Abstract:
Glaucoma patients with disease progression despite well-controlled IOPs present a management dilemma. Recent studies have shown that nocturnal IOP may be higher than pressures measured during normal office hours. Nocturnal hypotension in combination with over-night IOP spikes can place susceptible patients at increased risk for glaucomatous damage. The role of sleep position, perfusion pressure, and sleep quality on glaucoma will be discussed.

Learning Objectives:
1. Review perfusion pressure and its link to glaucoma through an evidence-based review of studies
2. Review nocturnal changes to IOP and blood pressure and how this influences glaucoma management
3. Review recent literature on sleep position and its influence on IOP
4. Review glaucoma treatment options and their effectiveness at curbing nocturnal IOP fluctuations
I. Ocular Perfusion Pressure

A. Difference between arterial BP and the intraocular pressure (IOP)
   1. Diastolic PP (DPP) = DBP − IOP
   2. Surrogate measurement of blood flow
   3. Reflects vascular status at optic disk

B. Alterations can cause ischemia and poor perfusion of tissues in optic nerve
   1. Can be due to low BP or relatively high IOP
   2. During nocturnal period, potential for both low BP and high IOP

C. Ocular Perfusion Pressure: risk factor for development of new glaucoma and progression of established glaucoma, defective autoregulatory mechanism
   1. Barbados Eye Study - low DPP (< 55 mm Hg) associated with 3 times increased risk of glaucoma, mean DPP: 63.2 healthy vs 53.8 glaucoma patients
   2. Baltimore Eye Survey – low DPP (<30 mm Hg) associated with 6 times higher risk than DPP > 50 mm Hg
   3. Egna-Neumarket Study – low DPP (< 68 mm Hg) associated with marked, progressive increase in frequency of glaucoma
   4. Singapore Malay Eye Study – Low diastolic BP and DPP < 56 risk factor for glaucoma, vascular mechanism in glaucoma development/progression
5. Los Angeles Latino Eye Study – both low diastolic and high systolic BP associated with increased prevalence of open-angle glaucoma

6. OCT Angiography Vessel Density and Severity VF Loss Glaucoma (Yarmohammadi et al)

II. Ocular Perfusion Pressure: Nocturnal influences on IOP
   A. Management Dilemma
      1. Glaucoma patients with advanced disease and/or progression despite low pressures during office visits
      2. Fragile Nerve? Weak supporting tissue?
      3. Compliance, patient ability to instill drops?
4. Washout Effect?
5. Diurnal curve
   i. Serial Tonometry, IOP checks in AM or PM
6. Ocular Perfusion Pressure in Low Tension Glaucoma
   i. Defective autoregulatory mechanisms, prevent maintenance of adequate blood flow in face of nighttime changes in IOP and BP

B. Nocturnal IOP
1. 24 hour IOP monitoring
   i. Highest IOPs often measured when patient is not in office.
   ii. Greater fluctuation of IOPs
   iii. 24 hour Contact Lens Sensors (CLS) – Sensimed Triggerfish

- NTG larger IOP fluctuations vs Non-Glaucoma patients, majority of highest IOP measurements during sleep for both groups (Tojo et al. J Glaucoma 2017).
2. Both healthy and glaucoma patients experience increase in IOP overnight (Mosaed et al. Correlation between office and peak nocturnal IOP in healthy subjects and glaucoma patients)

3. Office readings may not give accurate clinical picture
   i. Exercise caution when extrapolating results of in-office IOP measurements when making glaucoma treatment decisions

4. Sleeping on back - Supine position
   i. IOP increases – due to increased episcleral venous pressure?
   ii. Nocturnal IOP increase still seen even when all IOP measurements performed around the clock in supine position; more than just supine position involved

5. Supine position
   i. Glaucoma patients greater IOP rise when change from upright to horizontal vs. normals
   ii. Greater IOP variation with more advanced disease
   iii. Worsening of visual field in NTG associated with IOP in supine position and magnitude of IOP elevation with postural change

6. Lateral Decubitus Position
   i. Sleeping on side – majority of obese people, preference for LDP emerges in 35-45-year-old group, preferred position older age groups
   ii. Higher IOP dependent eye in healthy subjects, glaucoma suspects, glaucoma
iii. Larger C/D ratio on preferred side for sleeping
iv. Asymmetric visual field loss preferred sleep side
v. Narrow angles on Anterior Segment OCT (Park et al. J Glaucoma 2017)
   - Left lateral decubitus (OD temporal angle, OS nasal angle both narrow when switch from sitting to LLD)

7. Sleeping on stomach – Prone position
i. Significantly higher IOP than supine position
ii. Angle closure risk – A/C shallows due to gravity
iii. Spinal surgery studies – CRAO, PION
   - Risk factors: hypotension, anemia, length of surgery
iv. Reverse Trendelenburg position → fewer high IOP measurements
8. Head Position and IOP

i. 30 degree head-up position lower IOP 94% (Buys et al. Ophthalmology 2010)

ii. 20 degree head-up position w/ wedge pillow, 83.3% lower mean IOP (Lazzaro et al. J Glaucoma 2014)

iii. IOP neck flexion >> IOP neck extension (Malihi et al. Ophthal 2012) – too many pillows negates effect on lowering IOP?

iv. Bed head elevation better than multiple pillows, lower IOP (Park et al. Optom Vis Sci 2016) – Figure B position better than Figure C for lowering IOP.
9. Yoga Positions

i. 15 mmHg increase with headstand posture (Baskaran et al. Oph 2006)

ii. Compared to IOP while sitting: Position 1 – 12 mmHg higher
    Position 2 – 10 mmHg higher, Position 3 – 6 mmHg higher, Position 4 – 4 mmHg higher (Jasien et al. PLOS One 2015)
10. Management Pearls
   i. Elevating head by using wedge pillow neutralized IOP increase
   ii. Supine position better for IOP than prone position, especially in patients with potential for angle closure

C. IOP lowering treatment
   1. Aqueous humor production significantly lower at night, ~ 50%

![Graph showing aqueous humor flow at daytime and nighttime](image1)

2. Beta blockers and alpha 2 agonists not as effective during nocturnal period

![Graph showing habitual IOP](image2)
3. Prostaglandin analog have sustained 24-hour IOP lowering effect
   i. Liu et al. Am J Oph 2004 (Square = latanoprost, Triangle = Timolol),
      Circle = control; Orzalesi et al IOVS 2000

4. Carbonic anhydrase inhibitors shown to be better than beta blockers and
   alpha 2 agonists at controlling nocturnal IOP
   i. Orzalesi et al. IOVS 2000; Liu et al. Ophthalmology 2009 (graph below);

5. SLT showed benefit in nocturnal IOP measurements even if did not show
   response during the day

6. Trabeculectomy controlled 24-hour IOP better than maximum medications
III. Ocular Perfusion Pressure: Nocturnal Hypotension

A. Hypertension
   1. One of most important risk factors for cardiovascular morbidity and mortality
      i. Risk of cardiovascular mortality doubles with each 20 mm Hg rise in systolic BP and each 10 mm HG rise in diastolic BP

B. Hypotension – not ideal either
   1. Stroke, heart attack, heart failure, renal damage, end-organ damage
   2. “White Coat Syndrome” – over Tx and over-reduction BP
   3. Orthostatic Hypotension: flashes and floaters with postural changes
   4. During sleep, decrease in sympathetic nervous system – leads to nocturnal dip in blood pressure ~ 10-15%, more with blood pressure medications

C. Glaucoma: nocturnal hypotension risk factor development/progression
   1. Overdippers, BP drop > 20% during nocturnal period
   2. Hayreh Study (Am J Oph 1994): If diastolic BP decreased below critical level, beneficial effect is lost and mortality/morbidity rates increase again. Avoid excessive reduction of BP overnight
   3. Rotterdam Study (Muskens et al. Ophthalmology 2007)– only patients on antihypertensive medications, 4.68 times greater chance of developing glaucoma in patients with low DPP < 50 mm Hg compared to DPP > 65 mm Hg; increased risk POAG w/ calcium channel blockers
   4. Low Pressure Glaucoma Treatment Study – BP Medication was risk factor for optic disk hemorrhage (Am J Oph 2014) and VF progression (Am J Oph 2012)
   5. Thessaloniki Eye Study (Topouzis et al. Am J Oph 2006)– cup area, C/D ratio were increased and rim area decreased in subjects with lower DBP resulting from treatment compared to high DBP and untreated normal DBP groups
   6. Systolic BP increase of 10 mm HG is equivalent to 0.23 – 0.32 mmHg higher IOP.
      Diastolic BP increase of 10 mm Hg equivalent to 0.19 to 0.60 increase in IOP
   7. Low nocturnal BP (BP medication induced or spontaneous) increased risk glaucoma progression (Charlson, Oph 2014; Kwon et al. Am J Oph 2017)
   8. If not contraindicated, consider changing blood pressure medication dosage time to morning

D. Other Nocturnal Considerations
   1. Obstructive Sleep Apnea
      i. Pauses in breathing or abnormally low breathing during sleep
      ii. Characterized by snoring, restless sleep, daytime drowsiness
      iii. Continuous Positive Airway Pressure (CPAP)
         1. Keeps airway open during sleep
         2. Also increases IOP, but believed that oxygen delivery more important to glaucoma than IOP increase (Kiekens et al. IOVS 2008; Kadyan et al. Eye 2010)
iv. Glaucoma

1. Higher prevalence of glaucoma in OSA patients than general population (Mojon et al. Oph 1999)
2. Higher rates of Glaucoma in moderate/severe OSA
   - Lin et al. J Glaucoma 2011
3. Worse sleep apnea, more RNFL loss
   -- Zhao et al. J Glaucoma 2016
4. Ischemic Mechanism: disrupted blood flow from either less blood reaching optic nerve or less oxygen in blood that does reach optic nerve

2. Erectile Dysfunction Medications
   i. ED patients 2.85 fold greater POAG risk (Chung et al. Oph 2012)
   ii. Positive association between ED severity and severity of glaucoma
      (Law et al. J Glaucoma 2016)


Hughes BA, Bacharach J, Craven R. 3-Month, Multicenter, Double-Masked Study of the Safety and Efficacy of Travoprost 0.004%/Timolol 0.5% Ophthalmic Solution compared to Travoprost 0.004% Ophthalmic Solution and Timolol 0.5% Dosed Concomitantly in subjects with open angle glaucoma or ocular hypertension. J Glaucoma 2005; 14: 392-399


Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120 (6): 701-713


Kluchi T, Motoyama Y, Oshika T. Relationship of progression of visual field damage to postural changes in IOP in patients with normal tension glaucoma. Ophthalmology 2006; 113 (12): 2150-2155.

Korenfeld MS, Dueker DK. Occult IOP elevations and optic cup asymmetry, sleep posture may be a risk factor. Invest Ophthalmol Vis Sci. 1993:34. Abstract 994.


McMonnies CW. An examination of the hypothesis that IOP elevation episodes can have prognostic significance in glaucoma suspects. Journal of Optometry (2015) 8, 223-231.

Mehdizadeh M. Sleep position and eye pressure. Ophthalmology. 2007; 114 (12): 2362


