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ORIGINAL PAPER

The characteristic of intraocular pressure dynamic change in patients with glaucomatocyclitic crisis

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Abstract

Purpose To investigate the characteristic of intraocular pressure (IOP) dynamic change from episode to intermittent period in patients with Posner–Schlossman syndrome (PSS).

Patients and methods Seventeen cases of typical PSS were collected in this study. Both their random IOP in episodes/intermittent period and 24-h IOP in intermittent period were measured. The mean IOP as well as the peak and the valley value of 24-h IOP were calculated. Those data were statistically analyzed.

Results The IOP in affected eye in episodes is higher than that of the contralateral eye statistically; while in intermittent period the mean IOP ($p = 0.001$), the peak ($p = 0.029$) and the valley ($p = 0.004$) value of 24-h IOP in affected eye are statistically different with that of the contralateral eye. All of these parameters of the affected eye in intermittent period are lower than that of the contralateral eye obviously.

Conclusion The dynamic observations of IOP in episodes and intermittent period confirmed the IOP crossover phenomenon inpatients with typical PSS and this observation may be important in the differential diagnosis of PSS.

Keywords Glaucomatocyclitic crisis · Intraocular pressure · 24-h intraocular pressure measurement · Crossover phenomenon

Abbreviations

PSS	Posner–Schlossman syndrome
KP	Keratic precipitate
IOP	Intraocular pressure
C value	Coefficient of outflow facility
GOND	Glaucomatous optic nerve damage
CCTS	Central corneal thickness
POAG	Primary open-angle glaucoma's

Introduction

Glaucomatocyclitic crisis was initially described by Posner and Schlossman in 1948 [1, 2], as the so-called Posner–Schlossman syndrome (PSS). It is classified as an inflammatory glaucoma, because it is always accompanied by uveitis [3]. It is characterized by acute, recurrent, and monocular intraocular pressure (IOP) elevation and keratic precipitate (KP). Visual field and visual function are generally normal, but a reversible expanding of vascular shadow may occur during an acute onset of PSS. Coefficient of outflow

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facility (C value) descends in episodes and recovers in intermission. Various stimulation tests for glaucoma are negative in intermission.

Confirmation of the diagnosis of PSS may be difficult, even for typical cases. Misdiagnosis is not rare because of atypical symptoms and signs, such as delayed appearance or hiding in the anterior chamber angle, lack of the hoar and suet-shaped KP, corneal edema, and the absence of diagnostic symptoms and signs during intermittent periods. The prognosis of PSS is regarded as good when diagnosed at an early age, but glaucomatous optic nerve damage (GOND), similar to that in primary glaucoma cases, occurs in many of the PSS cases as the disease progresses, according to recent reports [4–6]. Early diagnosis and treatment are critical for PSS.

It has been reported that IOP of the affected eye is higher than that of the contralateral eye during PSS episodes and lower in intermittent periods, while the C value is opposite in typical PSS patients [7, 8]. This phenomenon is known as the IOP crossover phenomenon [9–12], which is important in the diagnosis or differential diagnosis of PSS. However, these studies were based on individual case reports or random IOP measurements taken during the day. IOP fluctuates with circadian rhythm, and the peak IOP usually appears in the night, especially while sleeping. Therefore, the conclusions described above may not be reliable. The current study investigated the characteristics of IOP change with PSS using a standard 24 h of IOP measurements.

Materials and methods

This descriptive study was approved by the Institutional Review Boards at Wuhan General Hospital of the Chinese People's Liberation Army, and was conducted in accordance with the Declaration of Helsinki. Consents were obtained from all subjects.

Seventeen patients with typical cases of PSS were recruited for the study from February 2014 to December 2015. Of these subjects, nine (52.94%) were male and eight (47.1%) were female. In 12 cases (70.6%), the left eye was involved and in five cases (29.4%) the right eye was involved.

Inclusion criteria for typical PSS cases were based on Jap's diagnostic standards [13] as follows:

(1) Unilateral.
(2) Recurrent episodes of mild, non-granulomatous cyclitis.
(3) Symptoms of mild discomfort, halos, and slight blurring of vision.
(4) Findings of elevated IOP, open angles, hoar and suet-shaped KP, no or minimal cells and flare, and mydriasis in the affected eye.
(5) Episodes lasting a few hours to a few weeks.
(6) Normal visual fields and optic disk.
(7) Normal IOP, tonography, and provocative tests between episodes.

The exclusion criteria were:

(1) Cases complicated with other types of glaucoma or other eye diseases, with the exception of mild refractive errors.
(2) Cases with cardio-cerebrovascular disease.
(3) Use of medications that affect IOP.

The validation of the intermittent period of PSS was required to be completed before the preparation for the 24-h IOP measurement. After an attack of PSS, the patient was followed up by Dr. Zhou for 4 weeks, with weekly examination including best-corrected vision acuity, office-time IOP, slit lamp, and direct ophthalmoscope. The confirmation standard of the intermittent period was by:

(1) IOP below 21 mmHg.
(2) Disappearance or significant reduction of KP.
(3) No recurrence of PSS after withdrawal of all drugs for at least 7 days.

Preparation for 24-h IOP measurement

The researchers obtained a detailed medical history of each patient, and recorded the office-time IOP in episodes of PSS.

Each subject was requested to comply with the following orders:

(1) Sleep for at least 8 h lying in bed with all lights turned off every night for the week before the measurement day.
(2) Do not consume any food affecting IOP (such as alcohol, coffee.) the day preceding the measurement day.

(3) Avoid drinking water within half an hour before every measurement.

Methods for 24-h IOP measurement

Patients were hospitalized at 7 AM and stayed for the following 24 h. They were asked to remain awake from 6:30 AM to 11:00 PM, and to lie in bed from 11:00 PM to 6:30 AM. IOP was measured at 7:30 AM, 9:30 AM, 11:30 AM, 1:30 PM, 3:30 PM, 5:30 PM, 7:30 PM, and 9:30 PM (awake time), and 11:30 PM, 1:30 AM, 3:30 AM, and 5:30 (sleeping time), according to the method recommended in the recent expert consensus of our country.

During the awake time, every measurement of IOP was completed with the patient in a sitting position, using a Goldmann applanation tonometer (HAAG-STREIT company in Switzerland) under bright light (500–1000 lx). During the sleeping time, the measurements were completed with the patient in a side-lying position, using a hand-held rebound (TAOLI ICARE tonometer of TIOLATO company in Finland tonometer under faint light (< 10 lx). The patient was awakened and turned to the side-lying position 10 min before each measurement. The superior eye was examined first, then the patient was turned over to the other side, and the other eye was measured after 10 min. At 7:30 AM, the sitting IOP was measured with both tonometers to correct for differences between the two tonometers. All measurements were taken by the same well-trained glaucoma doctor. If the results differed over 2 mmHg, a third measurement was taken, and the mean of the three measurements was recorded.

Intraocular pressure correction

Studies have shown that the IOP is positively correlated with central corneal thickness (CCT) [14]. Zhen and Wang [15] believe that the change in position is the important reason of intraocular pressure change during sleep.

Calibration of the measured IOP value was calculated by CCT correction and position effect correction [16].

$$\text{CCT correction} = [(520 - \text{CCT})/70] \times 5.$$

Position effect correction for different averaged IOP values is 2 mmHg for that < 15 mmHg, 3 mmHg for 15–20 mmHg, and 4 mmHg for that > 20 mmHg [12].

The corrected IOP value during awake time = IOP value in the sitting position (CCT correction).

The corrected IOP value during the sleeping time = (tested IOP value) − (CCT correction) − (the difference between the two tonometers) − (position effect correction).

Statistical analysis

After calibration of the measured values, the office-time IOP in episodes and the averages of the averaged IOP, peak and valley values of the affected and contralateral eye in intermittent period were calculated, respectively. SPSS 18.0 statistical software and Chi-square paired *t* tests were applied in the statistical processing of data.

Results

The baselines of the PSS patients are described in Table 1. The mean age was 30.8 ± 8.1 years and 44.3 ± 5.4 years in male and female patients, respectively. Left eyes were involved in 12 cases (8 male, 4 female), right eyes were involved in five cases (1 male, 4 female). Corneal edema was found in two cases (11.8%), while atypical KP was found in three cases (17.6%).

The fluctuation of 24-h IOP of both eyes during the intermittent period is depicted in Fig. 1. The curves of the IOP values of the affected eyes and the contralateral eyes were similar, with the peak values mainly found at 5:30 AM and the valley values at 1:30 PM. The IOP of the affected eyes were lower than that of the contralateral eyes at 7:30 AM, 9:30 AM, 11:30 AM, 1:30 PM, 3:30 PM, 5:30 PM, 7:30 PM, 9:30 PM, 11:30 PM, 1:30 AM, 3:30 AM, and 5:30 AM during the 24 h of measurements ($p < 0.001$, $p = 0.003$, $p = 0.004$, $p = 0.028$, $p = 0.001$, $p = 0.017$, $p = 0.006$, $p = 0.005$, $p = 0.047$, $p = 0.007$, $p = 0.044$, and $p < 0.001$, respectively).

The dynamic changes of IOP between episodes and intermission of the affected and the contralateral eyes are shown in Fig. 2 and Table 2.

Table 1 The baseline characteristics of the Posner–Schlossman Syndrome patients

Patient number	Sex	Affected eye	Age (y)	Duration of disease (y)	Highest IOP (mmHg)	Corneal edema	Atypical KP
1	M	L	38	**7**	46	+	−
2	M	L	47	4	39	−	−
3	M	L	33	4	42	−	+
4	M	L	23	8	60	+	−
5	F	L	50	4	37	−	−
6	F	L	63	3	41	−	−
7	M	L	43	3	38	−	−
8	M	R	30	2	52	−	−
9	F	L	50	1	60	−	−
10	M	L	45	6	43	−	−
11	F	R	32	2	46	−	−
12	M	L	57	3	39	−	−
13	M	L	42	3	47	−	+
14	F	R	37	2	48	−	−
15	F	R	39	1	55	−	+
16	F	R	50	1	49	−	−
17	F	L	33	1	53	−	−

M male, *F* female, *L* left, *R* right, *KP* keratic precipitate, *IOP* intraocular pressure

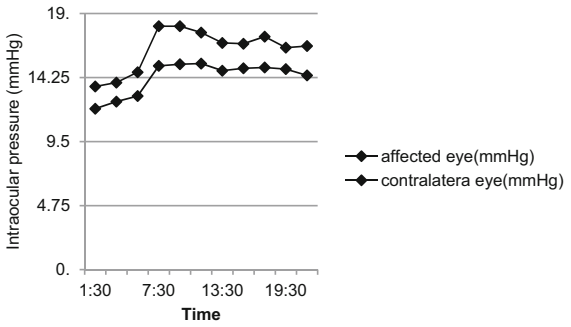

Fig. 1 Fluctuation of 24-h intraocular pressure during the intermittent period of the both eyes of Posner–Schlossman syndrome patients

During the PSS episodes, the mean IOP of the affected eyes was 47.00 mmHg, which was significantly higher than that of the contralateral eyes (17.00 mmHg). However, during the intermittent period, the mean, peak, and valley IOPs of the contralateral eyes detected by the 24-h measurements were all higher than those of the affected eyes ($p = 0.01$, $p = 0.002$, and $p = 0.046$, respectively). The IOP dynamic changes of the affected and the contralateral eyes from episodes to intermittent period presented a clear crossover phenomenon.

Discussion

Jap et al. [13] reported that both the anterior chamber and IOP returned to normal in PSS patients between episodes. From a study of IOP in 90 random cases with PSS, we found a unique characteristic of PSS, called the crossover phenomenon [12], where affected eyes had an increased IOP greater than that of the contralateral eyes during PSS episodes, but had a decreased IOP lower than that of the contralateral eyes in the intermittent period. However, IOP is a dynamic parameter with rhythms [17]. Peak and valley IOP values would have been neglected in random IOP measurements. As the above conclusion was based on the analysis of random IOP values, the validity of the conclusion needed further evidence.

This study revealed the changes of the IOP in patients under normal living conditions through 24-h IOP measurements. It showed that, although the peak IOP appeared at different times in different PSS patients, the peak IOP, valley IOP, and mean IOP of the affected eyes were all lower than those of the contralateral eyes over 24 h of measurements in the intermittent period. This result is consistent with previous research. This study also showed that the IOP

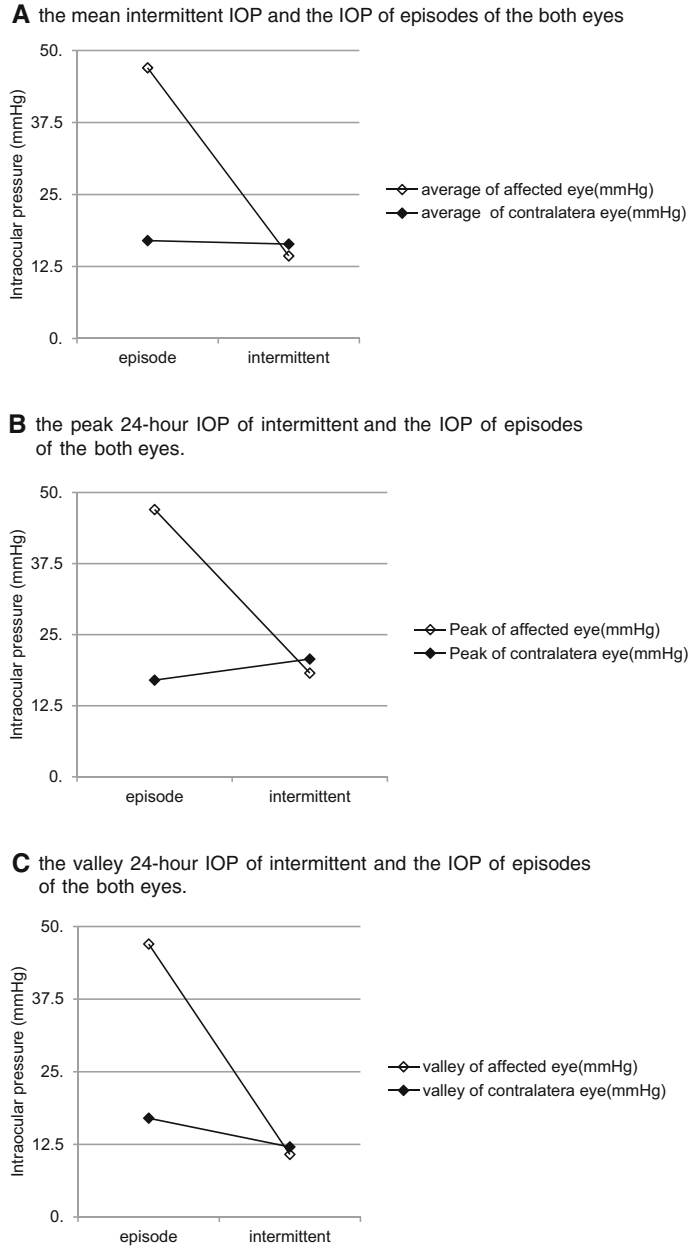

Fig. 2 The dynamic change of intraocular pressure (IOP) between episodes and intermittent of the affected and the contralateral eyes. **a** The mean intermittent IOP and the IOP of episodes of the both eyes. **b** The peak 24-h IOP of intermittent and the IOP of episodes of the both eyes. **c** The valley 24-h IOP of intermittent and the IOP of episodes of the both eyes

crossover phenomenon existed in typical PSS cases through the 24-h IOP measurements. This is the first report that used the 24-h IOP measurements to demonstrate the IOP crossover phenomenon.

Elevation of IOP during PSS episodes is due to the impairment of outflow facility secondary to inflammatory changes in the trabecular meshwork. The concentration of prostaglandins, particularly prostaglandin E, in the aqueous humor of PSS patients has been found significantly increased during acute episodes, but gradually decreasing between episodes, which is considered related to IOP changes [18]. The production of aqueous humor is remarkably elevated in episodes associated with significantly elevated prostaglandin E levels in the anterior chamber of PSS patients [16]. It was found that after the use of prostaglandin drops in rabbit eyes, the intraocular pressure in rabbit eyes first rises immediately and then

Table 2 Statistical comparative analysis of office time IOP in episodes and 24 h IOP measurements in intermittent period of the affected eye and the contralateral eye

IOP	Contralateral eye (mmHg)	Affect eye (mmHg)	*T*	*P*
Office-time IOP in episodes	17.00	47.00	16.833	< 0.001
Peak IOP in intermittent period	20.71	18.24	− 3.656	0.002
Valley IOP in intermittent period	12.06	10.76	− 2.161	0.046
Mean IOP in intermittent period	16.40	14.34	− 4.312	0.001

Statistical methods: paired *t* test

continues to decrease. The above results suggest that high levels of prostaglandin can cause an elevated IOP, while low concentrations of prostaglandin can reduce the IOP. Such an effect of prostaglandins is called a bidirectional reaction [19]. In fact, the concentration of various prostaglandin derivatives currently clinically used is very low. Whether the IOP crossover phenomenon relates to prostaglandins remains to be researched. In clinics, once the IOP crossover phenomenon disappears, the PSS may develop into glaucoma, so this phenomenon has an important predictive value on the outcome of the disease.

The prognosis of PSS was regarded as good at early age, but GOND similar to that in primary glaucoma cases occurred in many of the PSS cases, according to recent reports. According to Jap et al., the only factor that led PSS to develop into glaucoma was the duration of the disease. The risk of glaucoma developing in patients with a duration of PSS greater than 10 years is 2.8 times higher (95% confidence interval, 1.19–6.52) than those with a PSS duration of less than 10 years [14], so it is important to diagnose PSS at an early stage. Some cases of PSS are misdiagnosed because of atypical symptoms and signs, such as obvious corneal edema, lack of typical KP or heterochromia iridis, optic atrophy, and other factors. In this study, severe corneal edema was found in two (11.8%) cases and lack of typical KP in three (17.6%) cases. It can be difficult to differentiate PSS from other types of glaucoma. The IOP crossover phenomenon may be helpful to properly diagnose these cases.

Six special cases of PSS were observed in our hospital [20]. They initially showed typical clinical features of PSS with a remarkable IOP crossover phenomenon, but they lost this characteristic gradually after 5–8 years. After frequent episodes, the IOPs of the patients' affected eyes in intermittent periods became higher and higher, eventually surpassing the IOPs of the contralateral eyes. Some of the patients suffered from severe GOND. Four of the patients need to use drugs to control their IOP continuously, and two patients had to accept filtration surgery. In cases such as these, more aggressive treatment (especially in the intermittent period) should be applied as soon as possible after the disappearance of the IOP crossover phenomenon.

In conclusion, this study demonstrated the crossover phenomenon through 24-h IOP measurements, which will facilitate to the diagnosis and treatment of PSS. However, there are still several weaknesses of this study because of the small sample size. A large sample study should be conducted in the future.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Ethical approval This descriptive study was objectivity and transparency in research and accepted principles of ethical and professional conduct have been followed. All the co-authors of this paper have no financial interest in relation to the submission.

Informed consent Human participants in this research have given informed consent.

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