Ocular changes in OI in a Portuguese population

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Conflicts of interest

I, Rafael Barão, DO NOT have a financial interest/arrangement or affiliation with one or more organizations which could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Background

• OI can cause several ocular manifestations

• The most common (and noticeable) is the bluish coloration of the sclerae (+ type I)\(^1,2\)

• Other common manifestations include
  • Reduced corneal thickness\(^2,3,4\) and rigidity\(^4\)
  • High refractive errors\(^5\)
  • Keratoconus\(^6,7\)
  • Glaucoma (higher incidence *de per se* or higher risk?)\(^2,8,9,10,11\)

• Less common: scleral rupture\(^12\), retinal hemorrhages\(^13\), CNV\(^14\), among others

1. Silence *et. al.* 1993
2. Hald *et al.* 2018
3. Pedersen *et. al.* 1984
4. Lagrou *et. al.* 2018
5. Chau *et. al. in Osteogenesis Imperfecta*, 2014
7. Zeri *et. al.* 2018
8. Congdon *et. al.* 2006
9. Rosbach *et. al.* 2011
10. Wallace *et. al.* 2014
11. Pirouzian *et. al.* 2007
12. Mauri *et. al.* 2016
13. Ganesh *et. al.* 2004
Objectives

• Assess and explore the ocular features of OI patients in an adult Portuguese population

• Exploratory analysis of relationships between OI types and ocular phenotypes

• Exploratory analysis of relationships between several variables
Study design and setting

• An ongoing cross-sectional study on the ocular features in OI patients

• Protocol envolves coordinated visitations to several departments
  • Cardiology, Genetics, Rheumatology, Stomatology and Ophthalmology
Methods

• All patients underwent complete ophthalmological exam and extensive testing

  • BCVA, ocular motility and alignment testing
  • Slit-lamp biomicroscopy and fundus observation
  • Automated refractometry
  • Tonometry (GAT)
  • Corneal tomography (Pentacam® HR)
  • Non-mydriatic retinography
31 adult Portuguese patients have enrolled

- 24 ♀, 7 ♂
- Mean age: 43 ± 16y
- Height 146 ± 19 cm and weight 57 ± 16 kg
Visual acuity and refractive errors

- Mean BCVA $0.09 \pm 0.2$ logMAR (similar OU)
- Mean Sph $-1.3 \pm 5.2$ D, Cyl $-1.3 \pm 0.9$ D
  - 7 patients w/ high grade refractive errors
    - High myopia (range -6.5 to -24D): 8 eyes
    - High hyperopia (range 5.25 to 6.75D): 3 eyes
  - Cyl: 52% WTR, 25% ATR, 23% Obl
- BCVA correlated with Sph error ($r = -0.3; p = 0.01$)
Visual acuity and refractive errors

- No significant difference in BCVA or refractive errors between OI clinical or genetic types
Visual acuity and refractive errors

- **No significant difference** in BCVA or refractive errors **between OI clinical or genetic types**
Visual acuity and refractive errors

- **No significant difference** in BCVA or refractive errors **between OI clinical or genetic types**
Corneal thickness

- Avg CCT was \(481 \pm 54 \mu m\) (similar OU)
  - Significantly reduced vs. reference range\(^1\) \((p < 0.001)\)
  - Significantly different between OI type I and non-type I \((p = 0.01)\)
    - Types I vs. IV \((p = 0.026)\)
    - Types I vs. III \((p > 0.05)\)
- 77% of patients had thin corneas
  - 2 patients had thick corneas (avg 599 \(\mu m\))
    - 1 type IV and 1 thus far unclassified
  - 5 patients had normal CCT

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1. Hoffmann et. al 2013
Corneal thickness

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1. Hoffmann et. al 2013
Sclerae

- **80%** of patients had some form of (dis)coloration of the sclerae
- **CCT** was significantly lower in patients with blue sclerae ($p < 0.001$)
Intraocular pressure

- Mean IOP $13.8 \pm 4.8$ mmHg
- IOP correlated with CCT ($p < 0.001$)
  - Blue vs. white sclerae
    $13.2 \pm 4.9$ vs. $16.3 \pm 3.4$ mmHg ($p = 0.03$)
  - Did not differ significantly between OI types
Intraocular pressure

• Mean IOP 13,8 ± 4,8 mmHg

• IOP correlated with CCT  
  \((p < 0,001)\)
  • Blue vs. white sclerae  
  13,2 ± 4,9 vs. 16,3 ± 3,4 mmHg  
  \((p = 0,03)\)

• Did not differ significantly  
  between OI types
Corneal tomography

• Prevalence of corneal tomographic changes\(^{1,2}\): 77%

• Clinical bilateral keratoconus: 2 patients / Subclinical: 3 pts / Suspect corneas: 16 pts (10 bil.) bilateral

• No statistical difference between type I and non-type I groups (p > 0.05)

2. Shetty et. al 2017
Corneal tomography

Elevation (Front)

-Elevation (Back)

-Progression Index:
Min: 0.58
Max: 1.81
Av: 1.38
AF1max: 250

Corneal Thickness

Mean corneal thickness values on rings concentrically to the thinnest location

Corneal Thickness Spatial Profile (CTSP)

Percentage Thickness Increase (PTI)

Reference Database:
- Myopic/Normal
- Hyperopic/Mixed Cyl

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<th>Diameter</th>
<th>Myopic/Normal</th>
<th>Hyperopic/Mixed Cyl</th>
<th>Literature</th>
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Glaucoma

• Only 1 patient has been diagnosed with glaucoma...

... But she has active Behçet’s disease-associated uveitis
Retinal changes

• No relevant segment changes were detected
  ... Other than chorioretinal atrophy associated with high grade myopia
Discussion

• The majority of patients were OI type I and COL1A1 was the most common causative gene

• Clinical validity of these findings is stronger in type I disease

• Type I and type III populations seem similar (IOP, CCT, blue sclerae)
Discussion

• BCVA was moderately reduced, and there was a high incidence of high-grade ametropia
  • Do collagen anomalies affect the axial length of the eye?

• Reduced CCT is an hallmark of ocular disease in OI
  • Correlates negatively with IOP and is more associated to type I disease and with blue sclerae
  • What is its usefulness in diagnosis?¹
  • Is it a risk factor for the development of glaucoma?²
  • The COL1A1 gene has been associated with several forms of glaucoma³

• How is the relationship between blue sclerae and CCT relevant?
  • Is it dependent on the continuity of thinning of the sclerocorneal layer?
  • Or is it best explained by the molecular changes particular to OI type I?

¹. Hald et al. 2018
². Congdon et. al. 2006
Discussion

• Diagnosis of glaucoma in OI patients presents a clinical challenge

• Lower IOPs and lower CCTs

• Do the collagen changes in the sclerocorneal layer affect the way cupping develops?

• Since we did not perform posterior segment OCT or SAP the epidemiology of glaucoma in this population may be underestimated
Discussion

• Diagnosis of glaucoma in OI patients presents a clinical challenge

  • Lower IOPs and lower CCTs

  • Do the collagen changes in the sclerocorneal layer affect the way cupping develops?

  • Since we did not perform posterior segment OCT or SAP the epidemiology of glaucoma in this population may be underestimated
Discussion

• There was a significantly high prevalence of tomographically abnormal corneas...

... However

• There was no significant difference between OI clinical types

• There was no significant difference in BCVA between abnormal and normal córneas

• Are current keratoconus tomographic screening indices\(^1,2\) applicable in this populations?

1. Hashemi et. al 2016
2. Shetty et. al 2017
THANK YOU FOR YOUR ATTENTION!

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