

IOP-lowering effects for the application of human umbilical vein in non-penetrating deep sclerostomy in rabbits

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Abstract

• **AIM:** To estimate the effects of human umbilical vein (HUV) implanted under the sclera of glaucoma model on intraocular pressure (IOP) lowering and to investigate its related mechanisms

• **METHODS:** A total of 20 human umbilical veins (HUV) were collected from healthy fetus umbilical core. After the establishment of glaucoma model in rabbits, human freeze-dried umbilical vein was implanted under the sclera during NPDS, while for control group, sclerostomy was performed without implant. The formation of the filtration bleb and IOP were detected every 24 hours before surgery and on day 3, 7, 10 and 14 after surgery. Handheld pen-type Tono-pen II tonometer was used to measure IOP after topical anesthesia treatment. Each measurement has three duplicates. The incision recovery, filtration, conjunctiva congestion and anterior chamber inflammation were observed everyday after surgery.

• **RESULTS:** IOP was decreased dramatically with less inflammation than traditional sclerostomies with the application of HUV. The significant differences of IOP between the NPDS with and without HUV implant groups were shown up from 10 days after surgery. The average IOP in NPDS without HUV implant was 14.25mmHg, while for NPDS with HUV implant group, it was 12.30mmHg. This structure of filtration bleb, which allowed the aqueous humor to leave the eye, was formed for any type of surgery. However, 1-2 weeks later, filtration bleb was still existed in the group of sclerostomy with HUV implant and more stable than that of the surgery without HUV implant. Histological observations were performed on day 3, 7 and 14 after surgery. For the eyes under sclerostomy with HUV implant, HUV lumina was shown up on 3 days after surgery with few fibroblast cells

near the sclera. On 7 days after surgery, HUV lumina was stably maintained but with obvious fibroblast cells and inflammatory cell. On 14 days after surgery, HUV lumina was still clearly observed but with scarring formation, which suggests that the IOP lowering effects might result from an effective drainage structure formation.

• **CONCLUSION:** HUV might be an alternative material to make the drainage pathway for non-penetrating deep sclerostomy.

• **KEYWORDS:** IOP-lowering; non-penetrating deep sclerostomy; human umbilical vein

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INTRODUCTION

Due to the increasing of intraocular pressure (IOP), glaucoma can cause the progressive and irreversible damage on optic nerve, which is one of the main causes for blindness^[1,2]. Non-penetrating deep sclerostomy (NPDS) is the most effective means for lowering IOP by providing a new route for fluid to exit the eye. This new pathway is through the sclera of the eye into sub-conjunctival tissue, where a fluid filled bleb typically forms under the conjunctiva^[3]. Several biological materials are used to support the new channel structure, such as collagen transplant, sodium hyaluronate, amnion, SK Gel and so on^[4-8]. In our previous study, we found that umbilical vein can effectively inhibit the scar effects in both animal and clinical trials, which indicated that umbilical vein might be used as a alternative drain channel for aqueous humor in NPDS^[9]. In order to explore its clinical application on eyes, in this study, we transplanted the umbilical vein under the sclera to investigate the correspondent effects including inflammation, IOP and structure alterations. In this study, we will provide some valuable information to estimate the potential clinical application of umbilical vein in NPDS.

Surgery	IOP		Filtration bleb	
	HUV implant		With	Without
	With	Without		
1 day before	19.97±2.10	20.54±2.23		
3 days after	11.56±1.29	11.68±1.21	24/48	23/48
7 days after	11.77±1.40	12.09±1.24	16/32	14/32
10 days after	11.94±1.46	12.71±1.32 ^a	11/16	7/16
14 days after	12.30±1.64	14.25±1.63 ^b	6/16	3/16

^a*P*< 0.05, ^b*P*< 0.01 vs with HUV implant

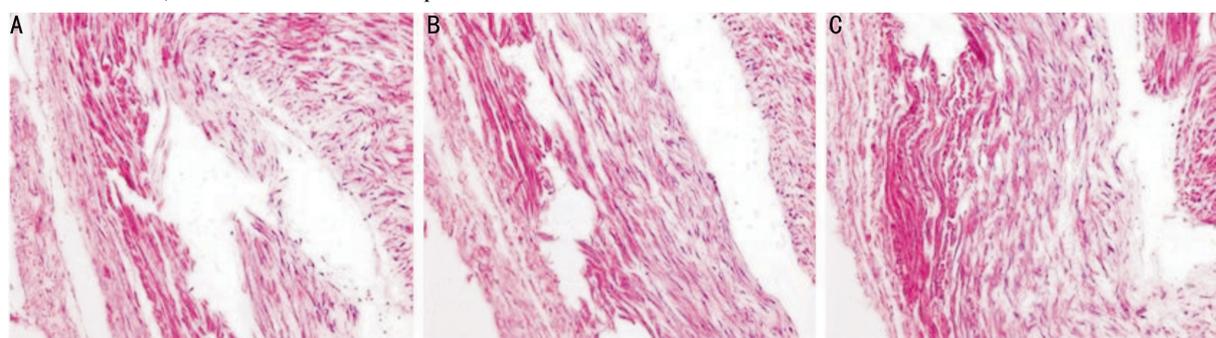


Figure 1 Tissue histology after surgery (magnifications×100) A: 3 days; B: 7 days; C: 14 days

MATERIALS AND METHODS

Materials A total of 20 human umbilical veins (HUV) were collected from healthy fetus umbilical core. HUV were treated with freeze-drying for 6 hours and ⁶⁰Co200cGy irradiation for 30 seconds.

Methods After the establishment of glaucoma model in rabbits, human freeze-dried umbilical vein was implanted under the sclera during NPDS, while for control group, sclerostomy was performed without implant. The formation of the filtration bleb and IOP were detected every 24 hours before surgery and on day 3, 7, 10 and 14 after surgery. Handheld pen-type Tono-pen II tonometer was used to measure IOP after topical anesthesia treatment. Each measurement has three duplicates. The incision recovery, filtration, conjunctiva congestion and anterior chamber inflammation were observed everyday after surgery. Histological observations were performed on day 3, 7 and 14 after surgery. The tissue of surgery location was stained by HE and observed underlympus BX51 microphotoscope to estimate fiber proliferation and scarring formation.

Statistical Analysis Statistical analysis was performed using SPSS 12.0. *P*<0.05 was considered statistically significant.

RESULTS

Intraocular Pressure The significant differences of IOP between the NPDS with and without HUV implant groups were found from 10 days after surgery. The average IOP in NPDS without HUV implant was 14.25mmHg, while for NPDS with HUV implant group, it was 12.30mmHg (Table 1).

Residual Filtration Bleb After the surgery, the aqueous humor began to flow through the sclerostomy hole and forms a small blister-like structure on the upper surface of

the eye. This structure was known as a filtration bleb, which allowed the aqueous humor to leave the eye in a controlled fashion. On day 3, the dispersed filtration bleb was formed for any type of surgery. However, 1-2 weeks later, filtration bleb was still existed in the group of sclerostomy with HUV implant and more stable than that of the surgery without HUV implant (Table 1).

Histological Assays To better understand the mechanism of IOP lowering effects, the tissue of surgery location was cut off to perform the histological assays with HE. For the eyes under sclerostomy with HUV implant, HUV lumina was shown up on 3 days after surgery with few fibroblast cells near the sclera (Figure 1A). On 7 days after surgery, HUV lumina was stably maintained but with obvious fibroblast cells and inflammatory cell (Figure 1B). On 14 days after surgery, HUV lumina was still clearly observed but with scarring formation (Figure 1C).

DISCUSSION

NPFS is a widely used filtration surgery for glaucoma with fewer complications than traditional sclerostomies [10,11]. The success of reduction in IOP by this surgery is associated with the assence of a filtering bled and depends on the duration of follow-up involved [12]. In order to obtain the long-term IOP regulation, implants were used as "aqueous shunts" or "drainage devices" to create a bypassing of the trabecular meshwork for increasing aqueous humor outflow from eye and decreasing IOP. Two types of implants were developed for clincial applications. One is to allow the aqueous fluid passes through it and the other one is to allow the flow of fluid along the surface. The current used implants include collagen [13-15], polymethylmethacrylate

implant^[16], SKGEL^[17], autologous scleral implant^[18-19], reticulated hyaluronic acid implant^[20,21] and Ex-PRESS X-200 implant^[22], The aqueous fluid out from eye by the implant's drainage will be reabsorbed by the capillaries and lymphatic system. The success of implants depends on the stable drainage formation. The main factors that cause the failure of implants include the closure of the opening of the tube, the excessive scarring around the external drainage. The late postoperative complications include iris prolapse^[23] and corneal injury, which can result from mechanical contact between the tube and the tissues of the eye. An ideal material should be smooth, effectively decrease IOP, induce less inflammation and scarring or even be absorbed by the body^[24]. In this study, we investigated the availability of implantation of HUV under sclera. The results showed that HUV effectively decreased IOP with an stable drainage pathway structure formation without corneal injury and caused less inflammation than traditional sclerostomies, which indicated that umbilical vein might be used as an alternative drain channel for aqueous humor in NPTS. Further long-term comparative clinical study is needed to evaluate its application prospect

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