

The role of warm compression in lowering the intraocular pressure in various conditions-a pilot studyHsieh-Ting Liu¹, Chi-Ting Horng^{2,*}¹ Department of Rehabilitation, Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan.² Department of Ophthalmology, Fooying University Hospital, Pingtung, Taiwan.* Corresponding author: Chi-Ting Horng, MD, PhD.; E- mail: h56041@gmail.com

Abstract: Purpose: This research aimed to determine the effect warm effect and ocular massage on lowering intraocular pressure (IOP) and relieving associated symptoms. **Methods:** A total of 50 subjects, with mean 43.2 ± 17.5 years and higher IOP (>25 mmHg), were enrolled in this study. In Taiwan, people sometimes use certain plants as heating source. In our study, heat in warm compression was generated from silicon rubber, and ocular was performed using fingers. In experiment 1 (N= 50; higher IOP in one eye), the different conditions (age, anterior chamber angle, and the existence of lens) of the patients were evaluated by the change in IOP after heating. In experiment 2 (N=50; higher IOP in both eyes), one eye receiving heating, whereas the other eyes were massaged for about 10 min. The difference in IOP change was then compared. In experiment 3, the subjective sensation of 50 volunteers was **Results:** The mean reduction of IOP (6-8 mmHg) after 10 min significant under all conditions, except for angle-closure glaucoma. In addition, ocular massage only decreased by 2-4 mmHg after 10 min. Moreover, decreased ocular pain and mood disorders in most patients were observed after therapy. **Conclusion:** This study is the first one to discuss the exact data on IOP lowering by warming and peri-ocular massage. IOP decreased significantly after heating and mildly reduced by massage in most subjects with higher IOP, consequently relieving ocular pain and psychological conditions. Therefore, warm compression with ocular massage may be beneficial to subjects with higher IOP and long-term near-distance workers.

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Keywords : eyelid warm, ocular massage, intraocular pressure

Introduction

Now medication becomes the most common method to treat glaucoma and ocular hypertension because of its effectiveness and efficiency. Medical therapy is currently the first line of strategic treatment to lower IOP and protect the axon of nerve. As for reduction of IOP, the mechanisms include two major groups by either decreasing the production or enhancing outflow drainage of the humor aqueous fluid [1]. The lowering IOP agents consist of many different classification including topical beta-blockers, alpha-2agonists, prostaglandins, para-sympathomimetics and carbonic anhydrase inhibitors. In clinics, most ophthalmologists always used the topical beta-blockers or prostaglandin analogs as the first-line of medical treatment for glaucoma and the IOP control. However, eye drugs have some side effects of cardiovascular impaction, asthma, allergic reaction, fibrosis of the conjunctiva, kerato-conjunctivitis, dry eye and thirsty, formation of renal stones, electrolytes imbalances, pigment deposition in the periocular region, and eyelash overgrowth are usually reported [2-4]. Ocular side effects to topical medications sometime altered the compliance of patients and the desire of using ophthalmic drops may decrease. Ocular intolerance and side effects have been reported until in 50% of the

cases with 10% of severe manifestations of intolerance. This associated problem may bother the doctors and patients [5-6].

A great number of patients can be controlled only by medications. However, if medical control failed, the more aggressive methods are necessary. For example, laser (laser peripheral iridotomy and argon laser trabeculoplasty) and surgical (surgical peripheral iridotomy, trabeculectomy and even cyclo-destruction) procedures for glaucoma and even ocular hypertension are used to retard the progression and reach the target IOP level effectively. Nevertheless, the failure rates (e.g. scar formation and obstruction of the iris hole) and its recurrences are high and unexpected in clinic. Besides, we first reported that the Cassiae seed extract may lower IOP in previous study in the world. In addition, many plants such as *Daucus carota* seed extract and fruit of *Aegle Marmelos* were proven to own the similar effects [7].

Warm pressure is a good method of rehabilitation fields with the physiological effect of improving blood flow and volume. Many researchers proposed many advantages about warm pressure which may use to treat infection wound, acute orbital cellulitis, meibomian gland dysfunction, kerato-conjunctivitis, blepharitis, chalazion, internal

and external hordeolum (styles), dry eye syndrome, ocular fatigue, congenital dacryocoele, and acute dacryocystitis. The physiologic mechanism of warm compression of eyelids is to melt solidified meibomian gland lipid, maintain the stability and uniformity of tear, improve tissue metabolism and blood flow by dilating the surrounding blood vessels [8-10]. In Taiwan, the people suffering from headache, ocular strain and periocular pain are always instructed to use the eyelid warmer to relieve the problems. Moreover, it is well known that one symptom of the increasing IOP is ocular pain. However, whether or not warming the eyelid may reduce IOP remained unknown. The aim of this study was to investigate the changes of IOP after warm compression with/without massage in various conditions. Moreover, we will discuss the possible mechanism [11-12].

Methods

All 50 subjects (25 man and 25 women); aged range, 20-65 years; mean \pm standard deviation age, 43.2 ± 17.5 years who complained about peri-ocular strain and increased IOP (> 25 mmHg) measured by non-contact tonometer (Kowa KT 800) were enrolled. We exclude the subject with eye disorders (e.g., infectious conjunctivitis, allergic diseases, autoimmune diseases, collagen diseases, retinopathy, uveitis, eyelid abnormality and previous ocular surgeries history). In addition, the patients with corneal edema, opacity and any types of keratopathy were also excluded because of checking the IOP difficultly. However, the patients with glaucoma or ocular hypertension who had taken medications or not all included in our study. At the same time, total volunteers had no history of systemic diseases (hypertension, diabetes, and hyperthyroidisms). Contact lens wears were accepted, but wearers were required to stop contact lens wearing for at least 10 minutes before treatment. All experimental protocols were conducted in accordance with the Declaration of Helsinki. Ethical approval for this study was obtained from the institution review board of our hospital (Kaohsiung Armed Forces General Hospital). Informed consent was obtained from each subject. All the experiments were performed in the laboratory of our hospital from February to July 2017. According to the previous studies, the temperature of the eye may vary significantly depending on the ambient temperature which revealed showed an increase of ocular temperature of 0.15 to 0.2°C per degree in room temperature. For example, under most environmental condition, the eye is at 35°C which is cooler than core body temperature. Besides, the humidity also affects the evaporation rate of tear which further result in the change of ocular temperature. Therefore, the ambient room temperature

and humidity should be stable to prevent from the bias. Therefore, the measurements were performed in wind-free room temperature ($25.5 \pm 0.5^\circ\text{C}$), humidity ($30 \pm 6\%$), and brightness under our control. Specifically, during contact heating, the time-temperature threshold at which the first sign of human skin thermal damage, tissue edema, occurs is when the skin temperature is 45°C after 35.5 minutes of uninterrupted exposure. Therefore, the warmer in our study is 45°C for 10 minutes for volunteers' safe concern. Methods current used for hyperthermia treatment include infra-red, radio frequency, microwave radiation and ultrasound. In this research, we applied to subjects' closed eyes by using eye-warmer system with generating heat from silicon rubber which is non-toxic and could maintain the constant temperature during experiments.

We compared the thermal effects from warm compression on patients' age, the existence of lens, and the angle of anterior chamber. Therefore, all participants underwent a complete ophthalmic evaluation including the IOP checking up, slit-lamp examination and anterior chamber angle measurement. At first, we checked the anterior chamber angle by using Goldman gonioscopy under the slit-lamp bio-microscopy. The three-mirror gonioscopy was attempted with contact lens at 16 X magnification. Since no mydriatic was used, the vertical slit beam was set to allow the maximum visualization. Before examination, the topical anesthesia was given into the conjunctival sac. In addition, the 2% hyperomellose gel was used as the coupling medium for the contact lens of gonioscopy. The common classification was introduced by Shaffer grading system which separated the degree of width of anterior chamber angle by several grades. According to the classification, grade 4, grade 3 and grade 2 were considered as wide open angle ($35^\circ - 45^\circ$), moderate open ($25^\circ - 34^\circ$), and moderately narrow ($10^\circ - 20^\circ$), respectively. In our study, we only separated two parts including open angle (grade 4 and 3) and angle closure (grade 2 or less) by Alonso's report. Narrow angle was determined in eyes in which the posterior trabecular meshwork could not be seen in two or more quadrants on non-indentation gonioscopy (grade 2 or less). Besides, we may find the existence of lens easily by slit-lamp examination. The normal peoples have the lens (so called "phakia") and the patients who had received cataract surgery may be found the "pseudo-phakia" (intraocular lens; IOLs) at the central part of pupil under examination.

In ophthalmic clinic, two methods of measuring IOP include Goldmann applanation tonometer (GAT) and noncontact air-puff tonometer (APT). However, the checking procedure from GAT is more complicated. Now the APT is largely available and

popular by most doctors due to its convenience. Nevertheless, the IOP data from APT is controversial and higher than the more actual IOP from GAT measurement in most ophthalmologists' experience. The major reason is that most of subjects may be afraid of the sudden air-puff from APT and their head may toward back which could affect the results. Therefore, we applied one drop of topical anesthesia (Alcan 0.5%, Alcon) into conjunctival surface of the subjects' eyes when checking IOP by APT. Thus, the IOP data from the anesthetic eye could decrease this confounding factor.

The source of heat generated of eye warmer ("MEDBEST" powered heating pad) used in our study is from silicon rubber which needs the electrical power supply continuously, and increases its energy and heat (Figure.1). Chemically, silicone rubber belongs to thermoset elastomers that have a backbone of alternating silicon and oxygen atoms and methyl or vinyl side groups. Some properties of silicon rubber such as elongation, creep, cyclic flexing, tear strength, compression set, dielectric strength, thermal conductivity, and fire resistance. Moreover, it can be found in a wide variety of products, including: automotive applications; cooking, baking, and food storage products; medical devices and implants; and in home repair and hardware with products. Silicone rubber is non-reactive, stable, and resistant to extreme environments and temperatures from -55°C to $+300^{\circ}\text{C}$ while still maintaining its useful properties. Because of these properties, the eye warmer in our study may be heated to $40-50^{\circ}\text{C}$. Furthermore, the important character of silicone rubber is highly inert and does not react with most chemicals. In this device, the heating temperature could be given to be set at three levels such as 40°C , 45°C and 50°C by one button. Besides, all subjects underwent warm compression may wear the goggles over the periorbital region for 10 minutes. Therefore, we could gain the more real data in this study.



Figure 1. The MEDBEST eye warmer could supply the heat by electronic power consistently without re-heating

Moreover, ocular symptoms were evaluated with visual analog scales (VAS). The questionnaire always included the symptoms such as "tiredness", "grittiness", "soreness", "dry sensation", "irritation", and "ocular discomfort". IN this study, all participants checked on the VAS sheets before and after various treatments. We could gain the demographic, IOP and VAS before treatment. Besides, the IOP and VAS of all subjects were evaluated again after therapy. Finally, we could analyze these results.

Experiment 1: Warm compression efficacy

Total 50 volunteers (with 50 eyes) with elevating IOP (> 25 mmHg) in one eye (OD) were enrolled. The eyelid warmer is a goggle type and could cover the whole eyelids and peri-ocular region. The subjects were instructive to close their both eyes during warming. The non-tested normal eyes were stuck by thick clothes to block the heat conduction. The total heating time is approximate to 10 minutes and the temperature is maintained at 45°C . After removing the eyelid warmer, we checked the IOP in the tested eyes of patients as soon as possible.

Experiment 2: Massage efficacy

All 50 subjects with the increasing IOP (> 25 mmHg) in both eyes (total 50 eyes) were recruited in experiment 2. In each case, one eye received randomly warmer compression for 10 minute (maintained at 45°C) and the other eye received finger massage around the peri-ocular region by experienced physiotherapists lasting for 10 minutes. We avoided directly compressing the central region of eyelid and the "force" of massage is gentle. After therapies, we checked their IOP in both eyes immediately. Therefore, we could compare the difference between various treatments.

Experiment 3: Visual analog scales measurement

In this experiment, we wanted to realize their feelings and improved level after treatment in experiment 1 and 2. Therefore, we used the easy method to evaluate their psychological and physiological condition after treatments. Therefore, 50 eyes were all recruited in experiment 3.

In clinics, visual analogs scales are used to evaluate the health outcome and life quality after treatment. Many researchers also used the VAS for the tool as primary or secondary outcomes or as the method to derive utility index. The VAS is a 10 cm long straight line, marked at each end with labels which anchor the scale. Each VAS item was given an introductory title and a short statement representing "no problem" at 0 mm and a short statement representing "worst imaginable problems" at 100 mm. For example, the patient with ocular pain are asked to place a mark on the line at a point representing the severity of their pain where the anchors are "no pain"

and “pain as bad as it could be” (labels vary between studies). Scores are noted in millimeter thus giving a total score range of 0-100 millimeters. In our study, the range of VAS was from 10 to 0. The volunteers may point out their subjective symptoms after treatment. We will use the method to further evaluate their condition before and after our treatments (experiment 1 and 2).

In general, there are five classic VAS items including patient’s self-reported mobility, self-care, ability to perform usual activities, pain, and the presence of anxiety or depression. In our study, we mildly modified the questionnaires. However, in experiment 3, we listed the five parameters about “perfect mobility”, “self-care”, “benefit to daily activity”, “periocular pain, ocular strain or headache” and “feeling about anxiety or depression”. All the 100 subjects were asked to mark the levels of their behavior condition and mood change just after any types of therapies.

All data were presented as mean \pm stand deviation (SD). The statistical analyses were performed using IBM SPSS statistics version 21 (Armonk, NY: IMB Corp). The ANOVA test was used to compare the change of IOP between pre- and post-treatment. A level of *P* values of less than 0.05 was considered to indicate a statistically significant difference.

Results

Experiment 1: Warm compression efficacy

First, we found that the mean IOP decreased significantly after eyelid heating with goggles for 10 minutes (30.5 ± 4.5 mmHg vs 23.4 ± 2.6 mmHg; *P* < 0.05) (Table 1). Secondly, we also divided 50 eyes into two groups based on their ages (> 40 or < 40 years old). The results revealed that the patients younger patients (< 40 years old) showed reduction of IOP (29.9 ± 4.5 mmHg vs 23.4 ± 2.6 mmHg; *P* < 0.05) and the older subjects (> 40 year old) also decline their mean IOP (31.5 ± 2.0 mmHg vs 24.2 ± 2.5 mmHg; *P* < 0.05) at the same time (Table 2).

Thirdly, we wanted to discover the heating effect on open angle and angle closure glaucoma induced higher IOP. The mean IOP of patients (N= 25) with POAG was 28.9 ± 3.1 mmHg and it decreased significantly to 21.4 ± 3.8 mmHg after warming (*P* < 0.05). Nevertheless, the mean IOP of patients (N=25) with PACG was 31.5 ± 4.0 mmHg and the IOP decreased to 27.4 ± 3.8 mmHg after eyelid heating (*P* > 0.05). In the cases of narrow anterior chamber angle, the mean IOP dropped apparently to 2-4 mmHg, however, the amplitude of decrease was not apparent (Table 3). Finally, we divided the subjects to two groups according to the persistence of lens. In the group of phakic (N=25), we found that the mean IOP

reduced significantly (29.9 ± 3.5 mmHg vs 22.4 ± 3.6 mmHg; *P* < 0.05) after treatment. At the same time, in the group of patients receiving cataract surgeries before (pseudophakic group; N= 23), the apparent phenomenon of lowering IOP was noted (30.5 ± 3.2 mmHg vs 23.8 ± 1.8 mmHg; *P* < 0.05).

Therefore, we concluded that warm compression is benefit for the decrease of IOP and the mean reduction is approximate to 6-8 mmHg. However, the effect of lowering IOP was not remarkable in the patients with narrow angle.

Experiment 2: Massage efficacy

There are 50 volunteers with higher IOP in both eyes were enrolled in experiment 2. The total volunteers with one eye receiving eyelid heating and the other eyes receiving periocular massage were arranged for 10 minutes. We found that the eyelid heating group showed good outcome (the mean IOP decreased from 30.2 ± 4.4 mmHg to 23.4 ± 2.6 mmHg; *P* < 0.05) (Table 4). However, the effect of finger massage was not significantly apparent (the mean IOP declined from 31.5 ± 3.2 mmHg to 28.2 ± 3.5 mmHg; *P* > 0.05) (Table 5). The mean level of lowering IOP was only 2-4 mmHg. The effectiveness of eyelid warming is significantly superior to the ocular massage. We speculated that the finger massage may reduce IOP; however, the force from incorrect massage possibly blocks the subconjunctival blood flow.

Experiment 3: Visual analog scales (VASs) measurement

In clinics, visual analogs scales are used to evaluate the health outcome and life quality after treatment which is a well-known and high reliable method. We found that the remarkable change about the improving subjective comfort about ocular fatigue and dry eye, enhancing the effectiveness of usual activities, and decreased the possibilities of anxiety or depressed mood. Furthermore, we believed that this improvement may furtherly help peoples to concentrate on reading and enhance the life quality and daily working efficacy (Table 6).

Discussion

Warm compression is applied in ophthalmic field has a long history. Heating devices have been used to treat ocular pathology (e.g., retinoblastoma, posterior uveal melanoma, decrease the recurrence of intraocular tumor after chemotherapy, proliferative vitreoretinopathy, scleromalacia). Moreover, it is currently most frequently prescribed for patients with varying presentations of mild to severe meibomian gland dysfunction and obstruction, improvement of tear evaporation, and subsequent symptoms of dry eye. Even the clinicians have been aware of the warm massage for contact lens wears who are the high risk

group of dry eye. Recently, the effect of periocular warming on accommodation was highly valued. Takahashi et al. demonstrated that 50% of eyes had an increase in the accommodation amplitude of at least 0.5 diopters immediately after application of warm compression. The mean near visual acuity immediately after application of warm compression and at 90 minutes significantly improved relative to the near acuity values after whole eyelids closure. In addition, the significant improvement of the high- and low- contrast sensitivity were also found. Many benign conditions, such as meibomian gland dysfunction, chalazion, and sebaceous blepharitis have been successfully. Moreover, warm compression often serve as a helpful adjunct to additional treatment methodologies (e.g., oral and topical antibiotics, cortico-steroid ointments and drops, manual

expression, etc.) in some researchers. In Asian countries, such as Japan, Korean and Taiwan (ROC), a traditional eye-warming instrument has long been used to treat hordeolum, meibomian gland obstruction and acute conjunctivitis. The ancient Chinese have been using hot hard-boiled egg to treat eyelid inflammation for a long time. The presumed purpose of heat is bring about vasodilation and increase blood flow, which in turn increases the circulation of naturally occurring immune compounds and prescribed antibiotics to the affected area. However, when used for indications such as posterior blepharitis, internal hordeolum and ocular rosacea, eye warmer must administer enough heat to liquefy the hardened or abnormal viscous meibomian secretion in deeper region. However, the actual data about the warm compression induced lowering IOP have never been reported.

Table 1. The changes of intraocular pressure before and after warm compression

	Pre-warm (N= 50)	Post-warm (N= 50)
Intraocular pressure	30.5 ± 4.5 mmHg	23.4 ± 2.6 mmHg*

N= 50 eyes * statically significant difference ($P < 0.05$)

Table 2. The changes of intraocular pressure before and after warm compression among different ages

	Pre-warm	Post-warm
< 40 years (N=25)	29.9 ± 3.5 mmHg	21.4 ± 3.6 mmHg*
> 40 years (N=25)	31.5 ± 2.05 mmHg	24.2 ± 2.5 mmHg*

* Statically significant difference ($P < 0.05$)

Table 3. The changes of intraocular pressure before and after warm compression among different types of glaucoma

	Pre-warm	Post-warm
Open angle (N=25)	28.9 ± 3.1 mmHg	21.4 ± 3.8 mmHg*
Angle close (N=25)	31.5 ± 4.0 mmHg	27.2 ± 3.5 mmHg

* Statically significant difference ($P < 0.05$)

Table 4. The changes of intraocular pressure before and after warm compression among whether the patient had received cataract surgery or not

	Pre-warm	Post-warm
Phakic (N=25)	29.9 ± 3.5 mmHg	22.4 ± 3.6 mmHg*
Aphakic (N=25)	31.5 ± 3.2 mmHg	23.8 ± 1.8 mmHg*

* Statically significant difference ($P < 0.05$)

Table 5. The changes of intraocular pressure before and after warm compression among whether the patient had received cataract surgery or not

	Pre-treatment	Post-treatment
Warmer (N=25)	30.2 ± 4.4 mmHg	23.4 ± 2.6 mmHg*
Massage (N=25)	31.5 ± 3.2 mmHg	28.2 ± 3.5 mmHg

* Statically significant difference ($P < 0.05$)

Table 6. The changes of intraocular pressure before and after warm compression among whether the patient had received cataract surgery or not

	Pre-treatment	Post-treatment
Warmer (N=25)	30.2 ± 4.4 mmHg	22.4 ± 2.6 mmHg*
Massage (N=25)	31.5 ± 3.2 mmHg	28.2 ± 2.8 mmHg

* Statically significant difference ($P < 0.05$).

The normal central lid margin temperature was $33.4 \pm 0.1^\circ\text{C}$ at a room temperature of 24°C . In addition, the central corneal temperature is approximate to 34.3°C , and the limbus is 0.45°C warmer than central corneal temperature. Moreover, corneal surface temperature is warmer nasally than centrally and temporally until 6 seconds and 8-10 seconds after blinking. Furthermore, an initial loss of corneal temperature of $0.033^\circ\text{C}/\text{second}$ in the absence of blinking was reported. There are different changes of temperature in various researches. For example, Matsumoto and his associates provided that an average increase of eyelid temperature and corneal temperature after 10 minutes of eye steamer application is $1.0 - 1.2^\circ\text{C}$ and $1.7 - 2.0^\circ\text{C}$, respectively. Mori et al. demonstrated that the temperature increased by 5.6°C and by 6.0°C in the lower eyelid after 5 minutes of warming, and the mean temperature of the cornea increased to 37.4°C with the eyelid close. Blackie et al. revealed that the best way to optimize warm compression efficiency is to heat to approximately 45°C . Besides, the clinicians must keep contact between the warm compression and outer eyelid surfaces for at least 4 minutes in order to achieve an inner lower eyelid temperature $\geq 40^\circ\text{C}$. They also reported that the mean maximum outer upper lid temperature of $42.2 \pm 1.3^\circ\text{C}$ was reached after 6 minutes. Palt and associates used the advanced warmer and they found that the temperature increased from $30.6 \pm 1.9^\circ\text{C}$ to $38.3 \pm 1.1^\circ\text{C}$ within the first 2 minutes during treatment. Subsequently, it elevated slightly to reach $40.5 \pm 0.9^\circ\text{C}$, resulting in a warming rate of about $+0.3^\circ\text{C}/\text{min}$. Besides, the temperature of eyelid increased from $30.5 \pm 1.9^\circ\text{C}$ to $38.1 \pm 1.5^\circ\text{C}$ during the first minute of warm compresses. Then, the temperature decreased with the cooling rate of about $-0.4^\circ\text{C}/\text{min}$. They usual testing time of various heated compression is from 10 to 15 minute. According to the maximum tolerance of eyelid and cornea are approximately $45 - 50^\circ\text{C}$ and $37 - 40^\circ\text{C}$, respectively in some studies. For instance, Moritz et al. suggested that during contact heating, the time-temperature threshold at which the first sign of human skin thermal damage, tissue edema, occurs when the temperature is 45°C after 35.5 minutes of uninterrupted exposure. Bilkhu and his associates demonstrated that the eyelid heated by the temperature of $46.2 \pm 0.6^\circ\text{C}$ from "EyeBag eyelid device" was safe. Mori and his co-workers found that the designed protocol about 45°C maintained for 15 minutes was no harm to peoples. They also suggested the importance of closed eyelids while warming.

Therefore, the heated time we choose is 10 minutes and the highest temperature is 45°C continuously in our study. Therefore, care must be

taken not to harm the eyelids of the subjects. In any situation, patient's care must be taken into consideration. Based on the previous studies, 45°C generated from eyelid warmer did not damage the deeper tissue, cornea and lens. In other words, this temperature from warmer does not result in the corneal opacity and possible cataract formation. Therefore, the safety of our warmer-device is beyond question and the maximal heating temperature should be not greater than 46°C in our experience.

One of the characters is that heat may transfer from adjacent structure by conduction and convection. During warm pressure application, there is heat transfer direct from the palpebral conjunctiva (through the closed eyelid), to the pre-corneal tear layer, cornea, aqueous humor, limbal vasculature, bulbar conjunctiva and even sclera. Besides, the closed eyelids may preserve heating energy and maintain the elevated temperature. Why the IOP should decrease after warm compression? In our study, we found that warmer may generate the heat from the elevation of temperature which is well known to induce the vaso-dilation including the sub-conjunctival blood vessels. The mechanisms of increasing IOP are obstruction of the routines of aqueous humor which are first produced by the epithelium of ciliary body and drained by the blood vessels of the subconjunctival space finally. The role of impaired outflow facility as the primary pathology leading to increased IOP. If the blood flow and volume increased, it may easily drain the aqueous humor and lower the IOP. In clinics, some anti-glaucoma drugs also have the similar mechanisms. For example, the effects of prostaglandins analogues ($\text{PGF}_{2\alpha}$) could exert micro-vascular effects indirectly by releasing nitric oxide (NO) which may enhance vasodilation. A large number of in vitro and in vivo preparations have been utilized showing NO to have an important role in regulation of regional ocular blood flow and vasodilation of the eye vasculature. Moreover, Ca^{2+} entry blockers were found to own the ability in relaxing the blood vessels and improving the ocular circulation. In addition, betaxolol and timolol (β -adrenergic antagonists) were proven to induce the vasodilation in retinal and other ocular vascular beds. Therefore, we suggested that the effects of lowering the IOP may be also from the heat-induced vasodilation of sub-conjunctival vessels during warm compression.

Massage is also procedure well-popular in rehabilitation field by any instruments. Moreover, periocular massage of the lids with a finger alone, or in combination with local applications of medications, warm compression or eyelid hygiene, may be used in the treatment of chronic blepharitis, meibomianitis,

chronic palpebral conjunctivitis, trachoma and chalazion. Ocular massage through the eyelid is also a common technique employed to aid filtration and avoid fluid obstruction after trabeculectomy in patients with glaucoma. Furthermore, the treatment of meibomian gland dysfunction and dry eye syndrome frequently involves massage to promote lipids secretion from obstruction glands following warm compression to the eyelids. The mechanism of ocular massage may enhance the vagus nerve activity. If combined eyelid warming, the synergic effects may reduce pain from higher IOP. Some authors believed that ocular massage is a simple procedure to reduce IOP. Lam and his workers found that IOP drop (> 1 mmHg) in 76% of the subjects (decreasing mean IOP is 3.73 mmHg; maximum reduction: 7 mmHg) which is approximately to our findings (mean IOP dropping: 2 mmHg by ocular massage). In our study, periocular massage is applied to promote the conduction which heat administered to the eyelid. The application of pressure, even mild pressure, is an integral component of warm compress, which also administers heat to the eyelid through conduction. Mild pressure also improves the apposition of the heating surface to the eyelid and peri-ocular skin and enhances the efficacy of the heat transfer. During massage, the pressure also may pass through the palpebral tarsal conjunctiva, pre-corneal tear layer, anterior layer, cornea and aqueous. Therefore, corneal epithelial temperature of 33.7°C and the temperature of surrounding blood vessels are approximate to 38°C. Mapstone also reported that eyelid massage may cause the anterior uveal hyperemia, and improve the aqueous flow and temperature. Besides, the increasing temperature is considered from the heat of aqueous humor fluid.

Why the results in our study only revealed that only mild and insignificant IOP change (only reduction of 2-4 mmHg) after ocular massage? At first, we suggested that several types of glaucoma own their characters. For example, the angle-closure glaucoma and even neo-vascular glaucoma which the abnormal anatomies may initial block the aqueous outflow within anterior and angle. In spite of the thermal heating to the eyes and vasodilation of the subconjunctival blood vessels, the aqueous humor still may not easily drain through the narrow angle, and the levels of lowering IOP is limited. Secondly, we conjectured that massive or in-correct massage had the opposite effect which may compress the lumens of subconjunctival blood vessels which possibly could block the outflow of aqueous humor fluid. Whether or not the theory may explain the phenomenon? It deserved further investigation in the future. Unfortunately, direct massage on the central eyeball may interfere with visual acuity within several

minutes due to the raising the corneal temperature and reducing corneal hysteresis and resistance factor in some researches. Furthermore, incorrect massage may result in corneal epithelial thinning, abnormal enzyme activity in the tear, susceptible to mechanical forces, change of corneal curvature and ocular rigidity, kerato-conus, and even larger IOP spikes. In our experience, even "light" force compressing the central eyeball may also induce IOP increment. Therefore we suggested that the correct technique is finger massage over the periocular region other than the central part of eyelid to prevent from the uncertain side effects.

Increased IOP has consistently been recognized as a risk factor for the development and progression of glaucoma. Large studies such as The Ocular Hypertension Treatment Study and The European Glaucoma Prevention Study recognized ocular hypertension (only increasing IOP) as the important factor for the development of POAG. Therefore, reducing IOP may decrease the risk of visual field progression and development of glaucoma. Now the use of visual terminal displays (VTDs) and smartphone in human, especially the official workers becomes very popular. However, long-term near work may impact on the ocular condition. For example, Sergienko et al demonstrated that it is likely that working hyperemia of the ciliary body and hyper-production of intraocular fluid occurred under long-term closer working [85]. Besides, Yan et al. found that near accommodation could induce transient IOP elevation in progressing myopic patients [86]. Simultaneously, the near work may cause the shallowing of anterior chamber space, narrow angle, and lens thickened with accommodation which always induced the peri-ocular pain, ocular fatigue and even headache. In this situation, warm compression with correct ocular massage (2-4 times per day; 10 minutes in one time) may lower IOP and relieve the VTDs associated problems such as ocular fatigue and dry eye.

Conclusion

Warm compression combined massage have been suggested as home therapy for the conscience and safe [51]. The IOP decreased significantly after heating and mild reduced by massage in most patients with higher IOP which also enhance the relief of periocular pain, and mood disorders. Therefore, we believed that warm compression combined with massage may be benefit to patients with increasing IOP, VTDs users with high prevalence of dry eye, long-term near-distance workers and the smartphone users [88]. Furthermore, these two treatments may furtherly improve the work efficacy and healthy conditions. Therefore, we strongly aggressed that the advantages of warm compression and correct finger

massage for human in high-developed modern society nowadays.

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