Clinical study of water drinking test and 24-hour intraocular pressure monitoring in patients with primary open angle glaucoma

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Abstract: This paper aims to observe the relevance of 24-hour intraocular pressure (IOP) monitoring and water drinking test (WDT) in patient with primary open angle glaucoma (POAG). 55 patients (90 eyes) with POAG was selected and randomly divided into operation group an drug group. Operation group, with 30 cases (48 eyes), were treat with trabeculectomy. And the other 25 cases (42 eyes) were treat with antiglaucoma medication. 24-hour intraocular pressure and WDT were measured before treatment and 6 months after treatment. The correlation between the peak value of 24-hour intraocular pressure (IOP) and intraocular pressure (IOP) fluctuation and the drinking water test were analyzed. Pearson correlation analysis showed a strong positive correlation between the peak value of diurnal IOP and the peak value of WDT IOP (r=0.758); and the Pearson correlation analysis also showed a strong positive correlation between the peak value of diurnal IOP and the peak value of WDT IOP after 6 months of POAG surgery or drug therapy (r=0.759,0.712). The peak value of IOP and IOP fluctuation in operation group were lower than those in the drug group at 6 months after operation, the difference was statistically significant. The peak value of WDT IOP can reflect the curve peak value of 24-hour IOP, which can be used to evaluate the current treatment. There were significant differences in IOP and IOP fluctuation between the drug group and the operation group at 6 months after treatment. Operation groups could achieve lower IOP and IOP fluctuation.

Keywords: Primary angle-closure glaucoma; IOP fluctuation.

INTRODUCTION

The treatment of primary open angle glaucoma (POAG) is mainly to reduce intraocular pressure (IOP) to the level of preventing the development of glaucomatous optic nerve damage. However, to some patients, even if the daytime IOP dropped to a satisfactory level, the vision field is still progressive. Studies have shown that the cause of progressive damage of visual field is that there is no 24-h IOP measurement, and the IOP fluctuation and IOP peak value are not observed (Zeimer *et al*., 1991, Katavisto 1964, Drance 2003). However, 24-hour of IOP measurement usually requires hospitalization, which has many disadvantages, such as time-consuming and complicated operation, so it can not be used as a routine survey and follow-up of POAG patients. Drinking water test (WDT) is the first diagnosis of glaucoma provocation test. The method is to drink a certain amount of water within 15 min according to the weight in kilograms, to measure the IOP peak value and IOP fluctuation range to assist in the diagnosis of POAG, with the characteristics of short time and easy operation. This study aims to find a more simple and effective method to evaluate the severity of POAG by observing the correlation between the WDT and 24-h IOP peak value and IOP fluctuation range in patients with POAG.

MATERIALS AND METHODS

Study objects

55 patients (90 eyes) with POAG were selected and randomly divided into the operation group an drug group. Operation group, with 30 cases (48 eyes), were treat with trabeculectomy and the other 25 cases (42 eyes) were treat with antiglaucoma medication. There was no significant difference in gender and age between the operation group and the drug group (P>0.05). As shown in table 1.

Inclusion criteria: (1) Patients diagnosed with POAG. (2) Newly diagnosed patients who did not receive beta blockers and other anti glaucoma drugs; if the anti glaucoma drugs has been used, the patients could included into this study 4 weeks after discontinuation. (3) Patients with the central corneal thickness in 500~550 µm. (4) Patients without major systemic disease. Exclusion criteria: Patients with other diseases that affect the structure and function of the angle of the eye.

Instrument

Slit lamp microscope (Type YZ5E, Suzhou medical instrument factory); Direct ophthalmoscope (Suzhou 66 Vision Technology Co., Ltd.); Non-contact tonometer (TOPCON Company, Japan).

Research methods

Implementation of trabeculectomy

(1) Operative procedures: Eye speculum was placed after anesthesia satisfaction, and the rectus traction line was used for fixing the upper rectus muscle; the conjunctival

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flap was made with fornix-based and the 5mm × 4mm trapezoidal scleral flap was made with corneal limbus-based; about 1.5mm × 1mm trabecular tissue was removed in the lamellar sclera cornea - trabecular border, and part of the iris tissue was removed; the two posterior angles of scleral flap were sutured with 10-0 suture in each of 1 needle; the conjunctival incision was carried out with interrupted suture; The cornea was used as the puncture mouth, and the saline solution was injected into the anterior chamber; anterior chamber was restored to understand whether the conjunctival incision was leaked.

(2) Postoperative treatment: Tobramycin and Dexamethasone and Pranopulin eyedrops were used to drop the eyes in the first week after operation, 1 time/2 hours, then changed into 4 times/day in the second week after operation. 2 weeks later, whether to continue medication was decided according to the recovery of the eye.

Medication

The following medication plans were referred to according to the basis of the IOP level (Zhou 2000, Stewart *et al*., 1993): (1) Latanoprost; (2) Latanoprost + Timolol; (3) Latanoprost + Timolol + Brinzolamide; (4) Latanoprost + Timolol + Brinzolamide + Alphagan. After medication, the type and frequency of the drug use were increased or reduced bases on the control of IOP.

Observation indexes

Non-contact tonometer was used to measure. The measuring time point of 24-h IOP were 7am, 10am, 1pm, 4pm, 7pm, 10pm, 1am, 4am, respectively. The peak value of IOP was the maximum value of IOP in the 8 times measurement. The fluctuation of IOP was the difference between the maximum and minimum value. Before treatment and 6 months after treatment, the 24-h IOP value of patients was measured on 7am, 10am, 1pm, 4pm, 7pm, 10pm, 1am, 4am everyday. And 15 ml/kg water was drunk every 15 min according to the weight in kilogram before treatment and 6 months after treatment, and the IOP was measured before drink and 15 min, 30 min, 45 min, 60m min after drink.

STATISTICAL ANALYSIS

SPSS 17.0 software was used for data statistical analysis. All data are expressed as mean + standard deviation (x±s). All data were tested for normality. The 24-h IOP in patients with POAG and the peak value and amplitude of intraocular pressure of WDT IOP were analyzed by Pearson correlation.

RESULTS

Correlation between POAG day and night IOP fluctuation and drinking water test before treatment

Before POAG treatment, the fluctuation amplitude of 24-h IOP and the WDT IOP fluctuation had the weak positive correlation by Pearson correlation analysis (r=0.284, *P*=0.007). The peak value of IOP before and after POAG treatment was positively correlated with the peak value of WDT (r=0.758, *P*=0.000). As shown in table 2 and table 3.

Correlation between diurnal IOP fluctuation and drinking water test 6 months after surgery

6 months after treatment of POAG patients, there was a weak positive correlation between the 24-h IOP fluctuation and WDT IOP fluctuations (r=0.248, *P*=0.018); There was a strong positive correlation between the peak value of 24-h IOP and the peak value of WDT IOP by Pearson (r=0.780, *P* =0.000). As shown in table 4 and table 5.

Comparison of the mean IOP, IOP peak value and IOP fluctuation between the drug group and the operation group

After t test, the difference of the mean IOP, IOP peak value and IOP fluctuation 6 month after treatment between the two groups were statistically significant (P=0.027, 0.018, 0.019). As shown in table 6.

DISCUSSION

At present, reducing intraocular pressure is the only confirmed way to control the damage of optic nerve in glaucoma. In the study of “Early Manifest Glaucoma Trial”, it clear shows that reducing IOP can reduce the risk of glaucoma by about 50%. However, for some patients, even if the intraocular pressure decreased to an ideal level in the daytime, the optic nerve damage continues. Large fluctuations in intraocular pressure has become an independent risk factor for glaucoma. Studies have shown that the progression of the disease in some patients is due to the fact that there is no 24-h intraocular pressure test, and the peak value of IOP and IOP are not observed (Zeimer *et al*., 1991, Katavisto 1964, Liu *et al*., 1998).

1. As the first diagnostic test for glaucoma, the method of WDT is to drink 15ml/kg water within in 15min according to the weight in kilogram, and the peak value of intraocular pressure and intraocular pressure fluctuations is measured in a short period of time to assist in the diagnosis of POAG. It is generally believed that elevated IOP 6~8mmHg and above is of diagnostic significance (Spaeth 1967). The mechanism of elevated intraocular pressure induced by WDT is the change of superficial scleral venous pressure and plasma osmotic pressure. Due to a large amount of water into the tissue fluid and blood in a short period of time, the osmotic pressure is reduced, and the formation of aqueous humor is increased. At the same time, because of the increase of blood moisture, central venous pressure and peripheral venous pressure is

Table 1: General condition of patients ($\bar{x}$±s)

Group	*n*	Age (years old)	Sex (male:female)
Operation group	30	49.30±14.31	17:13
Drug group	25	47.67±13.22	14:11

Table 2: The mean IOP at each time point of 24-h before treatment in POAG patients

Measurement time	7am	10am	1pm	4pm	7pm	10pm	1am	4am	Fluctuation range
Mean IOP	27.01 ±4.29	29.50 ±3.31	27.36 ±3.86	28.82 ±3.13	26.78 ±3.19	29.49 ±3.67	30.66 ±3.39	29.23 ±3.68	8.18 ±2.26

Table 3: Water drinking test IOP before treatment in POAG patients (mean IOP at each time points) (n=90, mmHg, $\bar{x}$±s)

Measurement time	Before drinking	15min	30min	45min	60min	Fluctuation range
Mean IOP	26.07±2.68	27.09±3.12	29.69±2.95	32.40±2.59	31.95±2.72	6.86±1.62

Table 4: 24-h intraocular pressure measurement in 6 months after POAG surgery (n=90, mmHg, $\bar{x}$±s)

Measurement time	7am	10am	1pm	4pm	7pm	10pm	1am	4am	Fluctuation range
Mean IOP	13.31 ±3.06	12.62 ±2.67	13.84 ±3.12	14.00 ±3.31	13.11 ±2.96	13.82 ±3.23	14.96 ±3.10	15.04 ±2.90	4.33 ±1.48

Table 5: Water drinking test in 6 months after POAG surgery (n=90, mmHg, $\bar{x}$±s)

Measurement time	Before drinking	15min	30min	45min	60min	Fluctuation range
Mean IOP	13.48±3.06	14.39±3.17	16.04±3.20	17.30±3.41	16.90±3.74	4.37±1.90

Table 6: The mean IOP, IOP peak value and IOP fluctuation between the drug group and the operation group

Group	Number of eyes	Mean IOP	IOP peak value	IOP fluctuation
Drug group	42	15.06±2.54	17.53±2.80	5.07±1.40
Operation group	48	13.84±2.76	16.04±3.10	4.33±1.48

evaluated, thus increasing the resistance of aqueous humor outflow (Susanna *et al*., 2005, Diestelhorst and Krieglstein 1994). Susanna *et al.* (2005, 2006) performed a follow-up study of WDT in patients with POAG, and the results found that in the case of intraocular pressure under the control of the outpatient time, the patients with high intraocular pressure peak value and large fluctuations in intraocular pressure were more likely to suffer further optic nerve damage. The transient ocular pressure caused by the large amount of drinking water in the normal eye can make the outflow of aqueous humor through the pressure dependent trabecular meshwork aqueous drainage. However, the reserve capacity and drainage capacity of the drainage pathway of the trabecular meshwork of POAG are decreased, which can not balance the generation and outflow of the aqueous humor in time, thereby causing the increase of intraocular pressure (Brucculeri *et al*., 1999).

24-h IOP and WDT were measured in patients with POAG before treatment, and there was significant positive correlation between the two testing methods. The 24-h IOP and WDT were measured again in patients with POAG 6 months after surgery, and the same conclusion was obtained, indicating that the peak value of WDT intraocular pressure can reflect the peak value of intraocular pressure measured by 24-h intraocular pressure, and can be used to evaluate the IOP control in patients with POAG. 24-h intraocular pressure measurement and WDT were performed in 25 patients with glaucoma by Kumar *et al* (2008), and the results showed that there was no significant difference between the two methods in the peak value of intraocular pressure and intraocular pressure fluctuation, suggesting that WDT was an ideal method to detect the peak value of intraocular pressure and intraocular pressure fluctuation. The study of Carlos and Remo (2008) and Danesh-Meyer (2008) also had confirmed this conclusion.

WDT has the advantages of short time and simple operation. It is an effective method to evaluate the change of intraocular pressure in patients with POAG, and it can reflect the drainage ability of aqueous humor drainage system of POAG patients. It helps to assess the current therapeutic effect in patients with POAG, and suggest whether there is a risk of further damage to the optic nerve and further progression of the disease. For the patients with high IOP peak value and IOP fluctuation after WDT examination, then further 24-h intraocular pressure measurement should be performed, so as to develop a reasonable treatment plan earlier. When the drug treatment can not control the intraocular pressure fluctuations and high intraocular pressure peak value, it should be as soon as possible to decide whether to accept early surgical treatment, so as not to miss the opportunity to treat.

CONCLUSION

In this study, the 24-h average intraocular pressure, intraocular pressure fluctuation and intraocular pressure peak value in the operation group were lower than those in the drug group, and the difference between the two groups was statistically significant ($P<0.05$), indicating that surgical treatment could better control the intraocular pressure fluctuation in POAG patients. Some clinical study had observed the curative effect of medicine, argon laser trabeculoplasty (ALT) and trabeculectomy to POAG, and the results found that the success rate of intraocular pressure control in the trabeculectomy group was higher than that in the drug treatment group and the ALT treatment group, and the probability of further impairment of visual field was reduced in POAG patients with early surgery (Welsh *et al*., 1998). The study of Mermoud *et al*. (1999) had shown that filtration surgery is superior to the treatment of anti glaucoma drugs in reducing diurnal IOP fluctuation. Luo *et al*. (2010) had observed the 24 h IOP in POAG patients treated with drugs and surgical treatment, and the results showed that the average IOP and IOP fluctuation in the operation group were lower than those in the drug group; after the water drinking test, the average intraocular pressure increased by 13% in the operation group and the drug group increased by 40%, indicating that the surgical treatment was better than drug treatment whether to reduce the average intraocular pressure or intraocular pressure fluctuations.

More and more doctors and scholars hold a positive attitude towards POAG surgical treatment. When the drug treatment and ALT treatment can not reduce the intraocular pressure POAG to the ideal intraocular pressure level of 15mmHg, trabeculectomy should be performed in the early period. Some scholars also believe that for diagnosed POAG patients, if the untreated intraocular pressure exceeds 30mmHg, and early changes of glaucoma appears in the field of vision, then the trabeculectomy can be performed.

REFERENCES

Brucculeri M, Hammel T, Harris A, Malinovsky V, Martin B (1999). Regulation of intraocular pressure after water drinking. *J. Glaucoma.*, **8**(2): 111-116.

Carlos GV and Remo S (2008). Correlation between the water drinking test and modified diurnal tension curve in untreated glaucomatous eyes. *Clinics*, **64**: 433-436.

Danesh-Meyer H (2008). The Water Drinking Test: Simple is Elegant. *Clin. Experiment Ophthalmol.*, **36**: 303-305.

Diestelhorst M and Krieglstein GK (1994). The effect of the water drinking test on aqueous humor dynamics in healthy volunteers. *Graefes. Arch Clin. Exp. Ophthalmol.*, **232**(3): 145-147.

Drance SM (2003). Diurnal variation of intraocular pressure in treated glaucoma. Significance in patients with chronic simple glaucoma. *Arch. Ophthalmol.*, **70**(11): 302-311.

Katavisto M (1964). The diuranl variations of ocular tension in glaucoma. Acta. Ophthalmol. (copenh)., **78**(suppl): 1-130.

Kumar RS, de Guzman MH, Ong PY and Goldberg I (2008). Does peak intraocular pressure measured by water drinking test reflect peak circadian levels? A pilot study. *Clin. Expe. Ophthalmol.*, **36**: 312-315.

Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L and Komaroff E (2003). Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment: The early manifest glaucoma trial. *Arch Ophthalmol.*, **121**: 48-56.

Liu JH, Kripke DF, Hofhllan RE, Twa MD, Loving RT, Rex KM, Gupta N and Weinreb RN (1998). Nocturnal elevation of intraocular pressure in young adults. *Invest Ophthalmol. Vis. Sci.*, **39**: 2707-2712.

Luo RJ, Zhuo YH, Liu SR, Lin MK and Tian Z (2010). Long-term effects of non-penetrating trabecular surgery versus trabeculectomy for treating glaucoma. *Chinese Journal of Ophthalmology*, **46**: 499-502.

Mermoud A, Schnyder CC, Sickenberg M, Chiou AG, Hédiguer SE and Faggioni R (1999). Comparison of deep sclerectomy with collagen implant and trabeculectomy in open-angle glaucoma. *J Cataract Refract Surg.*, **25**(3): 323-331.

Spaeth GL (1967). The water drinking test. Indications that factors other than osmotic considerations are involved. *Arch Ophthalmol.*, 77(1): 50-58.

Stewart WC, Chorak RP and Sethuraman G (1993). Factors associated with visual field loss in patients with advanced glaucomatous changes in the optic nerve head. *Am. J. Ophthalmol.*, **116**: 176-181.

Susanna R, Hatanaka M, Vessani RM, Pinheiro A and Morita C (2006). Correlation of asymmetric glaucomatous visual field damage and water-drinking test response. *Invest Ophthalmol. Vis. Sci.*, **47**(2): 641-644.

Susanna R, Vessani RM, Sakata L, Zacarias LC and Hatanaka M (2005). The relation between intraocular pressure peak in the water drinking test and visual field progression in glaucoma. *Br. J. Ophthalmol.*, **89**(10): 1298-1301.

Welsh NH, Delange J, Wasserman P and Ziémba SL (1998). The "deroofing" of schlemm's canal in patients with open-angle glaucoma through placement of a collagen drainage device. *Ophthalmic Surg Laster.*, **29**(3): 216-226.
Zeimer RC, Wilensky JT, Gieser DK and Viana MA (1991). Association between IOP peaks and progression of visual field loss. *Ophthalmology,* **98**(1): 64-69.
Zhou WB (2000). Clinical Glaucoma. People's Medical Publishing House. Beijing, China, pp.185-197.