# Experimental Studies

## Effect of irrigation solution temperature on the duration of intraocular bleeding during vitrectomy (experimental study)

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***Background:*** *Bleeding in vitreoretinal patients during and early after vitrectomy is still a challenge that needs to be addressed.*
***Purpose:*** *To assess the effect of irrigation fluid temperature on intraocular bleeding time in rabbits during vitrectomy.*
***Material and Methods:*** *Twelve Chinchilla rabbits (24 eyes) were included in this study and divided into four groups of 3 animals (6 eyes) each based on vitrectomy irrigation fluid temperature: group 1 (5° C), group 2 (10° C), group 3 (22° C), and group 4 (36° C). The ambient operating room temperature was between 22 °C and 24 °C.*
***Results:*** *The duration of intraocular bleeding in groups 1, 2, 3 and 4 was 88.3 ± 46.0 s, 34.8 ± 30 s, 63 ± 23.5 s, and 21.1 ± 9.5 s, respectively.*
***Conclusion:*** *In a rabbit model of intraocular bleeding, use of irrigation fluid of 36 °C (i.e., conditions of mild hypothermia) resulted in shorter intraocular bleeding in the perioperative period of vitrectomy compared to conventional use of room-temperature irrigation fluid (21.1 ± 9.5 s against 63 ± 23.5 s). Mild hypothermia may be recommended for use in vitreoretinal surgery in patients with a high risk of bleeding.*

### Introduction

Pars plana vitrectomy is widely used in the treatment of rhegmatogenous retinal detachments, proliferative diabetic retinopathy and other vitreoretinal disorders. The surgical intervention (e.g., in severe proliferative diabetic retinopathy) is often time consuming for the performing surgeon [1]. Despite continuous advances in vitrectomy technology, there still remain a wide range of challenges that need to be addressed [2-8]. One of these challenges is bleeding in vitreoretinal patients during and early after vitrectomy [9].

The temperature of irrigation solutions used during vitrectomy is commonly lower than that of the intraocular media, and neither of these temperatures is commonly monitored during the procedure [10]. Consequently, vitrectomy is performed under conditions of uncontrolled local ocular hypothermia.

Although there is no uniform protocol to administer hypothermia in intraocular surgery, some authors believe it reasonable to use low-temperature irrigating fluids to facilitate neuroprotection during vitrectomy [11-13]. In addition, currently, there are no clear recommendations on irrigation fluid temperature modes reducing the risk of bleeding during vitrectomy.

**The purpose** of the study was to assess the effect of irrigation fluid temperature on intraocular bleeding time in rabbits during vitrectomy.

### Material and Methods

Twelve Chinchilla rabbits (24 eyes; weight, 2.5-3.5 kg) were included in this study and divided into four groups of 3 animals (6 eyes) each based on vitrectomy irrigation fluid temperature: group 1 (5° C), group 2 (10° C), group 3 (22° C), and group 4 (36° C). The ambient operating room temperature was between 22 °C and 24 °C.

A 23-G three-port pars plana vitrectomy was performed using the Alcon Accurus 400VS vitrectomy system (Alcon Laboratories, Fort Worth, TX).

### Technique

The surgical site was prepared with antiseptic solution and epibulbar anesthetic was administered. Thereafter, core and peripheral vitrectomy was performed with cutting rates of 1500-1800 cuts/min, aspiration pressure of 150 mm Hg, and irrigation pressure of 20 mm Hg.

After vitrectomy, irrigation fluid circulation was maintained for 5 minutes to stabilize intraocular temperature [11]. Thereafter, the major retinal vessels running through the medullary bundles closely located nasally or temporarilly to the optic nerve were cut to induce intraocular bleeding [9, 14, 15], and the period from cutting the vessel (and the onset of bleeding) to complete arrest of bleeding from the damaged vessel was recorded. Irrigation and aspiration were not discontinued during this period.

BSS PLUS® (Alcon) was used as an intraocular irrigation fluid. Cool (5 °C or 10° C) fluid was prepared by cooling the solution inside the irrigating tube with cooling gel packs. Room-temperature (22 °C) fluid was obtained by placing the bottles with solution in the operating room for several hours before surgery. Warm (36 °C) fluid was prepared by warming the solution inside the irrigating tube with gel packs that were located outside the tube, and thus warming was performed in close proximity to the surgical site.

The temperature of the irrigation fluid delivered into the eye was monitored and controlled during surgery. A thermoelectric device [18] developed by the Institute of Thermoelectricity of the NAS of Ukraine and MES of Ukraine, and the Filatov Institute was used for measuring irrigation fluid temperature.

All animal experiments were performed in compliance with the Law of Ukraine on Protection of Animals from Cruel Treatment No. 3447-IV dated 21.02.2006 and European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes from the European Treaty Series (Strasbourg, 1986), and approved by a local Bioethics Committee of the Filatov Institute.

The animals were housed and bred conventionally. Each animal underwent biomicroscopy and ophthalmoscopy before surgery and the next day after surgery. In addition, rectal temperature measurements were made before surgery and before anesthesia.

Prior to surgery, animals were anesthetized with thiopental sodium 10% (1.0 mL/kg, intramuscularly). Immediately thereafter, both eyes received a drop of proxymetacaine HCl (0.5%) for topical anesthesia. The pupils were dilated with atropine sulphate. After surgery, a drop of sulfacyl natrium 20% and a drop of Ofloxacin 0.3% were applied to each operated eye immediately after surgery and four times daily for 5 days thereafter.

The experimental temperature data was subjected to statistical analysis. Data is presented as mean ± standard deviation (SD). Statistical analyses were conducted using Statistica 10.0 (StatSoft, Tulsa, OK, USA) software. The level of significance $p \leq 0.05$ was assumed.

### Results

No change in the cornea was observed, and the lens was clear during the surgical procedure. There was no significant difference in operation room temperature or baseline rectal temperature among the groups. Mean intraocular bleeding durations for the groups are presented in Table 1 and Figure 1.

Bleeding duration was significantly (p=0.000) shorter in rabbits with a vitrectomy irrigation fluid temperature of 36 °C (group 4) than in those with a vitrectomy irrigation fluid temperature of 22 °C (group 3) or 5 °C (group 1). There was no significant difference (p=0.14) in bleeding duration between animals of group 4 and those of group 2 (irrigation fluid temperature of 10 °C).

### Discussion

Vitrectomy is usually performed in patients who already have ischemic retinal injury, e.g., patients with diabetic retinopathy. In addition, IOP increase and systemic arterial pressure decrease during vitrectomy can result in decreased perfusion pressure, leading to additional intraoperative ischemic retinal and optic nerve injury [7]. As currently there is no classification for assessing the severity of eye tissue hypothermia, we were guided by the classification used in critical care intensive therapy units. Hypothermia can be classified based on the depth of cooling from a normal body temperature of 37-38°C: mild hypothermia (34-35.9 °C), moderate hypothermia (32-33.9 °C), intermediate hypothermia (30-31.9 °C), and deep hypothermia (< 30 °C) [17]. Mild hypothermia is known to have a positive effect on the structure and function of neural tissue under ischemic conditions. Mild hypothermia prevents blood–brain barrier disruption and its downstream effects under cerebral ischemic conditions [18], inhibits pro-inflammatory brain tissue responses [19], and suppresses cellular apoptosis [20]. Although mild therapeutic hypothermia (a reduction of a patient's core temperature to 34.0 - 35.9 °C) has been successfully applied in critical care practice for improving brain cell resistance to ischemic conditions [17, 20], to our knowledge, only animal studies have been reported on the effect of hypothermia on the ocular cells and tissues.

Intraocular temperatures undergo changes in the course of vitrectomy depending on irrigating fluid temperature. We have previously demonstrated [21] that, intraocular temperature decreased by 1°C with the use of 36°C irrigating fluid during vitrectomy (i.e., surgical interventions were performed under conditions of mild hypothermia). There has been histological evidence of apparent vacuolization of retinal structures at the microscopic slides from rabbit eyes that underwent vitrectomy under conditions of deep hypothermia, but not prolonged vitrectomy under conditions of mild hypothermia [22].

In the current study, duration of intraocular bleeding was significantly shorter in rabbits with a vitrectomy

irrigation fluid temperature of 36 °C than in those with a vitrectomy irrigation fluid temperature approximately equal to room temperature (22 °C). It has been reported that hypothermia does not begin to affect platelet function until temperature decreases below 35 °C; clotting factors are affected only when temperature decreases below 33 °C [17]. Therefore, conventional conditions under which vitrectomy is commonly performed (i.e., with the use of room-temperature irrigation fluid) are not the best for efficient perioperative hemostasis. In addition, duration of intraocular bleeding was shorter in rabbits with a vitrectomy irrigation fluid temperature of 10 °C than in those with a room- temperature irrigation fluid, which is in agreement with previous findings [11]. Moreover, in the current study, rabbits with a vitrectomy irrigation fluid temperature of 5 °C exhibited the longest intraocular bleeding duration.

Therefore, since mild hypothermia exerts a number of positive effects on neural tissue structures, does not result in cold-related damage to retinal tissue, and causes a reduction in duration of bleeding in the perioperative period, we find it reasonable to recommend it for prolonged vitreoretinal surgery, especially in patients with a high risk of bleeding (e.g., those with proliferative diabetic retinopathy).

### Conclusion

In a rabbit model of intraocular bleeding, use of irrigation fluid of 36 °C (i.e., conditions of mild hypothermia) resulted in shorter intraocular bleeding in the perioperative period of vitrectomy compared to conventional use of room-temperature irrigation fluid (21.1 ± 9.5 s against 63 ± 23.5 s). Mild hypothermia may be recommended for use in vitreoretinal surgery in patients with a high risk of bleeding.

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**Table 1.** Duration of intraocular bleeding in groups of experimental animals (6 eyes per group)

| **Animal group (irrigation fluid temperature)** | **Group 1 (5 °C)** | **Group 2 (10 °C)** | **Group 3 (22 °C)** | **Group 4 (36 °C)** |
|---|---|---|---|---|
| Bleeding duration, s | 88.3 ± 46.0 | 34.8 ± 30 | 63 ± 23.5 | 21.1 ± 9.5* |

Note: *, significant difference compared to groups 1 and 3

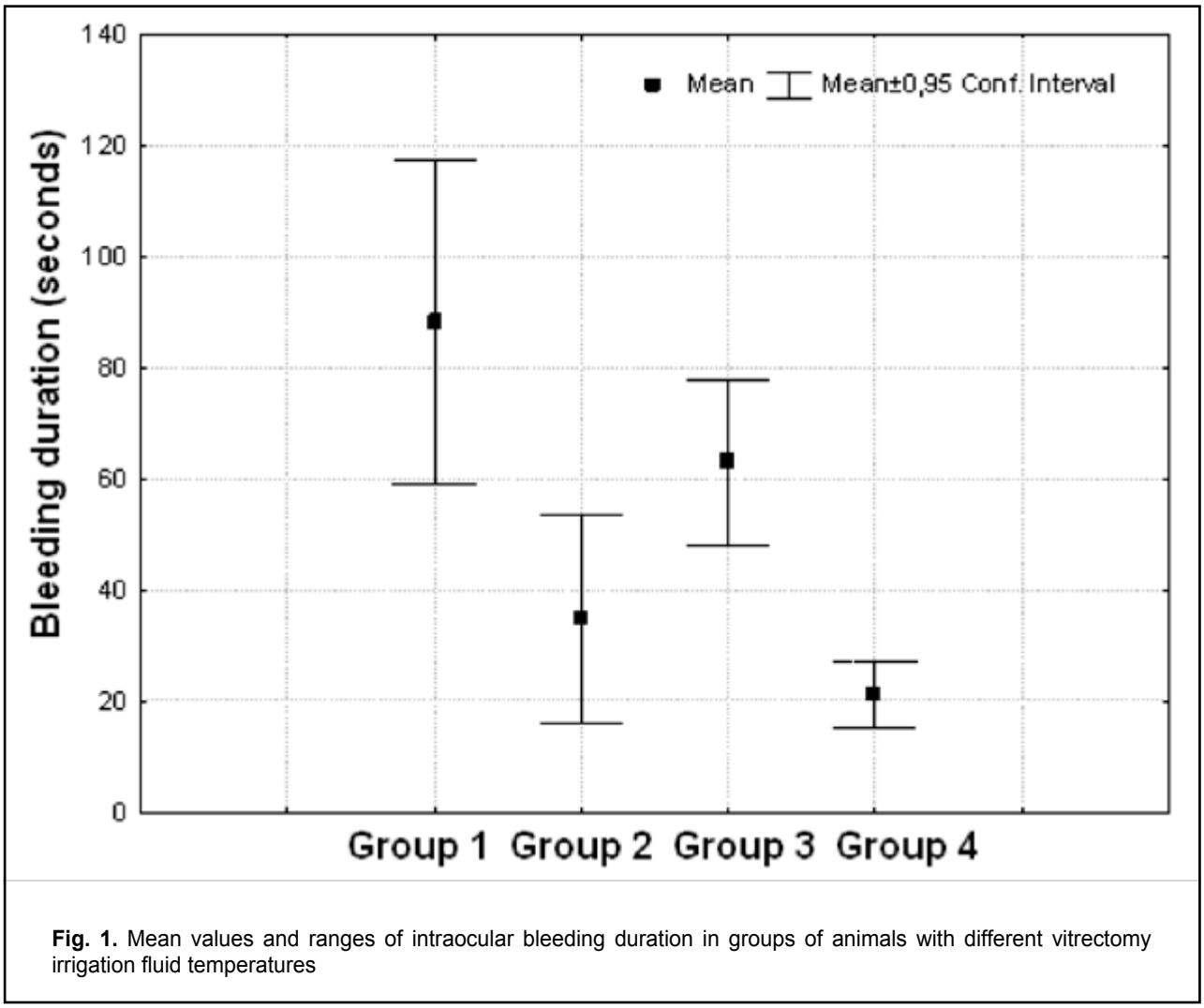


**Fig. 1.** Mean values and ranges of intraocular bleeding duration in groups of animals with different vitrectomy irrigation fluid temperatures