Experimental Laboratory Modeling of Choroidal Vasculature: A Study of the Dynamics of Intraoperative Choroidal Hemorrhage during Pars Plana Vitrectomy

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Abstract

Objectives: Choroidal hemorrhages (CH) result from rupture of choroidal vessels leading to extravasation of blood into the suprachoroidal space. In this study, we aimed to understand the hemodynamics of CH by developing a purpose-built scale model of the choroidal vasculature and calculating stress levels in the model under different conditions.

Materials and Methods: We modeled the choroidal vasculature using a rubber tube 10 cm in length and 1 cm in diameter that was wrapped with conductive thread to enable the measurement of stress at the walls of the tube. Stress levels across the tube were continuously measured under different systemic intravascular blood pressure levels (IVP), intraocular pressure (IOP) levels, and distortion.

Results: Stress values across the choroidal vessel model correlated negatively with IOP and positively with IVP and distortion. All correlations were statistically significant (p<0.05) and were stronger when the model was filled with expansile tamponade compared to non-expansile tamponades. Distortion showed the strongest correlation in terms of increasing stress across the model, while IVP showed stronger correlation compared to IOP. Raising IOP to counteract the stress in the model was effective when the stress in the model was secondary to increased IVP, but this approach was not effective when the stress in the model was caused by distortion.

Conclusion: Excessive distortion of the globe during surgical maneuvers could be the primary reason for the rarely observed intraoperative CH. Non-expansile ocular tamponade provides better support for the vascular bed against CH and should be the recommended choice of tamponade in patients with existing CH. Increasing IOP excessively is of limited effect in preventing CH in vessels that are under stress as a result of distorting surgical maneuvers.

Keywords: Choroid hemorrhage, vitrectomy, choroid, suprachoroidal space

Introduction

Choroidal hemorrhages (CH) are relatively uncommon but can lead to devastating outcomes. They result from rupture of arterioles, venules, and capillaries which initially lead to extravasation of blood into the choroid and subsequently into the suprachoroidal space.\(^1\) Possible mechanisms for vascular ruptures are believed to be drop in intraocular pressure (IOP), increase in systemic blood pressure, distortion of the vascular architecture, and direct injury to the blood vessels. However, these suppositions have not been supported by experimental data. Therefore, research to understand the hemodynamics of CH is important to enable surgeons to take effective measures to reduce the risks. Surgeons are generally advised to avoid hypotony during surgery, refrain from operating on patients with high systemic blood pressure, and minimize the use of expansile tamponades in high-risk patients. However, the role of avoiding inadvertent intraoperative distortion of ocular tissues in prevention of CH is generally underemphasized. Nevertheless, mathematical models showed that globe distortion from mechanical strain plays a more important role in causing CH.
role in causing CH compared to hypotony or increased systemic blood pressure. Therefore, in this study we aimed to understand the hemodynamics of CH by creating a purpose-built scale model of the choroidal vasculature and calculating stress levels in the model under different conditions.

Materials and Methods

The choroidal vasculature was modeled using a rubber tube 10 cm in length and 1 cm in diameter wrapped with conductive thread to enable the measurement of stress at the walls of the tube. The tube was filled with clear water and pressurized to various levels using an electric pump to simulate systemic intravascular blood pressure (IVP) and placed into a sealed container which was also pressurized to various levels to simulate variable IOP. A hydraulic actuator was also used to apply various longitudinal strain on the tube to simulate ocular distortion during surgical maneuvers. The stress levels in the tube were continuously monitored under different IVP, IOP, and distortion levels. IOP and IVP were measured in mmHg and stress was measured in Pascals (Pa), while distortion was measured as percentage of change in the length of the model (e.g., stretching the 10-cm rubber tube to 11 cm correlated to 10% distortion) (Figure 1, 2).

The experiments were carried out in two phases. Phase 1 consisted of 3 sets of experiments that aimed to observe changes in stress levels in the choroidal vasculature in relation to changes in IOP, systemic blood pressure, and longitudinal strain. Phase 2 consisted of 2 sets of experiments that aimed to observe the benefits of increasing the IOP to counteract high stress levels in the choroidal vasculature secondary to high systemic blood pressure and ocular distortion.

During phase 1, initial stress measurements were taken while dropping the IOP from 35 mmHg to 0 mmHg while maintaining IVP at 120 mmHg and distortion at 0%. These conditions reflected the effect of hypotony on the choroidal vasculature. Subsequently, stress measurements were taken while increasing IVP from 120 mmHg to 200 mmHg while maintaining IOP at 35 mmHg and distortion at 0%. These conditions reflected the effect of high systemic blood pressure on the choroidal vasculature. Finally, stress measurements were taken while gradually distorting the model up to 12% of its length while maintaining IOP at 35 mmHg and IVP at 120 mmHg. These conditions reflected the effect of perioperative ocular distortion on the choroidal vasculature.

In phase 2, stress levels in the choroidal vasculature were first increased up to 6 Pa by raising the IVP followed by a gradual increase in IOP from 35 mmHg to 80 mmHg to counteract the stress. These conditions reflected the role of increasing IOP during surgery to prevent CH in patients with high systemic blood pressure. Subsequently, the tests were repeated but this time distortion was used to raise the stress levels in the choroidal vasculature to 6 Pa while the IVP remained at 120 mmHg followed by a gradual increase in IOP from 35 mmHg to 80 mmHg to counteract the stress. These conditions reflected the role of increasing IOP during surgery to prevent CH in eyes subjected to distortion during surgery.

Statistical Analysis

All tests were performed separately while the container was filled with water and with air to reflect eyes filled with non-expansile tamponades and with expansile tamponades, respectively. To enhance accuracy and enable statistical analysis, each test was repeated 10 times. Spearman’s correlation was used to assess the statistical significance of the observations. Correlations were considered significant when p value was ≤0.05. Statistical analyses were performed using SPSS software version 18 (SPSS Inc., Chicago, IL, USA) (Table 1).

Results

The first set of experiments in phase 1 showed a statistically significant negative correlation between stress in the choroidal vasculature and IVP while IOP was fixed at 120 mmHg and distortion was 0%. The correlation was stronger when the model was filled with expansile tamponade. Spearman’s correlation rho was -0.504 (p<0.001) and stress levels reached 1.7 Pa when the model was filled with expansile tamponade compared to Spearman’s rho of -0.190 (p<0.001) and stress levels up to 0.1 Pa when the model was filled with non-expansile tamponade. The second set of experiments in phase 1 also showed a statistically significant but positive correlation between stress in the choroidal vasculature and IVP while IOP was fixed at 35 mmHg and distortion was 0%. The correlation was stronger when the model was filled with expansile tamponade, as Spearman’s correlation rho was -0.771 (p<0.001) and stress levels reached a maximum of 61 Pa when the model was filled with expansile tamponade compared to Spearman’s rho of 0.570 (p<0.001) and stress levels up to 9.9 Pa when the model was filled with non-expansile tamponade. The third set of experiments in phase 1 also showed a statistically significant positive correlation between stress in the choroidal vasculature and the extent of distortion applied on the tubular structure while IOP was fixed at 35 mmHg and IVP was fixed at 120 mmHg. However, the strength of the correlation was almost the same both when the container was filled with expansile tamponade (Spearman’s rho 0.624, p<0.001) and with non-expansile tamponade (Spearman’s rho 0.629, p<0.001) (Figure 3).

When the role of increasing IOP in counteracting stress in the choroidal vasculature was tested in phase 2, the first set of experiments showed a statistically significant negative correlation between IOP and stress in the choroidal vasculature when the stress was due to increased IVP. This correlation was marginally stronger when the container was filled with expansile...
tamponade (Spearman's rho -0.670, p<0.001) compared to non-expansile tamponade (Spearman's rho -0.580, p<0.001). However, the second set of experiments in phase 2 surprisingly showed a statistically significant positive correlation between IOP and stress in the choroidal vasculature when the stress was caused by distortion. This correlation was almost the same both when the container was filled with expansile tamponade (Spearman's rho 0.419, p<0.001) and non-expansile tamponade (Spearman's rho 0.413, p<0.001) (Figure 4).

**Discussion**

Hemorrhages in highly vascular choroid can arise from ciliary arteries, arterioles, venules, and capillaries. Hypotony and high systemic blood pressure are regarded as common contributing factors in addition to glaucoma, aphakia, and advanced age. It is believed that hypotony (e.g., caused by incising the eyeball) induces a vascular pressure gradient that leaves the vascular bed unsupported. Blood pressure can rise in the unsupported vascular bed, leading to a rupture, particularly in the presence of other contributing factors like arteriolar necrosis of the short and long posterior ciliary arteries. Alternatively, increased IVP (e.g., from obstructing the outflow of the vortex veins) can also increase pressure in the long and short posterior ciliary arteries, leading to rupture. Nevertheless, pressure in the choroidal vasculature is also susceptible to direct or indirect distortion, such as when the eyeball is inadvertently deformed during surgical maneuvers. Ocular distortion can force the outer and middle ocular coats to slide over each other, as these coats are only separated by a thin layer of fluid and sheets of fine collagen fibrils. Therefore, the vasculature around the suprachoroidal space must be competent enough to withstand not only the transmural pressure gradient but also the relative motion between ocular coats to avoid suprachoroidal hemorrhage.

Several reports in the literature have described experimental rabbit eye models of expulsive CH. In all these models, high IVP was induced by obstructing the venous flow through blocking or ligating the vortex veins or by inducing proptosis using latex bands, while hypotony in these models was induced by incising the globe or removing the corneal button. In contrast to earlier studies, we used a novel in vitro model of the choroidal vasculature, this approach enabled us to precisely calculate stress levels in the choroidal vasculature and study their relation with gradual changes in IOP, IVP, and distortion levels both when the model was filled with non-expansile and expansile tamponades.

**Table 1. Initial and final values for IOP, IVP, distortion, and stress in each experiment set in phase 1 and phase 2 while the model was filled with expansile and non-expansile tamponade. Note the final stress values are the average of 10 values measured at the end of each experiment**

| Phase | Set | Aim | Tamponade | No of tests | IOP (mmHg) | IVP (mmHg) | Distortion (%) | Stress (Pa) |
|-------|-----|-----|-----------|-------------|------------|-------------|--------------|-------------|
|       |     |     |           |             | Initial    | Final       | Initial      | Final       | Initial   | Final   |
| One   | 1   | To investigate the effect of low IOP on stress in choroidal vessels | Non-expansile | 10 | 35 | 0 | 120 | 120 | 0 | 0 | 0 | 0.1 |
|       |     |     |           |             | Expansile  | 10 | 35 | 0 | 120 | 120 | 0 | 0 | 0 | 1.7 |
|       | 2   | To investigate the effect of high IVP on stress in choroidal vessels | Non-expansile | 10 | 35 | 35 | 120 | 200 | 0 | 0 | 0 | 9.9 |
|       |     |     |           |             | Expansile  | 10 | 35 | 35 | 120 | 200 | 0 | 0 | 0 | 61 |
|       | 3   | To investigate the effect of distortion on stress in choroidal vessels | Non-expansile | 10 | 35 | 35 | 120 | 120 | 0 | 12 | 0 | 23 |
|       |     |     |           |             | Expansile  | 10 | 35 | 35 | 120 | 120 | 0 | 12 | 0 | 64 |
| Two   | 1   | To investigate the role of increasing IOP in counteracting stress in choroidal vessels caused by high IVP | Non-expansile | 10 | 35 | 80 | 180 | 180 | 0 | 0 | 6 | 0.6 |
|       |     |     |           |             | Expansile  | 10 | 35 | 80 | 180 | 180 | 0 | 0 | 6 | 0.4 |
|       | 2   | To investigate the role of increasing IOP in counteracting stress in choroidal vessels caused by distortion | Non-expansile | 10 | 35 | 80 | 120 | 120 | 12 | 12 | 6 | 6.5 |
|       |     |     |           |             | Expansile  | 10 | 35 | 80 | 120 | 120 | 12 | 12 | 6 | 6 |
Our model suggested that distorting the globe plays a more important role in inducing stress in the choroidal vasculature compared to increased IVP, which in turn has a greater effect than hypotony. Based on this, traumatic CH in patients with closed globe injuries and intraoperative CH during certain surgical maneuvers like indenting and tightening sutures over an external buckle could primarily be explained by distortion of the choroidal vasculature.\textsuperscript{15,16} It also explains the limited effect of hypotony in experimental induction of CH reported in previous studies.\textsuperscript{17,18} In fact, the reasons for CH in hypotonic eyes are believed to be indirectly related to distortion of the choroidal vasculature. It has been postulated that hypotony increases the filtration rate by magnifying the transmural pressure differential, resulting in choroidal effusion which in turn stretches and distorts the long and short ciliary blood vessels, leading to their rupture and hemorrhage.\textsuperscript{6,12,13,19,20,21,22,23,24}

The current model also showed that the risk of CH due to high systemic IVP and hypotony is higher when the eye is filled with expansile tamponades. This is most likely due to the extra support for the vascular bed provided by the density of non-expansile tamponades compared to expansile tamponades.\textsuperscript{7,11} This explains why it is advisable to use non-expansile tamponades if CH is detected or suspected during surgery.\textsuperscript{2}

The model also revealed that increasing IOP to counteract high stress in the choroidal vasculature is only effective when the stress in the vasculature is generated by high IVP. High IOP levels are not effective in reducing stress in the choroidal vascular if the stress was primarily generated by distortion. This is an important finding, as increasing IOP is the most
common strategy used to counteract intraoperative CH, while efforts to minimize surgical distortions are often ignored.

**Study Limitations**

One of the shortfalls of the study was that the model was a scaled up model of the choroidal vasculature. Although this method provided more precise measurement of the changes in stress levels, the actual stress levels in the choroidal vasculature could be different from those measured in our model.

**Conclusion**

Inadvertent excessive distortion of the globe during surgical maneuvers could be the primary reason for the rarely observed intra-operative CH. Therefore, care must be exercised to avoid unnecessary distortion of ocular tissues during surgery. Non-expandile ocular tamponade provides better support for the vascular bed against CH and should be the recommended choice of tamponade in patients with existing CH. Hypotony should be avoided during surgery, particularly when the eye is filled with expansile tamponade, and maximum effort should be made to avoid distorting a hypotonic globe filled with expansile tamponade. Finally, raising IOP excessively during intraocular surgery has limited effect in preventing CH that may arise from distortion of the delicate ocular tissues.
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Ethics
Ethics Committee Approval: Ethics committee approval was not obtained because our study was conducted with an experimental model in the laboratory without including human and animal elements.

Informed Consent: Peer-review: Externally peer reviewed.

Authorship Contributions
Concept: M.D., F Ş., Design: M.D., C.A., Data Collection or Processing: F.D., Analysis or Interpretation: M.D., C.A., Literature Search: M.D., F Ş., Writing: M.D., F.D.

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