Ocular hypothermia: anterior chamber perfusion

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SUMMARY The anterior chambers of 27 rabbit eyes were perfused at constant pressure with room temperature (25°C) or cooled (11°C) balanced salt solution at constant flow rates of 4.8 ml/min or 8.5 ml/min. Intraocular temperature changes in the anterior chamber, anterior vitreous, mid vitreous, and posterior vitreous and on the retina surface were monitored with an intraocular thermocouple probe. Perfusion of the anterior chamber of the pigmented rabbit eye with cooled fluid significantly reduced the temperature of the anterior chamber and anterior vitreous and even that of the retina. Both an increase in the rate of perfusion and a lowering of the perfusion temperature enhanced the cooling effect. The observed decrease in temperatures returned to approximately normal 4 minutes following the cessation of perfusion.

Hypothermia has been used to protect against ischaemia in cardiac surgery,^{1,2} urological surgery,³ neurosurgery,^{4,5} and for the preservation of ischaemic bowel.⁶ Hypothermia has been effective because with reduced tissue temperatures there is an associated decrease in the metabolic rate in the tissue involved. It has been shown that a decrease of 10°C in ocular tissue temperature can reduce the metabolic activity of the cornea by as much as 50%.⁷

During intraocular surgical procedures with prolonged perfusion the corneal endothelium may be damaged,^{8–11} resulting in a compromise of the corneal integrity. High levels of intraocular illumination such as used with deep vitrectomy surgery may be potentially damaging to retinal cells.^{12–17} In addition it is possible that a compromised circulation to the eye during the course of vitrectomy surgery may cause retinal cellular damage.¹⁸ (May DR, unpublished observation.) It was proposed by one of us (S.C.) that ocular hypothermia achieved with the use of refrigerated infusion fluid might reduce ocular tissue damage during intraocular surgical procedures.

Earlier investigators have studied the temperatures within the rabbit eye and have found a gradient

between the corneal surface and the retina of 6–10°C.^{19–21} Other investigators have evaluated the effects on this gradient of heating or cooling the eye. Using a heated thermophore applied to the rabbit cornea, Andrew observed an increase in intraocular temperatures with those structures closest to the heat source showing the greatest changes.²¹ The effects of lowered environmental temperatures have also been evaluated and have shown that ocular temperatures can be lowered by exposure to decreased ambient temperatures.^{7,22}

Actual perfusion studies conducted by Wolin and Massopust on cat eyes utilised a cooled perfusion fluid pumped through the vitreous.²³ Their study demonstrated that a selective cooling of the in-vivo eye was possible, resulting in evidence of decreased retinal activity as measured with electroretinography.

Our study was designed to evaluate the changes in intraocular temperature as a result of anterior chamber perfusion. We chose to determine the speed and extent of the intraocular temperature changes in the rabbit eye. Subsequent studies will evaluate the effects of anterior chamber perfusion on the cellular anatomy and physiology of the cornea and also posterior perfusion of the vitrectomised eye on retina integrity and function.

We began with anterior chamber perfusion because of its simplicity and also its frequent use in modern ophthalmic surgery.

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Materials and methods

Twenty-four eyes of 17 Dutch-belted rabbits weighing approximately 2.5 kg each were used in this experiment. The eyes were dilated with 1% cyclopentolate hydrochloride and 1% atropine sulphate ophthalmic solution prior to the procedure. The rabbits were injected with 10 mg of acepromazine maleate and 100 mg of ketamine hydrochloride intramuscularly for anaesthesia. Topical 0.5% proparacaine hydrochloride ophthalmic solution was applied for local anaesthesia.

The rabbits were placed on their side for surgery, the lids were retracted with a paediatric wire speculum, and a 180° peritomy was made at the superior limbus. The superior rectus muscle was isolated. A muscle hook was placed beneath the muscle for control of the eye during the procedure.

Corneal incisions were made by first passing a 22 gauge needle through the cornea 1 mm anterior to the limbus and enlarging the opening to 3 mm with corneal-scleral scissors. Perfusion was carried out through a nasal corneal incision with a 21 gauge blunt needle inserted into the mid-anterior chamber. Drainage of the perfusate was through a temporal corneal incision located 180° from the first.

A temporal pars plana puncture incision was made 4 mm posterior to the limbus. The intraocular temperature probe was inserted here for the intra-vitreous and retina temperature measurements. Temperature measurements in each eye were at the surface of the retina and in the posterior vitreous,

mid-vitreous, and anterior chamber. The anterior chamber temperature measurements were made through the temporal corneal incision. The temperature probe was positioned by direct visualisation within the anterior chamber and anterior vitreous and by indirect ophthalmoscopic visualisation for positioning in the mid and posterior vitreous and at the retina surface.

Perfusion of each rabbit eye was with Balanced Salt Solution (registered trademark of Alcon Laboratories Inc.) flowing at 4.8 ml/min or 8.5 ml/min. The Balanced Salt Solution was maintained at 120 cm above the level of the eye. Flow rates were monitored with a Gilmont no. 12 flowmeter which was calibrated against a standard graduated cylinder.

Two different perfusion temperatures of the Balanced Salt Solution were used: room temperature (25°C), and a cooled solution (11°C). The perfusion temperatures were monitored during the procedure and varied no more than $\pm 1^\circ\text{C}$ from the desired temperature setting.

The Balanced Salt Solution was cooled by running it through a Borg-Warner thermoelectric heat pump Model 920AHP-4. The heat pump was powered by a Borg-Warner TC-102 temperature controller regulated by a feedback signal from a temperature transducer at the distal end of the perfusion tube (Fig. 1).

The intraocular temperature monitoring probe was a Bailey 23 g thermocouple model MT-5 with a 2.5 cm blunt tip of 0.64 mm diameter. The probe was sealed, and only stainless steel came in contact with the ocular

Fig. 1 Controlled cooling system for perfusion fluid. BSS=Balanced Salt Solution (Alcon Laboratories, Inc.).

tissue. A Doric 400A Trendicator (Type T) was used to measure and display the thermocouple output with $\pm 1^\circ\text{C}$ accuracy. This accuracy included inherent electronic variation and also $\pm 10\%$ line voltage variations at $25 \pm 3^\circ\text{C}$. Room temperatures were monitored by this same thermocouple during the procedure and were maintained at $25 \pm 1^\circ\text{C}$.

Rectal temperatures were monitored with a veterinary mercury-in-glass thermometer accurate to $\pm 0.2^\circ\text{C}$. Intraocular pressures were monitored throughout the procedure by Schiøtz tonometry. During the procedure the intraocular pressures remained within a range of approximately 16–24 mmHg.

Intraocular temperatures were recorded prior to the start of the perfusion and at 1-minute intervals during the 10 minutes of perfusion. Sixteen eyes were studied for 4 additional minutes and one eye for 3 additional minutes after the perfusion was completed. All measurements were taken along the ocular axis. The rabbits were killed after the procedure with a 1 ml intracardiac injection of T61 euthanasia solution (National Laboratories).

Results

The temperatures recorded within the rabbit eyes during perfusion and during the 4 minutes post perfusion were averaged for each temperature measuring position in the eye within each of the 4 experimental groups and plotted against elapsed time (Figs. 2–5). The core body temperature of the animals was measured with the rectal thermometer; it averaged 39.4°C and did not significantly change during the course of the procedure. Preinfusion temperatures of the eyes had the following average temperatures: anterior chamber, 32.5°C ; anterior vitreous, 35.0°C ; mid-vitreous, 35.5°C ; posterior vitreous, 36.6°C ; retina surface, 36.8°C .

Perfusion with 25°C Balanced Salt Solution at 4.8 ml/min produced a rapid drop in the average anterior chamber temperature to 25.4°C within the first 1 minute of elapsed time. Lesser amounts of temperature decrease were recorded as measurements progressed posteriorly in the eye from the anterior vitreous to the retina surface. The maximum temperature change in each eye was recorded in the

Fig. 2 Perfusion of the anterior chamber with 25°C infusion fluid at 4.8 ml/min. Intraocular temperature changes plotted as a function of elapsed perfusion time.

Fig. 3 Perfusion of the anterior chamber with 25°C infusion fluid at 8.5 ml/min. Intraocular temperature changes plotted as a function of elapsed perfusion time.

Ocular hypothermia: anterior chamber perfusion

anterior chamber. Likewise, progressively lesser amounts of temperature changes were noted as the temperature measurements progressed posteriorly from the anterior vitreous to the retina surface. When perfusion was stopped after 10 minutes, the intraocular temperatures increased progressively during the next 4 minutes of monitoring. At 4 minutes post infusion the intraocular temperatures approached the preperfusion levels.

Perfusion of the rabbit eyes with 25°C Balanced Salt Solution at 8.5 ml/min produced more rapid changes in the intraocular temperatures than with 4.8 ml/min. The lowest temperatures recorded for each time interval were also slightly lower than with perfusion at 4.8 ml/min. There was not a significant change in the rate of return of the intraocular temperature to preperfusion levels. As with the perfusion at 4.8 ml/min, a relatively stable level of temperature was achieved in each eye after approximately 3–4 minutes of perfusion temperature, with slight additional decreases noted over the duration of the perfusion.

When the temperature of the Balanced Salt

Fig. 4 Perfusion of the anterior chamber with 11°C infusion fluid at 4.8 ml/min. Intraocular temperature changes plotted as a function of elapsed perfusion time.

Solution was decreased to 11°C and perfusion was carried out at 4.8 ml/min, a more precipitous drop of the temperature in the anterior chamber, anterior vitreous, and mid-vitreous was noted. The posterior vitreous and retina surface temperatures also dropped more rapidly than with perfusion of Balanced Salt Solution at 4.8 ml/min.

With 11°C perfusion at a rate of 8.5 ml/min a rapid drop in intraocular temperature was again noted at all levels within the eye. The lowest temperatures achieved with their perfusion were lower than with 11°C perfusion at 4.8 ml/min. After the cessation of perfusion, the temperatures rapidly returned to higher levels but did not reach the preperfusion levels by 4 minutes.

In comparing the changes of retina temperatures (Table 1), we noted that as the temperature of the perfusion fluid was decreased from 25° to 11°C, the final retinal temperature achieved was lower. This lower retinal temperature was also noted as the rate of infusion was increased in both temperature groups.

Statistical analysis by a one-way analysis of variance of the ΔT over the 10-minute perfusion period

Fig. 5 Perfusion of the anterior chamber with 11°C infusion fluid at 8.5 ml/min. Intraocular temperature changes plotted as a function of elapsed perfusion time.

demonstrated that the temperature changes in each of the 4 experimental groups were significantly different ($p < 0.001$). Furthermore, by a paired comparison of the data for treatment effects both the 8.5 ml/min group ($p < 0.005$) and the 11°C temperature group ($p < 0.001$) were found to have a significantly greater cooling effect on the retinal surface temperature than the 4.8 ml/min group of 25°C temperature groups respectively. An analysis of the statistical significance of the changes in intraocular temperatures with perfusion was limited to the retinal surface temperature changes (Table 1).

Discussion

Two main sources of error are encountered in any intraocular temperature measuring study. These are increased blood flow to the eye secondary to the ocular manipulation and heat conduction along the temperature probe.^{7 24 25} The effects of the first were decreased by omitting any data from eyes that were observed to have gross evidence of trauma—either damage to the lens or intraocular haemorrhage. Errors associated with metallic probes have been found to increase as measurements are made in the more anterior parts of the eye.²⁵ This error is greatly reduced when the probe is 15–20 mm within the eye. Tests for significance of results were made with only the retinal treatments, which, being the deepest measurements, would have the least amount of error.

The calculated significance between the different treatment groups was computed on the assumption that the responses were independently and normally distributed with constant variance. These assumptions may not all be met by these data; however, we feel that the results are still meaningful even without these assumptions.

Table 1 Changes in retina temperature (ΔT) after 10 minutes of perfusion

Perfusion fluid temperature	Rate of perfusion					
	4.8 ml/min			8.5 ml/min		
	Rabbit no.	Eye	ΔT (°C)	Rabbit no.	Eye	ΔT (°C)
25°C	44	OS	-1.5	44	OD	-1.0
	50	OS	-2.0	49	OD	-2.0
	50	OD	-1.0	49	OS	-2.0
	51	OD	-1.0	48	OS	-2.0
	52	OS	-1.0	53	OD	-1.0
	48	OD	-0	NK36	OD	-2.0
11°C	42	OD	-2.0	40	OS	-4.0
	nnB	OS	-4.0	40	OD	-4.0
	45	OD	-2.0	41	OS	-4.0
	42	OD	-2.0	nnA	OD	-3.0
				46	OS	-2.0
				39	OD	-3.0

This study has shown that perfusion of the anterior chamber in vivo effectively reduces the intraocular temperatures. The observed reduced intraocular temperatures achieved as a result of the perfusion were found to return to approximately normal within 4 minutes following cessation of perfusion.

It was noted in each experimental group that the closer the temperature measurements were made to the anterior chamber the more marked was the rate of decrease of the temperature and the lower the final temperature achieved. This would be expected because of heat continually conducted into the eye from the retina and choroidal circulation. In spite of this we noted that we could decrease the retina temperature of each eye with anterior chamber perfusion. The effect of these changes on the rabbit eye or the human eye in a surgical situation can at present only be guessed at.

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