Cover Story

Data on IOP are usually obtained three to four times a year in a typical glaucoma patient. The IOP is typically collected during office hours in the clinic and, although it fluctuates, it is considered representative of daytime IOP. We know very little about the IOP during non-office hours, which includes IOP during sleep. Systemic blood pressure, concurrent obstructive sleep apnea (OSA), and sleeping position, for example, can also have an effect on glaucoma and its management. The implications of these are described in this article.

Sleeping IOP and Circadian Rhythms
An individual’s true IOP during sleep is unknown. Studies investigated the diurnal, nocturnal, and 24-hour IOP in supine, sitting, and habitual positions among patients with glaucoma and healthy controls.\(^1\)\(^2\) The IOP is lower for the sitting position than the supine position in both normal and glaucomatous eyes.\(^1\) The daytime variation in the sitting as well as supine IOP was found to be greater in glaucomatous compared with healthy eyes. In the nocturnal period, however, variations in supine IOP were not different between healthy and glaucomatous eyes.\(^1\)

Waking IOP Spikes
IOP is lowest during REM sleep and highest during slow-wave sleep.\(^3\) When people awake, however, the IOP rises in both normal as well as glaucomatous eyes compared with presleep levels, and this pressure decreases to baseline levels over 12 minutes in healthy individuals.\(^4\)\(^5\) The exponential decrease in IOP during those 12 minutes is accompanied by an exponential decrease after a blood pressure (BP) spike that occurs on waking.\(^5\) The BP spike does not dissipate in 12 minutes in glaucoma patients who have an obstructed outflow mechanism.\(^4\) The reason for the nocturnal IOP elevation is unclear, because aqueous flow decreases by approximately 50% at night. Possible mechanisms that have been suggested include a rise in episcleral venous pressure associated with waking from REM sleep,\(^6\) choroidal engorgement due to a rise in BP with increased ocular volume,\(^7\) and changes in uveoscleral outflow.\(^8\)

There is no known way to check IOP during sleep. Although peak IOP has been found to occur during the nocturnal/sleep period in 24-hour studies,\(^3\)\(^3\)\(^9\) it is difficult to determine whether this represents the IOP associated with the waking phenomenon or if it is representative of the patient’s true sleeping IOP.\(^3\) Control of nocturnal IOP through the use of long-acting drugs or surgical therapies may be necessary for patients whose glaucoma is progressing despite control of their daytime IOP.\(^10\) There is also the possibility that a corresponding rise in cerebrospinal fluid pressure in the supine position may counterbalance the effects of the raised IOP on the lamina cribrosa.\(^11\)

Sleep Studies and Circadian Rhythms: Connecting Glaucoma and Sleep

IOP changes in the nocturnal period.

By Sanjay G. Asrani, MD
**IMPACT OF NOCTURNAL SYSTEMIC HYPOTENSION**

Low nighttime BP is a risk factor for glaucomatous progression. Both in normal-tension glaucoma (NTG) and in primary open-angle glaucoma, worse visual fields are associated with minimal nighttime BP, especially in hypertensive patients taking oral antihypertensive therapy. It has been suggested that aggressive antihypertensive treatment may make such individuals more vulnerable to disease progression.12-15

Patients with NTG showed increased variability of nighttime BP compared with controls. Increased fluctuation in BP may lead to fluctuation in ocular perfusion pressure and cause ischemic episodes at the optic nerve head.16 Greater variation in mean ocular perfusion pressure has been shown to be associated with nocturnal hypotension in NTG patients.17 In fact, 24-hour fluctuation in mean ocular perfusion pressure was the most consistent risk factor for glaucomatous progression in a cohort of 101 NTG eyes.18

**OSA AND GLAUCOMA**

OSA is a sleep-related breathing disorder that is associated with multiple hypoxic nocturnal episodes and excessive daytime sleepiness. Increased sympathetic system activation occurs in patients with OSA along with higher incidences of cardiovascular disease and open-angle glaucoma.19

With disturbed autoregulation, such as in OSA, a mild reduction in perfusion pressure may lead to significant changes in ocular blood flow. This problem is more likely to occur at lower-than-normal diastolic BP, such as with nocturnal dips in BP. Unstable ocular blood flow may result in ischemia-reperfusion injury to the optic nerve head (site of concentrated mitochondria), which is associated with oxidative damage and the release of free radicals. Fluctuations at high IOP levels (or even with normal IOP levels associated with disturbed autoregulation) also destabilize ocular perfusion. Significant variations in IOP (mean range, 6.7 mm Hg) occur in a majority (85%) of OSA patients and are possibly associated with multiple awakenings.19 Significant fluctuation in ocular perfusion pressure is seen in patients with OSA. Variations in IOP, especially at times of fluctuations in perfusion pressure, can overwhelm the autoregulation of blood flow to the optic nerve.

In OSA, both IOP fluctuations and perfusion pressure disturbance occur simultaneously. Unfortunately, the treatment of OSA with the current gold standard, continuous positive airway pressure, is associated with worse IOP fluctuations and a further decrease in perfusion pressure.19,20

**SLEEPING POSITION AND GLAUCOMA**

Patients with OSA typically sleep in the prone position. Floppy lid syndrome (due to lax eyelids and rubbing of the conjunctiva on the pillow) is commonly associated with OSA. Thus, a diagnosis of floppy lid syndrome can suggest a diagnosis of OSA and associated glaucoma.

Rarely, unilateral glaucoma is associated with sleep position. Patients may sleep with one of their eyes pressing into their elbows, which might result in unilaterally increased pressure during the night. When the patient’s eyes have hypotony, it is important to caution him or her regarding sleeping position (or to wear a shield at bedtime) so as to minimize the risk of corneal endothelial damage due to inadvertent pressure on and collapse of the anterior chamber.

**CONCLUSION**

Knowledge about the various changes in IOP during sleep and on waking up may help us better understand the pathogenesis of glaucoma. It may help explain why some of our patients continue to worsen despite seemingly good control of daytime IOPs. New long-acting medications and surgeries that blunt these changes need to be developed. A history of OSA, unusual sleeping position, and systemic BP may help us better guide our patients in their glaucoma management.

Sanjay G. Asrani, MD, is an associate professor of ophthalmology and the director of education at the Duke Eye Center in Durham, North Carolina. Dr. Asrani may be reached at (919) 684-8656; asran002@mc.duke.edu.

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