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# Intraocular pressure decrease after local ocular cooling is underestimated by applanation tonometry

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## Abstract

*Background:* The effects of intense systemic or local cooling on aqueous humor dynamics in animals are an increased total outflow facility and a decreased aqueous flow. Few studies suggest that only vasoconstriction of arteriolar segments of the episcleral vasculature may be the cause for a decrease in intraocular pressure after local cooling in humans. Because corneal changes may have influenced such studies, the effect of local cooling was assessed in normal subjects. *Methods:* Intraocular pressure and corneal thickness were measured in 18 healthy human subjects before and after exposure of the right eye to both, an air stream at 20° C, and an air stream at 0° C. *Results:* No significant changes in IOP or corneal thickness occurred under 20° C conditions. After local cooling, the mean corneal thickness increased from $0.52 \pm 0.01$ mm to $0.57 \pm 0.02$ mm ($p < 0.001$). Mean intraocular pressure decreased from $13.8 \pm 2.9$ mmHg to $12.9 \pm 3.1$ mmHg ($p < 0.026$). The observed decrease in IOP correlated significantly but negatively ($R = -0.53$; $p = 0.024$) with the increase in corneal thickness, indicating that the cooling effect on IOP may be rather underestimated. *Conclusion:* The eye is very sensitive to local cooling effects, which may, however, partially be masked by changes in corneal thickness.

## Introduction

The effect of hypothermia on ocular physiology has been investigated broadly in animal studies [1–6]. The effect of intense systemic or local cooling on aqueous humor dynamics consists of increased total outflow facility and decreased aqueous flow. Only few studies on humans have addressed the effect of local cooling on aqueous humor dynamics. Local cooling conditions have been suggested to decrease the intraocular pressure (IOP) in humans with no changes in total outflow facility or aqueous flow [7]. In fact, the changes in IOP after exposure of the eye to a cold air stream have been suggested to be a result of a decrease in episcleral venous pressure [7]. The authors of the above-mentioned study used a cold air stream at -19° C for 40 minutes. These extreme conditions, however, may have induced a corneal edema [8, 9]. Corneal edema, in turn, is known to cause an underestimation of IOP [10]. Thus, whether local cooling conditions in humans may reduce the IOP or whether the measured effect on IOP is, instead, an artifact due to corneal edema remains to be clarified. Therefore, we measured the effect of local cooling on corneal thickness and IOP in 18 healthy humans.

## Patients and methods

The right eyes of 18 healthy volunteer subjects were tested after obtaining informed consent.

Prior to each IOP measurement, corneal thickness was determined on the right eye with a Haag-Streit pachymeter (Bern, Switzerland). The scale was set to 0 mm before taking the measurement. Central corneal thickness was determined, and the value was not read until the examiner removed the slit-lamp. Afterwards, IOP was measured using a Goldmann applanation tonometer under topical anesthesia with 0.4% oxybuprocaine chlorate, following careful application of a fluorescein strip in the inferior conjunctival fornix, according to a standard protocol. The tonometer was set to 10 mmHg before taking the pressure, and the value was not read until the examiner removed the tonometer from the cornea. The mean of three consecutive measurements was taken for IOP as well as for corneal thickness for each step throughout the experiment.

After IOP measurement, the patient was asked to lean back in the chair, and an air stream at 20° C was directed toward his right eye for 5 minutes. The air stream was generated by a ventilator (Prototype of Linde Kältetechnik AG, Basel, Switzerland), allowing continuous adjustment of the air-stream flow between 5 and 65 $m^3$/hr through an insulated tube 5 cm in diameter. The air stream was maintained at 30 $m^3$/h throughout the procedure. None of the subjects complained of pain. The temperature of the air stream was constantly monitored at the exit orifice of the tube, 2 cm in front of the eye.

After 5 minutes of local air-stream exposure at 20° C, corneal thickness and IOP were recorded according to the protocol described above. Afterwards, the patient was asked to lean back again, and then an air stream at 0° C was directed toward his right eye for 5 minutes. At this temperature, a regulating circuit maintained the ventilator at constant conditions with a variability of less than ± 2.0° C. Finally, corneal thickness and IOP were recorded a last time according to the same protocol.

Data are expressed as mean ± standard deviation and were compared by means of a t-test for paired variables. The correlation between the IOP reading and the corneal thickness after exposure to cold air was calculated by means of Pearson's Linear Correlation Factor.

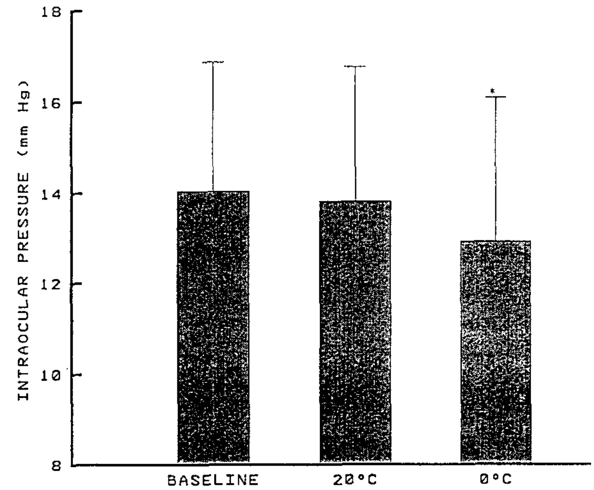


*Fig. 1.* The IOP (mean± SD) decreased significantly (p = 0.026) only after cooling at 0° C (*), but not with an air stream at room temperature (20° C).

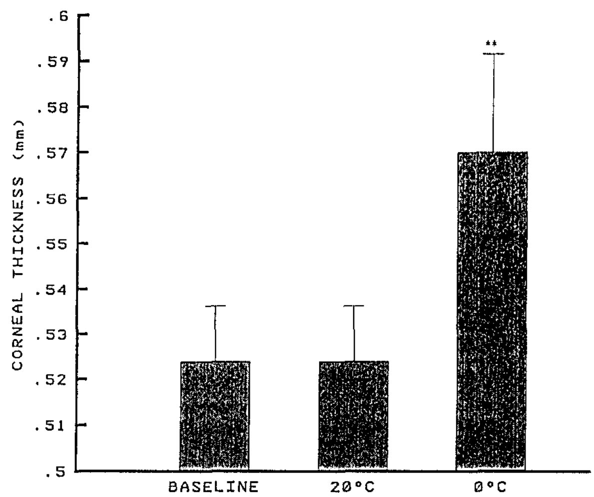


*Fig. 2.* The corneal thickness (mean ± SD) increased significantly (p < 0.001) after cooling at 0° C (**), but not with an air stream at room temperature (20° C).

## Results

In this group of 18 healthy subjects, the mean age (± SD) was 33.8 ± 7.8 years. The changes in the mean IOP values and the mean corneal thickness values after each step of the experimental procedure are shown in Fig. 1 and Fig. 2. Baseline mean IOP and corneal thickness were, respectively, 14.1 ± 2.8 mmHg and 0.52 ± 0.01 mm. After exposure to an air stream at 20° C, the mean IOP and corneal thickness were, respectively, 13.8 ± 2.9 mmHg and 0.52 ± 0.01 mm. After exposure to an air stream at 0° C, the mean IOP and corneal thickness were 12.9 ± 3.1 mmHg and 0.57 ± 0.02 mm, respectively. No significant decrease in IOP occurred after exposure to 20° C air (p = 0.104). The decrease in IOP after local cooling, however, was statistically significant (p = 0.02) (Fig. 1). As well, no changes in pachymetric readings were observed after exposure to 20° C air while local cooling produced a statistically significant increase in corneal thickness (p < 0.001) (Fig. 2). A statistically significant correlation was found between the decrease in IOP and the increase in corneal thickness observed after exposure to cold air (R = - 0.53; p = 0.024). Subjects with only slight increase in corneal thickness had a large

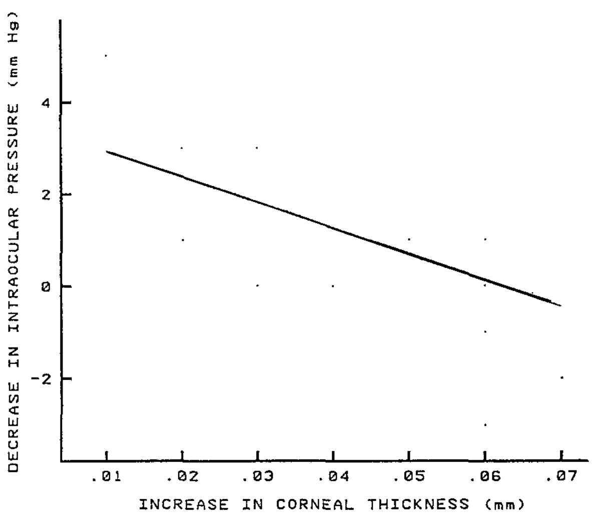


*Fig. 3.* The decrease in IOP and the increase in corneal thickness observed after exposure to cold air correlated significantly (R = - 0.53; p = 0.024). Subjects with only slight increase in corneal thickness had a large decrease in IOP, while subjects with more pronounced increase in corneal thickness had a minor decrease in IOP (negative decrease values indicate an increase for the measured difference of IOP). Consequently, the measured effect of local cooling on IOP has been rather underestimated.

decrease in IOP, while subjects with more pronounced increase in corneal thickness had a minor decrease in IOP (Fig. 3).

## Discussion

The effect of local cooling on corneal thickness and IOP was measured in 18 healthy subjects. In this population, local cooling by means of cold-air stream provoked a decrease in IOP and an increase in corneal thickness. No changes in corneal thickness occurred after exposure to 20° C. This suggests that the reason for the increase in corneal thickness was the local cooling effect. The decrease in IOP and the increase in corneal thickness observed after exposure to cold air correlated significantly but negatively. Subjects with only slight increase in corneal thickness had a large decrease in IOP, while subjects with more pronounced increase in corneal thickness had only a minor decrease in IOP. Consequently, the measured effect of local cooling on IOP has rather been underestimated in this study because of the increase in corneal thickness. Thus, the decrease in IOP in eyes without increased corneal thickness would be expected to be even more prominent. The slight and statistically not significant decrease in IOP after exposure to 20° C might, most probably, have been induced by repeated measurements [10]. Whether a same effect might have caused the decrease after local cooling seems doubtful. Indeed, the effect of repeated measurements diminishes progressively [10]. The decrease in IOP after local cooling was not only higher but has seemingly even been underestimated. Of course, a prerequisite for our hypothesis is that in corneas displaying no change in thickness after local cooling the bending properties remain normal.

The mechanisms for the changes in IOP and in corneal thickness have not been investigated in the present study. An increase in corneal thickness was observed in each subject after local cooling. Corneal swelling during local cooling has been reported in patients with trigeminal nerve dysfunction and seems to occur in normals only under severe environmental conditions [8, 9, 11]. However, the effect of local cooling has been tested under local anesthesia in the present study. Therefore, hypothetically, in addition to the cold air, a further cause for the observed increase in corneal thickness after this relatively mild local cooling may be the local anesthesia, which was an unavoidable aspect of the present study. Indeed, the subjects were all exposed to local cooling within 1–2 minutes after intraocular pressure measurement which was always done in local anesthesia. Therefore, a reduced corneal sensitivity during local ocular cooling must be expected. Corneal thickness is known to influence IOP readings [10, 12, 13]. Whereas applanation readings may be too high in thick corneas (thickness made up of collagen fibrils), manifest corneal edema seems to cause rather an underestimation of IOP [10]. A manifest corneal edema was never observed during this study. Only a slight increase in pachymetric readings was recorded. Furthermore, subjects with only slight increase in corneal thickness had a pronounced decrease in IOP, while subjects with larger increase in corneal thickness displayed a less pronounced decrease in IOP. If this slightly increased corneal thickness had caused an overestimation of the decrease in intraocular pressure, we would expect a larger decrease in patients with large increase in corneal thickness and a smaller decrease in patients with slight increase in corneal thickness. We observed exactly the contrary, suggesting rather an underestimation of the decrease in intraocular pressure after local cooling. We do not know what led to the slight increase in corneal thickness. We believe that it was most probably due to an increase in corneal water content, but we do not know in which part of the cornea. We also do not know how a very slight increase in corneal water content would affect applanatory intraocular pressure readings. Possibly, local changes in corneal thickness may lead to changes in corneal radius, which might explain why corneal changes expected to provoke an underestimation of applanatory IOP readings lead actually to an overestimation. Further investigations are required to elucidate this question. Our results suggest that the slight increase observed in corneal thickness rather induced an overestimation of the IOP after local cooling and that the latter's real effect on IOP might have been underestimated.

The present study not only confirms previous results in animals and humans that local ocular cooling reduces IOP, but also shows that aqueous humor dynamics may be influenced with relatively mild cooling conditions. Furthermore, even under such mild conditions, the negative correlation between decrease in IOP and increase in corneal thickness suggests that an assessment of IOP by applanation tonometry rather underestimates the real effect of the experimental manipulation. Therefore, previous interpretations of the effect of local cooling on IOP in humans might be more debatable. Local cooling conditions have been suggested to decrease the intraocular pressure (IOP) in humans without changes in total outflow facility or aqueous flow [7]. In fact, the changes in IOP after exposure of the eye to a cold air stream have been suggested to be a result of a decrease in episcleral venous pressure [7]. Hypothermia is known to cause arteriolar vasoconstriction. Hence, as a result of episcleral hypothermia, a concomitant decrease in pressure within the episcleral veins would be expected, which, in turn, may induce a decrease in IOP. This hypothesis is supported by the recent observation of decreased IOP and increased aqueous outflow in rabbits after pharmacologic vasoconstriction of arteriolar segments of the episcleral vasculature [8]. Unfortunately, the values of the pachymetric readings were not communicated in the above-mentioned study [7]. However, under the rather intense cooling conditions used, the corneal thickness might have changed. The present data suggest that IOP readings may be overestimated after local cooling. Therefore, the reported correlation between the decrease in IOP and the decrease in episcleral venous pressure may not account for the whole effect of local cooling. In fact, a decrease of more than 25% of total outflow facility has been found which was statistically not significant. However, because only 5 subjects could be included in their evaluation, the power of their statistical analysis to conclude a statistical difference in total outflow facility was only 44%.

Local eye cooling induced a decrease in IOP and an increase in corneal thickness in 18 healthy subjects. The present results suggest that the real effect might be more important than that measured by applanation tonometry. The mechanisms which provoke a decrease in IOP after local cooling in humans are not clear. An arterial vasoconstriction of episcleral vessels alone seems not to be the answer. However, aqueous humor dynamics alone may not account for the whole effect either [7]. Several reports suggests that substances which regulate vascular tonus may influence aqueous humor dynamics and corneal metabolism [15–17]. The significance of these findings remains to be investigated. Because of the high sensitivity of the eye to local cooling, hypothermia may prove to be an interesting research tool.

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