A Patient with Primary Open-Angle Glaucoma with Re-Elevated Nocturnal Sitting Intraocular Pressure after Restarting Medical Therapy due to a Bleb Failure

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We describe the case of a primary open-angle glaucoma patient with re-elevated nocturnal sitting intraocular pressure (IOP) after restarting medical therapy due to a failing bleb. IOP was markedly higher than diurnal IOP during multiple-drug therapy in both eyes, but it did not increase in the left eye with a functional bleb without medical therapy after trabeculectomy with adjuvant mitomycin. However, nocturnal sitting IOP was re-elevated after restarting multiple-drug therapy due to a failing bleb, while diurnal IOP was maintained at a low level. (J Nippon Med Sch 2021; 88: 509-511)

Key words: 24-hour intraocular pressure, trabeculectomy, diurnal intraocular pressure variation, nocturnal intraocular pressure, glaucoma

Introduction
Glaucoma is a leading cause of visual function loss. The only reliable treatment at present is the use of intraocular pressure (IOP) reduction therapy. Antiglaucoma eye drops are generally started as the initial treatment for primary open-angle glaucoma (POAG). Prostaglandin F2α analogs (PGF2α) have been commonly used as the first-line treatment for glaucoma. PGF2α has a 24-hour IOP-lowering effect in POAG and normal tension glaucoma. However, with combination therapy of glaucoma eye drops, sitting IOP tends to increase during the nighttime in open-angle glaucoma and POAG. In contrast, trabeculectomy with adjunctive mitomycin C (TLE) can lower IOP much more than drug therapy during not only the daytime, but also the nighttime. However, if clinic IOP re-elevates over the target IOP due to a failing bleb, glaucoma eye drops are generally re-started. In relation to both selective laser trabeculoplasty and trabeculotomy combined with sinusotomy, there are some reports that nocturnal sitting IOP was significantly lower than preoperative sitting IOP, although there was no significant diurnal sitting IOP reduction. However, it is unclear whether nocturnal sitting IOP re-elevates after restarting multiple-drug therapy due to a failing bleb after TLE while diurnal IOP maintains at a low level.

In the following report, we describe the case of a POAG patient with re-elevated nocturnal sitting IOP after restarting medical therapy due to a failing bleb.

Case Report
A 47-year-old woman with POAG was referred to our hospital for further examination and treatment due to rapid visual field deterioration in the left eye despite a well-controlled clinic IOP of approximately 12 mmHg. Her untreated clinic IOP was 18 mmHg in both eyes according to her referral letter from a previous doctor. At her first visit, her preoperative spherical equivalents were 0.5 D in both eyes, and her corrected visual acuity was 20/20 in both eyes, with an IOP using Goldmann applanation tonometry (GAT) of 14 mmHg in both eyes. Both her eyes were being treated with latanoprost ophthalmic solution 0.005% (latanoprost) eye drops once per day each night and timolol gel-forming solution 0.5% (timolol) eye drops once per day each morning. Slit lamp
Fig. 1 Twenty-four-hour sitting IOP during multiple-drug therapy
Nocturnal IOP at 1 AM and 3 AM were markedly higher than diurnal IOP during multiple-drug therapy in both eyes.

Fig. 2 Twenty-four-hour sitting IOP without medical therapy with a functional bleb after TLE
There was no nocturnal IOP elevation in the left eye, in contrast with the right eye. TLE: trabeculectomy with adjunctive mitomycin C.

Fig. 3 Twenty-four-hour sitting IOP after restarting medical therapy due to a failing bleb
Nocturnal IOP was re-elevated at 1 AM and 3 AM in both eyes, although the IOP of the left eye is lower than that of the right eye at all 8 time points.

examination showed normal findings in both eyes. Gonioscopy showed open angles in both eyes. Fundus examination showed definite inferior temporal and superior temporal retinal nerve fiber defects and enlargement of optic disk cupping in both eyes. Humphrey perimetry program 30-2 performed by a previous doctor showed corresponding superior nasal and inferior nasal visual field defects in both eyes, and definite progression in the left eye. Because IOP elevation outside clinic hours was suspected, sitting IOP was measured at 10 AM, 1 PM, 4 PM, 7 PM, 10 PM, 1 AM, 3 AM, and 7 AM through 24-h periods by GAT during the medical therapy in the hospital (Fig. 1). Nocturnal IOPs at 1 AM and 3 AM were markedly higher than diurnal IOPs in both eyes. For the purpose of lowering 24-h IOP, TLE was performed in the left eye. At about 18 months after TLE, 24-h sitting IOP of the right eye during medical therapy (latanoprost, timolol, and brinzolamide 1% ophthalmic suspension twice per day each morning and night) and of the left eye without medical therapy were measured in the hospital (Fig. 2). There was no nocturnal IOP elevation in the left eye, in contrast with the right eye. However, left IOP increased to 15 mmHg without glaucoma eye drops along with a failing bleb. Needle revisions of the bleb were performed twice in the left eye, but left IOP re-elevated to 15-16 mmHg. Then, latanoprost and dorzolamide/timolol fixed combination (dorzolamide/timolol) twice per day each morning and night were instilled into both eyes. The clinic IOP in both eyes remained at 10-13 mmHg thereafter, but clinic IOP of the left eye was almost always lower than that of the right eye. At about 5 years after TLE, 24-h sitting IOP of both eyes was re-measured during medical therapy (latanoprost and dorzolamide/timolol) in the hospital. The nocturnal IOP was re-elevated at 1 AM and 3 AM in both eyes, although IOP of the left eye was lower than that of the right eye at all 8 time points (Fig. 3).

Discussion
IOP reduction treatment is the only evidence-based treatment for glaucoma at present. It is well-known that there are not a few patients whose sitting IOP measured outside clinic hours is high among those with rapid visual field defect progression despite low clinic IOP treated with anti-glaucoma eye drops\(^\text{10}\). In addition, nocturnal sitting IOP tends to be higher than diurnal sitting IOP during combination glaucoma drug therapy\(^\text{7,7}\). The mechanism remains unclear, but it may be due to a smaller pharmacological effect of almost all glaucoma drugs during the nighttime than during the daytime\(^\text{10,12}\).
In contrast, successful TLE can lower 24-hour IOP much more than drug therapy throughout the day\(^6\), mainly because functional TLE has an aqueous pathway to the subconjunctival space\(^7\).

The present patient also had nocturnal sitting IOP elevation during combination glaucoma drug therapy. However, while the filtering bleb remained functional and medication was not needed, there was no nocturnal IOP elevation. In contrast, when the bleb function failed and multiple-drug therapy was again required, the nocturnal sitting IOP was re-elevated during the nighttime in the left eye, although the IOP of the left eye was lower than that of the right eye at all time points. We previously reported a significant positive correlation between mean sitting IOP and 24-h sitting IOP fluctuation in POAG patients without medication after TLE\(^9\). Thus, in order to maintain low sitting IOP throughout the day, keeping good bleb function and sitting IOP as low as possible without medication may be needed.

In summary, the present POAG patient developed re-elevated nocturnal sitting IOPs after restarting medical therapy due to a failing bleb although the nocturnal elevation of IOP was suppressed with a functional bleb after TLE. This indicates that caution must be taken in patients with re-elevated nocturnal sitting IOP when restarting medical therapy after TLE even if clinic IOP is maintained at a low level.

**Conflict of Interest:** The authors have no conflicts of interest.

**References**


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