



Arthur J Sit

Cheryl Guttman
in Las Vegas

INTRAOCULAR pressure is a “sleeping giant”, rising at night to play a possible role in glaucoma development and progression. Based on that premise, greater attention is needed to understand the efficacy of glaucoma therapy for providing 24-hour IOP control, said Arthur J Sit MD, at the 2006 glaucoma subspecialty day meeting of the American Academy of Ophthalmology.

“Research is currently ongoing examining a number of factors that might explain the cause of the nocturnal rise in IOP, and there are no studies that have demonstrated its role as an independent risk factor for glaucoma. However, there are good reasons to suspect nocturnal IOP elevation is clinically relevant in glaucoma development and progression,” said Dr Sit, assistant professor of ophthalmology, Mayo Clinic College of Medicine, Rochester, Minnesota, US.

Dr Sit reviewed studies characterising the circadian behaviour of IOP, a hypothesis regarding the pathophysiological role of the nocturnal increase, effects of glaucoma treatments on nocturnal IOP, and research being conducted to understand its cause.

Dr Sit told attendees that the idea that IOP is a dynamic physiologic parameter governed by circadian rhythms is not new. It has been almost 50 years since Drance first described diurnal variation in IOP, showing a peak occurred in early morning in most individuals and that glaucoma patients manifested greater variation compared with normal people. However, his studies covered only the waking period.

Subsequently, researchers investigating 24-hour variation of IOP showed that IOP was highest in the morning and slightly lower at night during sleep. As a limitation, however, IOP in those studies was measured with subjects in a sitting position during the entire 24-hour period.

Using a sleep laboratory setting, investigators at the Hamilton Glaucoma Center, University of California San Diego, measured IOP in habitual positions with subjects sitting and supine during the day

and supine at night. They also reported that IOP fell during the day as Drance initially described, but found it increased rapidly at bedtime when the study subjects assumed the supine position.

“After eliminating the effect of body position change, most of the nocturnal rise was eliminated. However, peak IOP was still observed during sleep in most of the normal subjects. Among patients with glaucoma, the peak IOP was early in the morning when position changes were eliminated but IOP was highest at night considering data when measured in the habitual positions,” Dr Sit said.

Those findings suggested that change in body position plays a role in the nocturnal rise in IOP. However, it does not appear to be the whole story. In contrast to IOP, aqueous production drops by about 50 per cent at night in both normal and glaucomatous eyes.

“If all other factors remain equal, the change in aqueous production would be expected to lead to a decrease in nocturnal IOP rather than a rise,” Dr Sit said.

In order to understand the reason for the nocturnal rise in IOP, Dr Sit and colleagues at the Mayo Clinic are currently investigating the role of nocturnal changes in outflow facility and of position independent change in episcleral venous pressure. They are also examining the possibility that there is individual variation in aqueous production rates.

Discussing the possible pathogenic role of the nocturnal rise in IOP, Dr Sit observed that the fact that it appears to be a physiologic process raises the question of whether it matters clinically. The answer may come from another physiologic process – the drop in systemic blood pressure that occurs at night corresponding to the rise in IOP, Dr Sit said.

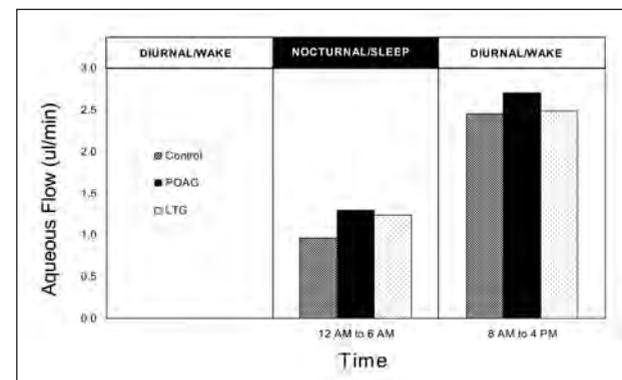
“Conceivably, those two events may act in concert to compromise optic nerve head circulation and lead to the development or progression of glaucoma in susceptible individuals. In fact, it has been reported that an exaggerated dip in nocturnal BP may be an additional risk

factor for glaucomatous visual field loss,” he explained.

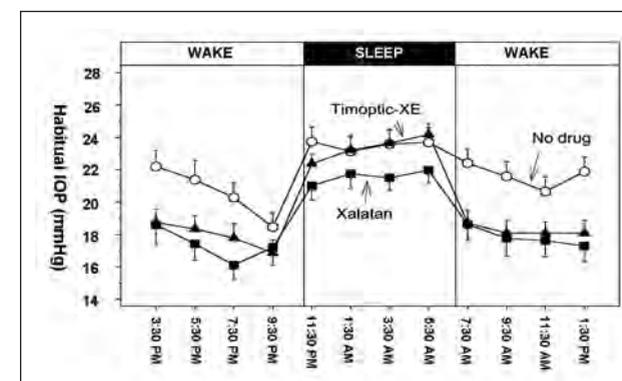
Results from studies conducted in the sleep laboratory at the Hamilton Glaucoma Center also showed that not all IOP-lowering medications are alike when it comes to 24-hour IOP control. In an initial study comparing latanoprost and timolol, those investigators found the prostaglandin analogue provided good control for the entire 24-hour period and was associated with lower IOP during the nocturnal hours compared with during the day. In contrast, the beta-blocker provided good efficacy during the day, but IOP returned to baseline while the subjects were asleep.

“Subsequent studies show that 24-hour efficacy appears to be a class effect of prostaglandin analogues and that therapies increasing outflow appear to be better for stabilising IOP than those reducing aqueous production. The lack of efficacy of aqueous suppressants may reflect their limited ability to further decrease aqueous production that is already reduced to a basal level during sleep,” Dr Sit said.

He noted results of studies comparing 24-hour IOP control achieved after trabeculectomy versus with medical management suggest that surgery may be better for stabilising IOP. Compared with their counterparts being treated with ocular hypotensive medications, patients who had undergone trabeculectomy in those trials were found to have fewer IOP



Diurnal to nocturnal change in aqueous flow rate in normal subjects and glaucoma patients



24-hour efficacy of latanoprost vs timolol

Courtesy of Arthur J Sit MD

fluctuations and more consistent IOP control, Dr Sit reported.

“Fortunately, we have therapeutic modalities that can control the elevation in IOP occurring at night. However, we are still waiting for a 24-hour ambulatory monitoring system that would provide an easier way to measure IOP around the clock, and in the future, it will be important that investigations of therapies for glaucoma include examination of their effects on nocturnal IOP,” he commented.

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