Fluid Dynamics of Tubes Used in Membrane-Tube Type Glaucoma Shunt Devices

Jong Chul Han  
Samsung Medical Center

Young Hoon Hwang  (brainh@kimeye.com)  
Kim's Eye Hospital  https://orcid.org/0000-0003-3716-6496

Byung Heon Ahn  
Kim’s Eye Hospital

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Abstract

Purpose: To investigate the outflow characteristics of silicone tubes with intraluminal stents used in membrane-tube (MT) type glaucoma shunt devices (MT-device).

Methods: The silicone tubes used in MicroMT (internal diameter of 100 µm with 7-0 nylon intraluminal stent) and Finetube MT (internal diameter of 200 µm with 5-0 nylon intraluminal stent) were connected to a syringe-pump that delivered a continuous flow of distilled water at flow rates of 2, 5, 10, and 25 µl/min. The pressures and resistances of tubes were measured at a steady flow rate with full-length, half-length, and absence of intraluminal stents.

Results: At flow rates between 2 and 25 µl/min, the mean outflow resistance of tubes ranged from 3.0 ± 1.9 to 3.8 ± 1.7 mmHg/µl/min with a full-length intraluminal stent, 1.8 ± 1.1 to 2.2 ± 1.1 mmHg/µl/min with a half-length intraluminal stent, and 0.1 ± 0 to 0.2 ± 0 mmHg/µl/min without an intraluminal stent. At a physiologic state with a flow rate of 2 µl/min and episcleral venous pressure of 6 mmHg, the mean pressures of tubes were expected to be 13.2 ± 3.0, 10.5 ± 2.4, and 6.4 ± 0.2 mmHg in MicroMT with full-length, half-length, and absence of intraluminal stents, respectively, and 12.5 ± 3.9, 9.6 ± 2.4, and 6.2 ± 0.2 mmHg in Finetube MT with full-length, half-length, and absence of intraluminal stents, respectively. Variance of the pressure decreased according to the intraluminal stent retraction (P < 0.01).

Conclusion: The tubes with intraluminal stents used in the MT-device showed safe (with a minimal risk of postoperative ocular hypotony) and effective (sufficient for intraocular pressure control) outflow characteristics.

Introduction

Glaucoma drainage devices (GDDs) have been introduced to control intraocular pressure (IOP), especially in eyes with refractory glaucoma, such as neovascular glaucoma, uveitic glaucoma, and previously failed glaucoma surgery. Theoretically, the amount of aqueous drainage through the GDD is determined based on the profiles of GDDs. Thus, GDDs may offer a standardized and predictable control of IOP. However, despite the use of temporal ligation of the tube, staged operations, and valve type GDDs, postoperative ocular hypotony due to excessive aqueous drainage still occurs.\(^1\text{-}^7\)

To overcome this limitation, we introduced two types of membrane-tube (MT) type glaucoma shunt devices (MT-device; MicroMT and Finetube MT).\(^8\text{-}^9\) MT-devices consist of thin expanded-polytetrafluoroethylene membranes and small silicone tubes with intraluminal stents that prevent postoperative ocular hypotony and provide a stepwise reduction in IOP after the surgery by retracting the stent.\(^8\text{-}^9\) During the development of the MT-device, various in vivo and in vitro experiments were performed in order to determine the proper profiles of tubes with safe (minimal risk of postoperative ocular hypotony) and effective (sufficient for IOP control) outflow characteristics.\(^8\text{-}^{15}\) In the present study,
we report the pressure and resistance of silicone tubes with intraluminal stents used in MT-devices at various steady-state flow rates.

**Methods**

**Preparation of the tubes**

The study protocol was waived by the Institutional Review Board of Kim's Eye Hospital, Seoul, Korea. Two types of silicone tubes used in MicroMT\(^8\) and Finetube MT\(^9\) were investigated; these devices are still investigational and not commercially available yet. The tube used in MicroMT has a 200 µm external diameter and 100 µm internal diameter (Silicone No. 1, ARAM Micro Tubing, Japan) with a 7-0 nylon thread intraluminal stent. The tube of Finetube MT has a 300 µm external diameter and 200 µm internal diameter (Silicone No. 2, ARAM Micro Tubing, Japan) with a 5-0 nylon thread intraluminal stent. The MT-devices were designed to induce aqueous drainage from the anterior chamber to the post-limbal (MicroMT) and post-equatorial (Finetube MT) subconjunctival space, respectively. Therefore, the tube length used for MicroMT and Finetube MT was set as 5 and 10 mm, respectively. In this experiment, a total of 60 tubes (30 tubes for MicroMT and 30 tubes for Finetube MT) were used.

**Devices for measuring pressure and resistance**

Experiments were performed based on the experimental design described in the previous studies.\(^{13,16}\) The instrument consisted of three components: (1) a perfusion pump and syringe, (2) a pressure transducer and detector, and (3) a housing unit where the glaucoma implant was submerged in distilled water (Fig. 1). The perfusion pump with a stepper motor (Model 11; Harvard Apparatus, MA, USA) was adopted. The perfusion pump was connected to a 1 mL glass syringe (Hamilton Co., Reno, NV, USA). A three-way stopcock was connected to the end of the glass syringe and calibration reservoir. A pressure transducer (PX260; Edwards Life Sciences, Irvine, USA) and detector (8SP; ADInstrument, Colorado Springs, CO, USA) were connected to a personal computer, which monitored the pressure change in units of 0.01 mmHg using Chart v5.1 software (ADInstrument). We verified the pressure gauges whenever the calibration of the pressure gauges was performed. A hole 1.5 cm from the base was made in the housing unit and a 26-gauge needle sleeve was attached to hole using silicone glue. The plastic plate, which was made using half of the plastic syringe to fix the silicone tubes, was attached beneath the hole. The silicone tubes were submerged and connected to the pump and pressure gauze through the needle sleeve in the housing unit. The zero reference line was marked beyond the level of hole (approximately 3 cm height from the base) and the pressure was measured as approximately 2.4 mmHg at the level. The height of this fluid was maintained by suction to maintain a zero reference line. This height of fluid level was selected because the level was easy to handle in our housing unit (6 cm of the height of plastic box) and the glaucoma implant could be submerged completely at the level. Resistance was calculated using Poiseuille's equation and data from the step experiments. Assuming ideal fluid flow in a noncollapsible tube, the
equation can be simplified to resistance \( R = \frac{(P_{in} - P_{out})}{\text{rate of steady flow (Q)}} \). \( P_{in} \) was measured using the pressure transducer and \( P_{out} \) was set constantly submerging the apparatus under a fluid column at a given height as described above.

**Measurement of pressure and resistance of the tubes**

In the experiments, the perfusion rate increased in a stepwise manner from 0 to 2, to 10, and to 25 µl/min. Each pressure at each flow rate was recorded (Fig. 2). Because we hypothesized the episcleral venous pressure in human eye as 6 mmHg, we corrected the baseline pressure into 6 mmHg. Then, the pressure at each flow rate was changed into corrected pressure by adjusting the baseline pressure. Flow was maintained for up to 20 min at each step so that resistance was calculated from steady-state flow and pressure conditions. Three step experiments were performed in each tube; (1) tubes with a full-length intraluminal stent, (2) after pulling the intraluminal stent by a half-length of the tube, (3) after complete removal of the stent.

**Statistical analysis**

Friedman's test with post hoc analysis was used for the comparison of pressure and resistance among the tubes with a full-length intraluminal stent, with a half-length intraluminal stent, and without the intraluminal stent. In addition to the mean pressure and resistance level, variance of pressure may provide information regarding the predictability of pressure; a lower variance may reflect a greater predictability. Therefore, to compare the variance of the pressure among the tubes with a full-length intraluminal stent, with a half-length intraluminal stent, and without an intraluminal stent, a Brown-Forsythe test was performed. All statistical analyses were performed with SPSS software version 18.0 (SPSS, Inc., Chicago, IL). A P value less than 0.05 was considered statistically significant.

**Results**

In the tubes of MicroMT, mean corrected pressures with a full-length intraluminal stent were 13.2 ± 3.0, 24.6 ± 8.1, 43.8 ± 16.5, and 98.1 ± 40.8 mmHg at flow rates of 2, 5, 10, and 25 µl/min, respectively. With a half-length intraluminal stent, mean corrected pressures were 10.5 ± 2.4, 16.7 ± 5.1, 26.4 ± 8.6, and 54.7 ± 21.2 mmHg at flow rates of 2, 5, 10, and 25 µl/min, respectively. Without the intraluminal stent, mean corrected pressures were 6.4 ± 0.2, 7.0 ± 0.2, 8.0 ± 0.4, and 10.9 ± 0.9 mmHg at flow rates of 2, 5, 10, and 25 µl/min, respectively. Mean outflow resistance ranged from 3.6 ± 1.5 to 3.8 ± 1.7 mmHg/µl/min with a full-length intraluminal stent, 2.0 ± 0.9 to 2.2 ± 1.1 mmHg/µl/min with a half-length intraluminal stent, and 0.2 ± 0 mmHg/µl/min without the intraluminal stent (P < 0.001, Table 1).
In the tubes of Finetube MT, mean corrected pressures with a full-length intraluminal stent were $12.5 \pm 3.9$, $21.8 \pm 9.6$, $37.6 \pm 19.1$, and $82.0 \pm 46.5$ mmHg at flow rates of $2$, $5$, $10$, and $25 \mu l/min$, respectively. With a half-length intraluminal stent, mean corrected pressures were $9.6 \pm 2.4$, $14.9 \pm 5.9$, $23.9 \pm 11.5$, and $49.9 \pm 27.5$ mmHg at flow rates of $2$, $5$, $10$, and $25 \mu l/min$, respectively. Without the intraluminal stent, mean corrected pressures were $6.2 \pm 0.2$, $6.4 \pm 0.2$, $6.8 \pm 0.2$, and $7.9 \pm 0.3$ mmHg at flow rates of $2$, $5$, $10$, and $25 \mu l/min$, respectively. Mean outflow resistance ranged from $3.0 \pm 1.9$ to $3.2 \pm 1.9$ mmHg/µl/min with a full-length intraluminal stent, $1.8 \pm 1.2$ mmHg/µl/min with a half-length intraluminal stent, and $0.1 \pm 0$ mmHg/µl/min without intraluminal stent ($P < 0.001$, Table 2).

Variances of pressure in the tubes of MicroMT and Finetube MT are presented in Figure 3. Variances of the pressure decreased based on the intraluminal stent retraction; variance was highest with a full-length intraluminal stent and lowest without an intraluminal stent ($P < 0.001$ at all flow rates).

**Discussion**

The present study demonstrated that silicone tubes with intraluminal stents used in MT-devices induced consistent and predictable pressures and resistances at various flow rates. In addition, when the intraluminal stent was partially and completely removed, the pressure and resistance gradually decreased. Therefore, GDDs using these tubes may contribute to safe and effective control of IOP with stepwise reduction.

Ocular hypotony is an important complication of GDD implantation, especially at the early postoperative period. To prevent this complication, various methods have been introduced.\(^1\text{-7}\) For instance, tube ligation with or without intraluminal or extraluminal stents during the surgery has been introduced.\(^1\text{-4,6,7}\) However, tube ligation may not produce predictable pressure; when the ligation is too tight or too loose, unexpected high or low pressures can occur, respectively. Other procedures, such as fenestrations or slit formations are performed to prevent postoperative peaks in IOP.\(^4\) Rietveld et al.\(^17\) showed that adjustable pressure regulation by focal tube constriction similar to tube ligation was disappointing because the maintenance of steady pressure levels at a given flow rate was difficult. They suggest that tube ligature to reliably regulate pressure may only be trustworthy with highly sophisticated microarchitecture under well-controlled conditions.

Given that an intraluminal stent can induce the entire area of the tube to occlude, it may provide more predictable pressure control compared to that of focal tube constriction. However, it has not been widely used. This may be due to the silicone tubes of conventional GDDs, such as the Ahmed Glaucoma Valve (New World Medical, Rancho Cucamonga, CA, USA) and the Baerveldt Glaucoma Implant (Abbott Laboratories Inc., Abbott Park, IL, USA) cannot provide the proper pressure to prevent ocular hypotony with the intraluminal stent. The inner diameter of the silicone tubes of the conventional GDDs are approximately 300 µm. Therefore, a 3-0 nylon thread with a diameter between 200 and 250 µm can be used as an intraluminal stent. However, results from a previous study show that the conventional silicone tube with a 3-0 polypropylene intraluminal stent would not successfully prevent ocular hypotony.\(^18\)
Sheybani et al.\textsuperscript{19} also report that a conventional tube with intraluminal 4-0 and 5-0 suture threads only provide pressures of 1.16 and 0.3 mmHg, respectively, at the flow rate of 2.5 μl/min. Therefore, intraluminal stenting of conventional tubes by using 3-0, 4-0, and 5-0 suture materials may not prevent ocular hypotony. The 2-0 nylon thread with a diameter of 300–350 μm can completely obstruct the lumen of the tube or may not even be able to be inserted into the lumen. For this reason, pressure control with an intraluminal stent in GDDs have not been widely used for the prevention of postoperative ocular hypotony. Therefore, we hypothesized that a smaller tube with intraluminal stent may be a good alternative to conventional tubes.

The results from the present study demonstrated that at a physiologic flow rate of 2 μl/min with an episcleral venous pressure of 6 mmHg, the mean pressure formed by the tubes of MicroMT were 13.2 and 10.5 mmHg with full-length and half-length intraluminal stents, respectively. By using the tubes of Finetube MT, the mean pressures were 12.5 and 9.6 mmHg with full-length and half-length intraluminal stents, respectively. These pressure levels may be appropriate for the control of IOP with a minimal risk of ocular hypotony. When the flow rate increased, the pressure increased accordingly. However, the resistance remained consistent irrespective of the flow rate. In addition, when the intraluminal stents were partially and completely removed, variance of pressure decreased. These findings suggest that the tubes of MT-devices may confer a consistent and predictable IOP level. To validate these \textit{in vitro} experimental results, we analyzed the clinical data of MT-devices and found that 1 year after the surgery, mean IOP decreased from a preoperative value of 23 to 15 mmHg after MicroMT implantation and 33 to 17 mmHg after Finetube MT implantation without ocular hypotony.\textsuperscript{8,9}

An additional advantage to using an intraluminal stent is that it can allow stepwise IOP control through retraction of the stent. When the tube is focally constricted by ligation, two-staged pressure control is available by postoperative removal of the ligation. However, after removal of the ligation, IOP can drop abruptly, causing ocular hypotony. In contrast, by using small silicone tubes with intraluminal stents, sudden IOP decreases can be prevented; in the present study, stent retraction induced a stepwise and gradual decrease in the mean and variance of pressure. After the implantation of the MT-device, the intraluminal stent can be retracted if the pressure needs to be lowered. Our clinical results show that retracting the intraluminal stent half the length of the tube after the operation reduced the IOP by an additional 3–5 mmHg and complete removal of the stent 4 weeks after the operation induced an additional 40% reduction in IOP without ocular hypotony.\textsuperscript{8,9}

Tubes of MT-devices have smaller diameters than tubes of conventional GDDs, lowering the chance of conjunctival erosion or tube exposure. Based on the clinical data, no eye showed conjunctival erosion or tube exposure after the implantation of an MT-device.\textsuperscript{8,9} The use of a smaller tube may have a higher possibility of tube occlusion by blood clots, inflammatory materials, or silicone oil droplets. Our clinical results showed that there was no tube occlusion after implantation of an MT-device.\textsuperscript{8,9} Nevertheless, when using small tubes, the possibility of tube occlusion should be considered.
In conclusion, the tubes of an MT-device provided pressure and resistance sufficient for control of IOP with a minimal risk of ocular hypotony. Furthermore, it could provide stepwise reduction of IOP by retraction of the intraluminal stent. Therefore, these tubes may be a useful option for safe and effective control of IOP.

**Declarations**

**List of abbreviations**

GDD: glaucoma drainage device, IOP: intraocular pressure, MT: membrane-tube

**Ethics approval and consent to participate**

Need for approval was waived by the Institutional Review Board of Kim's Eye Hospital, Korea

**Consent for publication**

Not applicable

**Availability of data and material**

The datasets used and analysed during the current study are available from the corresponding author on reasonable request

**Competing interests**

The authors declare that they have no competing interests

**Funding**

Not applicable

**Authors' contributions**
JCH, YHH, and BHA made substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data. JCH, YHH, and BHA have been involved in drafting the manuscript and revising it critically for important intellectual content and given final approval of the version to be published.

Author details

1Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University, School of Medicine, Seoul, Republic of Korea

2Department of Ophthalmology, Konyang University, Kim's Eye Hospital, Myung-Gok Eye Research Institute, Seoul, Republic of Korea

References

1. Barton K, Feuer WJ, Budenz DL, et al. Three-year treatment outcomes in the Ahmed Baerveldt comparison study. Ophthalmology 2014;121:1547-57.

2. Bailey AK, Sarkisian SR Jr. Complications of tube implants and their management. Curr Opin Ophthalmol 2014;25:148-53.

3. Trible JR, Brown DB. Occlusive ligature and standardized fenestration of a Baerveldt tube with and without antimetabolites for early postoperative intraocular pressure control. Ophthalmology 1998;105:2243-50.

4. Sherwood MB, Smith MF. Prevention of early hypotony associated with Molteno implants by a new occluding stent technique. Ophthalmology 1993;100:85-90.

5. Tong L, Frazao K, LaBree L, et al. Intraocular pressure control and complications with two-stage insertion of the Baerveldt implant. Ophthalmology 2003;110:353-8.

6. Kee C. Prevention of early postoperative hypotony by partial ligation of silicone tube in Ahmed glaucoma valve implantation. J Glaucoma 2001;10:466-9.

7. Lee JJ, Park KH, Kim DM, Kim TW. Clinical outcomes of Ahmed glaucoma valve implantation using tube ligation and removable external stents. Korean J Ophthalmol 2009;23:86-92.

8. Ahn BH, Hwang YH, Han JC. Novel membrane-tube type glaucoma shunt device for glaucoma surgery. Clin Exp Ophthalmol 2016;44:776-82.

9. Han JC, Hwang YH, Ahn BH. Membrane-tube-type glaucoma shunt device for refractory glaucoma surgery. Graefes Arch Clin Exp Ophthalmol 2017;255:163-9.

10. Kim C, Kim Y, Choi S, et al. Clinical experience of e-PTFE membrane implant surgery for refractory glaucoma. Br J Ophthalmol 2003;87:63-70.

11. Choi YJ, Kim CS, Ahn BH. A comparison of the clinical effect between e-PTFE membrane-tube implant and Ahmed glaucoma valve implant for the treatment of refractory glaucoma. Korean J
12. Bae HB, Kim CS, Ahn BH. A membranous drainage implant in glaucoma filtering surgery: animal trial. Korean J Ophthalmol 1988;2:49-56.

13. Sohn SW, Noh MD, Lee JH, et al. Performance of and pressure elevation formed by small-diameter microtubes used in constant-flow sets. Korean J Ophthalmol 2016;30:225-33.

14. Kim DW, Hwang YH, Ahn BH, Lee EK, Kim CS. Safety and efficacy of a membrane-tube-type glaucoma shunt device: an animal trial. Curr Eye Res 2017;31:1-7.

15. Kim MK, Hwang YH, Ahn BH. Implantation of a modified Baerveldt glaucoma implant with a smaller tube and intraluminal stent. Korean J Ophthalmol 2017;31:90-91.

16. Francis BA, Cortes A, Chen J, et al. Characteristics of glaucoma drainage implants during dynamic and steady-state flow conditions. Ophthalmology 1998;105:1708-14.

17. Rietveld E, van der Veen AJ. Postoperative pressure regulation in glaucoma shunt surgery: focal tube constriction is not the answer. J Glaucoma 2004;13:216-20.

18. Hoare Nairne JE, Sherwood D, Jacob JS, Rich WJ. Single stage insertion of the Molteno tube for glaucoma and modifications to reduce postoperative hypotony. Br J Ophthalmol 1988;72:846-51.

19. Sheybani A, Reitsamer H, Ahmed II. Fluid dynamics of a novel micro-fistula implant for the surgical treatment of glaucoma. Invest Ophthalmol Vis Sci 2015;56:4789-95.

Figures
Figure 1

Schematic diagram of the perfusion apparatus used in the present experiment. The instrument consisted of a perfusion pump and syringe, a pressure transducer and detector, and a housing unit where the glaucoma implant was submerged in fluid. The height of the fluid was fixed at 3 cm (approximately 2.4 mmHg) from the plastic plate. The three-way stopcock was used to remove the fluid to maintain the baseline pressure during the experiments.
Step function tests that were performed to measure the pressure according to the each flow rate (2, 5, 10, and 25 µl/min). Flow was maintained for up to 20 min at each step so that resistance was calculated from steady-state flow and pressure conditions.
Figure 3

Variances of the pressure in the tubes of membrane-tube (MT) type glaucoma shunt devices at each flow rate (2, 5, 10, and 25 μl/min). (A) MicroMT, (B), Finetube MT. Variances of the pressure decreased according to the intraluminal stent retraction (P < 0.001 at all flow rates, Brown-Forsythe test).