et al., 2015)
- 19% of UK school children have a visual problem requiring attention (Thomson, 2002)

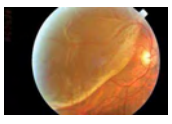
Why does myopia matter?

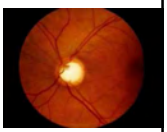
- Common and increasing prevalence
  - 93% of Taiwanese medical students are myopic (Lin et al., 1996)
  - Prevalence of myopia in USA has increased in last 30 years from 25% to 42% (Vitale et al, 2009)
  - 50-53% of UK university students are myopic (Logan et al., 2005)
  - Prevalence of myopia in UK has more than doubled in last 50y (McCullough et al., 2016)
- Significant health impact
  - High myopia (≤-6) increases risk of retinal detachment, myopic macular degeneration, glaucoma, & other conditions
    - "no evidence of a safe threshold level of myopia for any of the known ocular diseases linked to myopia" (Flitcroft, 2012)
  - In the Copenhagen study myopia-related diseases were the most common cause of impaired vision (Holden et al., 2014)



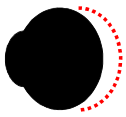
Realistic goals of myopia control

- 20% slowing of rate of myopia
  - Person destined to be -4.00 would be -3.25
  - Person destined to be -6.00 would be -4.75
  - Person destined to be -8.00 would be -6.50
- 33%
  - Person destined to be -4.00 would be -2.50
  - Person destined to be -6.00 would be -4.00
  - Person destined to be -8.00 would be -5.25
- Reducing the rate of myopia progression by 50% would lead to reduction in frequency of high myopia of over 90% (Brennan, 2012)
- Average…means no guarantee!

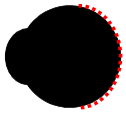




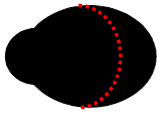
Refractive error: conventional view



Hypermetropia (long-sighted)
- image shell focused behind retina

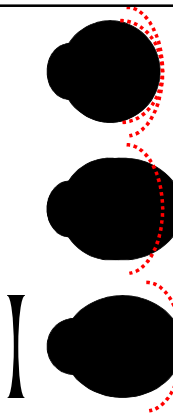


Emmetropia (normal vision)
- image shell focused on retina



Myopia (short-sighted)
- image shell focused in front of retina

Myopia: the new view



Patient about to become myopic
- image shell focused on retina at fovea
- image focused behind retina in periphery
- *relative peripheral hyperopic defocus* - RPHD

Reviews: Charman & Radhakrishnan (2010); Earl Smith (2011); Flitcroft (2012)

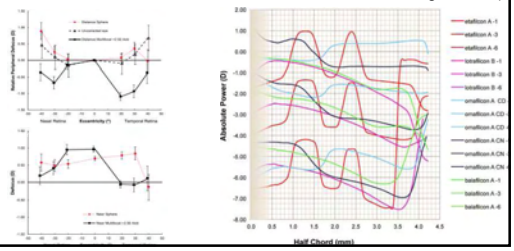
The eye grows so the peripheral image is in focus causing myopia at the fovea

Spectacles or contact lenses correct the focus at the fovea, but not the RPHD so myopia progresses

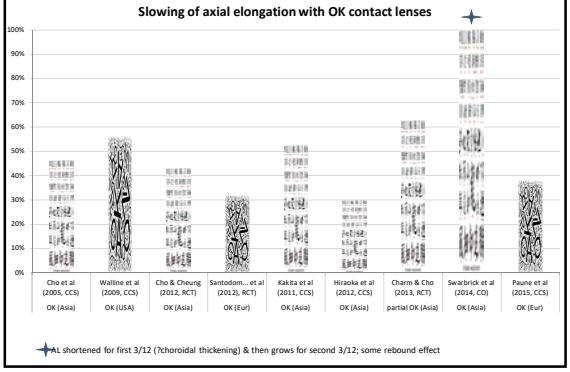
BUT: see Atchison et al. (2015) Relative peripheral hyperopia does not predict development and progression of myopia in children

Can we reduce peripheral hyperopic defocus?

- RPHD eliminated by orthokeratology (OK) (Ticak & Walline, 2013)
- Large pupil diameters facilitate OK myopia control (Chen et al., 2012)
- Centre-distance multifocal SCL creates peripheral myopic defocus during DV and to lesser extent during NV (Berntsen & Kramer, 2013)
- CD multifocals creat RPMD (Wagner et al., 2014; Kang et al, 2013)



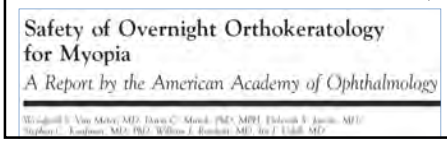
Slowing of axial elongation with OK contact lenses



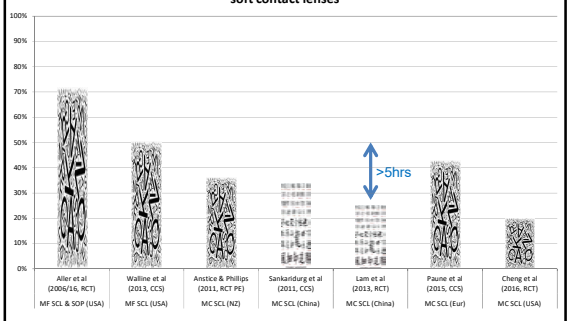
AL shortened for first 3/12 (?choroidal thickening) & then grows for second 3/12; some rebound effect

Safety of overnight orthokeratology (OOK)

- For soft contact lenses, overnight wear increases risk of microbial keratitis (MK) by 10x
- Several cases of (MK) reported, mainly in Asian countries thought to be associated with poor hygiene Watt & Swarbrick (2007)
  - Tap water, old contact lens cases, suction holders
- Prevalence of complications from OOK has not been established Van Meter et al. (2008)
- Risk of OOK similar to other overnight wear of contact lenses Bullimore et al. (2013)



Slowing of myopia progression with multifocal (MF) or myopia control (MC) soft contact lenses



Not included: Fujikado et al (2014) – small pilot study of experimental lens only 0.50D add

Myopia control with multifocal CL: practical tips

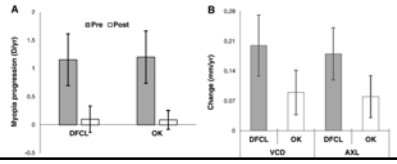
Used in research studies

- Prescribe:
  - Add that eliminates eso-fixation disparity at near (Aller, 2014)
  - If no esophoria, maximum add giving acceptable DV
  - Myopia control requires lens centration (Kang et al., 2013)
- Wear for schoolwork
  - Daily wear
  - Can wear all waking hours if desired & safe – more treatment effect
  - Remove when swimming
  - Don't shower in CL
  - E-seg glasses for backup
- Monitor every 6/12
  - CL check and eye exam
  - "natural" stimulus so rebound effects unlikely (Holden et al., 2014)

Myopia control: comparisons between methods

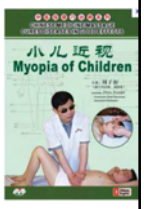
Turnbull, Munro, Phillips (2016)

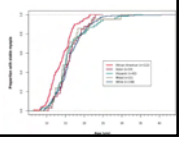
- 110 patients: 4-43y, mean12y, 62% female
- Options: OrthoK, dual focus soft lenses (DFCL), 0.01% atropine, "no preferential recommendations"
- Px choice: 56 OrthoK, 32 dual focus SCL, 22 advice only, 3 chose 0.01% atropine
- No difference in efficacy between OrthoK & DFSCL
- VA during treatment NS different in 3 main groups
- OrthoK pxs seen 7 times ±4, DFSCL 4.7±2; hours in clinic 8.6 cf 4.3
- One adverse event (?central ulcer) in an OrthoK px, 5 OrthoK with lens adherence



Caveats

- Need more RCTs
  - But myopia control effective "on balance of probabilities" and need to start young
- Persistence of treatment effect
  - Unclear whether the treatment effect is sustained
  - May be rebound effect when stop intervention
  - Perhaps unlikely with optical interventions & can keep in MF CL until myopia likely to be stable
- Check for DV blur –max add for good DV
- Axial length changes correlated with myopia changes (r^2 = 65%)
- Followers of a theory tend to ignore other theories
  - If myopia wasn't multifactorial, then we would have solved it by now!





Conclusions: myopia control in European children

- If NV esophoria or high accommodative lag, recommend multifocals
  - MF glasses (E-seg) likely to reduce progression rate by 30-40%
  - MF CL may reduce progression by up to 70%
  - Aim to eliminate esophoria; typical add +2.00 to +2.50, CD
- If not esophoric and normal lag, effect reduced
  - MF glasses likely to reduce progression by only 15%
  - MF CL success unclear, perhaps 36-50% if perform like dual focus
- OrthoK slows myopia progression by 32-63%
- Only fit CL if child & parents motivated & hygienic
- Also encourage child to experience outdoor daylight

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Myopia: What would be your treatment of choice?
Orthokeratology

Katie Harrop MCOptom FBCLA

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Conflicts of Interest

- Professional Services Manager
  - No7 Contact Lenses
    - Manufacturer of EyeDream Orthokeratology

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History

- Development of OrthoK was practitioner led
- Jessen
  - Showed flattening to temporarily correct myopia is possible with standard hard lens designs
- Reverse geometry lenses
  - Developed to stabilise fit
  - As a side effect increased levels of myopia could be corrected
    - Up to 5.00D corrected consistently
- Anecdotal reports of myopia control
  - No change in lens parameters and no change in baseline myopia when OK ceased
  - No mechanism proposed

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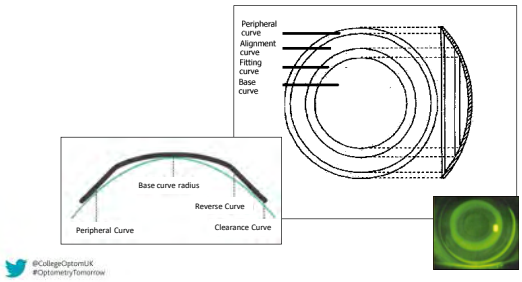
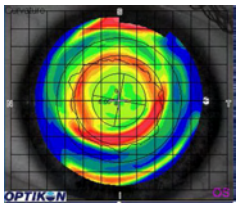
Basics of OrthoK lens design

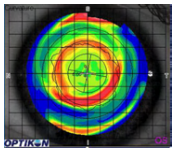


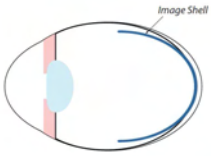
Corneal shape post OK

- Tear film forces lead to
  - central epithelial thinning
  - mid peripheral thickening
- This generates
  - Central Flattening
  - Mid peripheral steepening



Corneal shape and image shell





The Evidence

- First significant paper published in 2005

The longitudinal orthokeratology research in children (LORIC) in Hong Kong: a pilot study on refractive changes and myopic control.

- Cho et al, Current Eye Research.
  - Showed a significant myopia control effect but generated as many questions as answers
    - Large amounts of variation between subjects
    - Can the effect be predicted for individual patients?

The Evidence

- **Corneal reshaping and myopia progression. (CRAYON Study)**
- Walline et al, Br J Ophthalmol. 2009
  - **CONCLUSION:** Results confirm previous reports of slowed eye growth following corneal reshaping contact lens wear.
  - i.e. results repeated with American children.

The Evidence

- **Influence of Overnight Orthokeratology on Axial Elongation in Childhood Myopia**-Kakita et al, Investigative Ophthalmology & Visual Science, 2011
  - 2 year study
  - 210 children
    - 45 in OrthoK group
    - 60 in matched spectacle wearing control group
  - Again showed axial length increase was smaller in OK group compared to control group

The Evidence

- **Retardation of Myopia in Orthokeratology (ROMIO) Study**: - Cho et al, Invest. Ophthalmol. Vis. Sci. 2012
- On average, the increase in axial elongation for Ortho k subjects was slower by 43% compared to subjects wearing single-vision glasses.
  - 20% of the 7-8 year old OrthoK patients progressed at greater than 1.00D/yr
    - while 63% of the control group did so.
  - Rates slowed down significantly by ages 9-10
    - when only 13% of the controls and 9% of the OrthoK patients progressed at that rate.

The Evidence

- **Long-Term Effect of Overnight Orthokeratology on Axial Length Elongation in Childhood Myopia: A 5-Year Follow-Up Study**-Hiraoka et al, Investigative Ophthalmology & Visual Science, 2012,
- Overall a 37% reduction in progression
- Compared their axial length data to published studies using other methods.
  - Inhibitory effect exceeded all studies on soft lens designs and spectacles
    - Only outperformed by Atropine 0.5% +MF specs and Atropine

The Evidence

- **Long-term Efficacy of Orthokeratology Contact Lens Wear in Controlling the Progression of Childhood Myopia** -Santodomingo-Rubido et al, Current Eye Research 2016
  - **7 year long study**
- A trend toward a reduction in the rate of axial elongation of the order of 33% was found in the OK group in comparison to the CT group following 7 years of lens wear

The Evidence

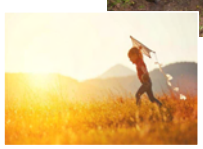
- **Orthokeratology for Myopia Control: A Meta Analysis**-Si et al, Optometry and Vision Science 2015
- **Orthokeratology to Control Myopia Progression: A Meta Analysis**-Sun et al, PLOS ONE 2015
- Included seven studies
  - 435 subjects – OK group 218, Control group 217
  - Age 6 to 16 years
  - Follow up time 2 years
- Si -Weighted mean difference of -0.26mm in axial length elongation for OK group - 56% reduction
- Sun - Myopia Progression reduced by approximately 45%

Benefits of Ortho K for myopia control

- Optics are presented to the eye all waking hours
  - Soft lenses may not be worn all day
- Increased peripheral plus for higher myopes
  - Peripheral plus is equal the amount of myopia corrected
  - Therefore over a 2.50D correction peripheral plus is greater than available from currently available soft lenses

Other Benefits of OrthoK

- Freedom from contact lens wear during the day
  - Great for active children
  - Sports e.g. cycling, rugby
- Can go about life as normal
  - Play
  - Paint
  - Rub eyes



Other Benefits of OrthoK

- Lens free at school
  - No specs or contact lenses to worry about for PE
  - Nothing to get in the way of schooling

Other Benefits of OrthoK

- All lens wear is done at home
  - Lens wear only when asleep
  - Less likely to lose lenses

Practice Building

- Orthokeratology is a 'specialist' lens system
  - Although not difficult
- Lens supply not available via retail outlets/online lens suppliers
  - And unlikely to be in the future
- Patients are very loyal and recommend both Orthokeratology and your practice to friends and family

My experience

- Started fitting Ortho K lenses in 2004
- Initially saw the early adopters
  - Or bungee jumpers
- Next big group were becoming intolerant to soft contact lens wear due to dryness
- Next group were children for myopia control
  - Initially parent led

My experience

- Fitted children as young as 5
- Average starting age 8 -12
- For many children there is no change in lens parameters
  - Or prescription if discontinue OK
- Children successfully wear and care for the lenses
- Report many benefits of being lens free in the day

Future?

- We know that the retina is not spherical in shape and can't be described simply
- Current optical methods work with an over-simplified model of the image shell
- To provide peripheral relative myopia for all eyes we need to:
  - Understand the shape better
    - Map it for individuals
  - Create lenses to create the correct image shell for each patient

Future?

- Soft lenses are unlikely to be able to be manufactured with the levels of accuracy that are needed
- And they drape over the cornea
- Single base curve lenses exaggerate this problem
- Ortho K lenses are rigid and lathe cut
  - Therefore will be able to produce lenses with suitable accuracy as our understanding increases and specific lens designs are developed

Thank you

Myopia: What would be your treatment of choice?
Drugs

Simon Barnard

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Disclosures/Conflicts of Interest

Professor Barnard is Chief Medical Officer of IRISS Medical Technologies which has developed technology to assist multifocal contact lens fitting

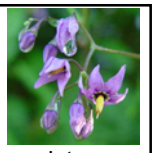
I have received funding for presenting lectures for Asda, Carl Zeiss Meditec; Cerium Visual Technologies; Interoptik Norway, IRISS Medical Technologies; Leightons; Optos plc , Sightcare, Specsavers, Synsam Norway, Vision Express

I have a general interest in paediatric optometry

What pharmaceutical agents?

Tropicamide
Cyclopentolate
Atropine
Pirenzipine
Timolol

Atropine



Competitive, non-selective antagonist of muscarinic acetylcholine receptors

Used as
- Cycloplegic to temporarily paralyse accommodation reflex
- Mydriatic to dilate pupils

Atropine standard doses (1.0% & 0.5%)

- Peak cycloplegia after 1 hour
- Duration of mydriasis and cycloplegia 7 - 14 days
- Use is avoided for routine diagnostic cycloplegia
- Duration may cause intermittent esotropia ⇒ constant

Used therapeutically

- Anterior uveitis
- Penalisation as amblyopia therapy

Atropine, has long been known to be effective in reducing myopia progression in children (Gimbel,1973; Kelly et al, 1975)

Gimbel HV (1973), The control of myopia with atropine. *Can J Ophthalmol, 8; 527-532*
Kelly et al (1975) Clinical assessment of the arrest of myopia, *Br J Ophthalmol,* 59; 529-538

Unwanted side effects in its standard 1% or 0.5% concentration

- Cycloplegia
- Mydriasis and photophobia
- Allergy

Atropine is also very toxic

Not widely used for myopia control

Serendipity

A trial in Singapore demonstrated that atropine 0.01% remained effective at reducing the rate of progression of myopia whilst having minimal effects on pupil size and accommodation (Chua et al, 2006)

Chua WH, et al 2006, Atropine for the treatment of childhood myopia, *Ophthalmology,* 113; 2285 - 91

The effects of different doses of atropine

Atropine for the Treatment of Myopia (ATOM) studies 1 & 2 demonstrated a dose-related response to atropine over 2-years

- Higher doses inhibited myopia progression to a slightly higher degree than lower doses (Chua et al, 2006; Chia et al, 2012)

Chia et al (2012) Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1% and 0.01% doses (ATOM 2) *Ophthalmology, 119, 347-354*

Effect of ceasing atropine of different doses

When atropine was stopped after 24 months for a period of 12 months (Phase 2 of ATOM 2 - *wash out period)*

- Rapid increase in myopia in children originally treated with higher concentrations of atropine

- Lowest concentration (0.01%) ⇒ minimal change (Tong et al, 2009; Chia et al, 2014)

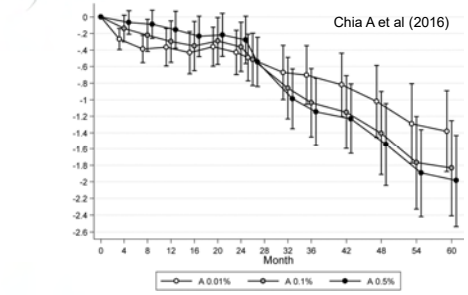
Tong L et al (2009) Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. *Ophthalmology, 116; 572-579*
Chia A et al (2014) Atropine for the treatment of myopia : changes after stopping atropine 0.01%, 0.1% and 0.5% (ATOM 2) *Am J Ophthalmol, 157; 451-457*

- Net result - myopia progression significantly lower in children treated with 0.01% (-0.72D) at 36 months cf.
  0.1% (-1.04D) and
  0.5% (-1.15D)
- 0.01% caused
  - less photopic pupil dilation
  - no clinically significant loss of accommodation or
  - near VA (Chia et al, 2014)

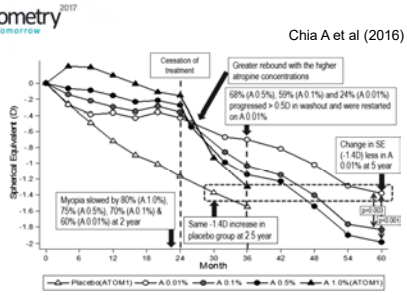
Long term effectiveness

Phase 3 of the ATOM study looked at the effect of recommencing treatment (at 36 months) with 0.01% atropine for a further 24 months (Chia et al, 2016)

Chia A et al (2016) Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2: Myopia Control with Atropine 0.01% Eyedrops . *Ophthalmol, 123:2; 391-399*



Mean change in spherical equivalent over time within different treatment groups (atropine 0.01%, 0.1%, and 0.5%). Error bars represent 1 standard deviation.



Summary of findings from the ATOM1 and ATOM2 studies: change in spherical equivalent (SE). ATOM = Atropine for the Treatment of Myopia; D = diopter.

Over 5 years, atropine 0.01% eyedrops were more effective in slowing myopia progression with less visual side effects compared with higher doses of atropine

The story so far

- Atropine 0.01% eyedrops instilled nightly has been shown to be an effective treatment to prevent (reduce) myopia progression
- Safe; minimal visual side effects
- Study groups mostly Asian with heavily pigmented irides

How about lighter coloured irides?

- 14 university students (18-27 years) received 1 drop atropine 0.01% daily into each eye over 5 days
- Range of physiological, functional and quality of life measures assessed at baseline, day 3 and day 5 (Loughman & Flitcroft, 2017)

Loughman J & Flitcroft DI (2017) The acceptability and visual impact of 0.01% atropine in a Caucasian population. *Br J Ophthalmol,* 100; 1525-1529

- Pupil size increased > 1.0 mm
- Pupillary response significantly more sluggish
- NPC receded slightly (not statistically significant)
- Binocular amplitude of accommodation reduced (not statistically significant)
- WRRT reading speed unchanged
- Distance VA and near VA not significantly affected

Quality of life (n = 14)

4 subjects entirely asymptomatic

8 subjects reported a one-grade increase in their level of difficulty (0 ⇒ a little) with one of the 14 vision related tasks

2 subjects reported a one-grade increase in their level of difficulty (0 ⇒ a little) with two tasks

Glare was the most commonly reported symptom by six subjects

Conclusions

- Use of atropine 0.01% slows the progression of myopia in children
- Minimal side effects
- Safety over a 5-year period has been demonstrated

The future

- Atropine 0.01% not currently available in multidose or single dose units
- Studies required to assess the efficacy of combination therapies (atropine + contact lenses intervention)

Conclusion

What would be my treatment of choice?

1. Atropine 0.01% together with
2. Multifocal contact lenses and
3. Advice on playing in the sun

(Lagreze WA et al 2017)

Lagreze WA Joachimsen L Scheffel F (2017) Current recommendations for deceleration of myopia progression. *Ophthalmologe.* Jan;114 (1): 24-29.