The Association between Glaucoma Medication Adherence and Intraocular Pressure Variability in the Collaborative Initial Glaucoma Treatment Study (CIGTS)

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#1965

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PURPOSE

- Because variability of intraocular pressure (IOP) is an established risk factor for visual field loss, we investigated the association between IOP variability and medication adherence in participants randomized to the medication arm of the CIGTS

METHODS

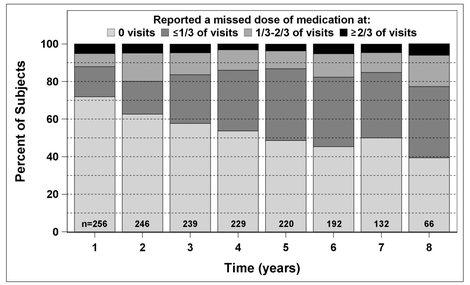
- 607 newly-diagnosed, open-angle glaucoma patients participated in the CIGTS, of which 307 were randomized to treatment with medication
- Participants were followed every 6 months up to 10 years at clinic visits, where measures of IOP were taken, and in telephone interviews, where self-reported medication adherence information was obtained
  - Cumulative measures of IOP variability (range, SD, maximum) were calculated over all available visits for years 1-8
  - Medication adherence was assessed by responses (Yes or No) to "*Did you happen to miss any dose of your medication yesterday?*"

Statistical Methods

- The effect of adherence on measures of IOP variability over time (1-8 years) was assessed with linear mixed models (unadjusted and adjusted for baseline IOP, baseline mean deviation [MD], and time [years])
- Adherence was measured as the percentage of follow-up visits where a patient reported missing a dose of their medication on the previous day
- Models excluded visits after trabeculoplasty or trabeculectomy

RESULTS

- Participants (n=307) were 53% male, 54% White, on average 57.4 years old (SD=11.2), and followed for an average of 7.3 years (SD=2.3)

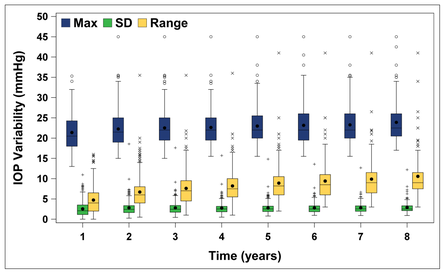


- Over all available follow-up, missing a medication dose was reported as follows:
  - 46% (n=142) never reported missing a dose
  - 37% (n=112) reported missed at ≤1/3 of visits
  - 10% (n=31) reported missed at 1/3-2/3 of visits
  - 7% (n=21) reported missed at ≥2/3 of visits
- 1 subject dropped out prior to follow-up

Baseline Variables	0 Missed (n=142) Mean (SD)	≤⅓ Missed (n=112) Mean (SD)	⅓-⅔ Missed (n=31) Mean (SD)	≥⅔ Missed (n=21) Mean (SD)	P-value*
Age (years)	58.5 (11.0)	57.9 (11.3)	56.4 (9.7)	48.4 (10.8)	0.0011
MD (dB)	-4.7 (4.1)	-5.2 (3.9)	-6.7 (5.3)	-6.3 (5.3)	0.0159
IOP (mmHg)	27.7 (5.5)	26.7 (5.0)	29.7 (6.8)	28.2 (5.8)	0.3794
	# (%)	# (%)	# (%)	# (%)	P-value*
Gender					
Male	82 (57.8)	58 (51.8)	15 (48.4)	9 (42.9)	0.1217
Female	60 (42.2)	54 (48.2)	16 (51.6)	12 (57.1)	
Race					
White/Other	92 (64.8)	70 (62.5)	17 (54.8)	7 (33.3)	0.0119
Black	50 (35.2)	42 (37.5)	14 (45.2)	14 (66.7)	

*Linear trend test

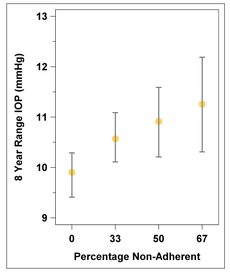
- Younger participants (p=0.0011), those with worse baseline MD (p=0.0159), and those of Black race (p=0.0119) were more likely to have worse adherence



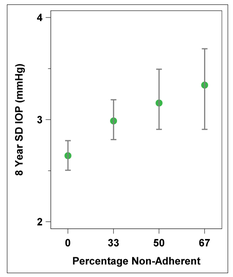
- Range of IOP increased from an average of 4.7 mmHg at year 1 to 10.6 mmHg by year 8
- SD of IOP increased from an average of 2.5 mmHg at year 1 to 2.9 mmHg by year 8
- Max IOP increased from an average of 21.4 mmHg at year 1 to 23.9 mmHg by year 8
- Measures of IOP variability were highly correlated (r=0.82 to 0.97, p<0.0001)

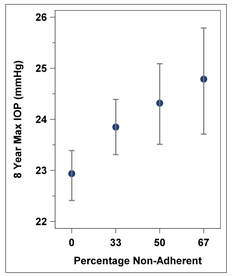
Increase in IOP Variability per 10% increase in Nonadherence			
Outcome	Estimate	95% CI	P-value
Unadjusted			
Range IOP	0.22	(0.04, 0.40)	0.0190
SD IOP	0.11	(0.04, 0.19)	0.0030
Max IOP	0.27	(0.05, 0.50)	0.0166
Adjusted			
Range IOP	0.20	(0.03, 0.37)	0.0192
SD IOP	0.10	(0.03, 0.17)	0.0039
Max IOP	0.28	(0.09, 0.46)	0.0033

- In unadjusted and adjusted models, worse adherence was associated with larger range IOP, larger SD IOP, and higher maximum IOP
- In adjusted models, a 10% increase in nonadherence was associated with a 0.20 mmHg increase in IOP range, a 0.10 mmHg increase in IOP SD, and a 0.28 mmHg increase in IOP Max



- The average IOP range at 8 years for a participant who reported never missing a dose of medication over follow-up was 9.9 mmHg (95% confidence interval, CI=9.4-10.3), whereas a participant who reported missing a dose of medication at 1/3, 1/2, and 2/3 of follow-up visits had an average IOP range at 8 years of 10.6 mmHg (CI=10.1-11.1), 10.9 mmHg (CI=10.2-11.6), and 11.3 mmHg (CI=10.3-12.2); (p=0.0192)





- A similar assocation of decreasing adherence with increasing SD IOP (p=0.0039) and increasing Max IOP (p=0.0033) was observed

CONCLUSIONS

- These results link medication non-adherence to increased IOP variability
- IOP variability has been shown to be a risk factor for visual field loss (*Musch DC, Gillespie BW, Niziol LM, Lichter PR, Varma R; CIGTS Study Group. Intraocular pressure control and long-term visual field loss in the Collaborative Initial Glaucoma Treatment Study. Ophthalmology 2011;118(9):1766-73*)
- Limitations include self-reported medication adherence, and being queried about missing medication only twice a year on only the previous day
- Further study will explore pathways between medication adherence, IOP variability, and visual field progression to capture the inter-relationship between these factors

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