

Patching retinal breaks with Seprafilm[®] in experimental rhegmatogenous retinal detachment of rabbit eyes

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Abstract

Purpose To examine the short-term effect of Seprafilm[®] for patching retinal breaks in experimental rhegmatogenous retinal detachment of rabbit eyes.

Methods Experimental retinal detachment with a break was made and repaired by fluid–gas exchange during vitreous surgery in 10 rabbit eyes. In seven eyes, Seprafilm[®] was applied to cover iatrogenic retinal breaks entirely (study group) and in other three eyes operations were finished without Seprafilm[®] application (control group). Funduscopy examination was carried out in both groups and in study group optical coherence tomography (OCT) was performed to observe Seprafilm[®] on the retinal break. Eyes of study group were enucleated on 7th and 14th postoperative day for histological evaluation.

Results The funduscopy examination showed that the retina was reattached in all eyes of study group. Meanwhile all three eyes of control group resulted in proliferative vitreoretinopathy. OCT showed that Seprafilm[®] adhered to the retina tightly. Funduscopy examination and OCT showed Seprafilm[®] dissolved within 14 days. Histological examination revealed that Seprafilm[®] adhered tightly to the retina and there was no inflammatory change at the Seprafilm[®] application sites.

Conclusions In our small number of this study, Seprafilm[®] was found to be beneficial to patch small and posteriorly located retinal breaks in vitreous surgery for rhegmatogenous retinal detachment.

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Introduction

In vitreous surgery for rhegmatogenous retinal detachment, thermal coagulation such as photocoagulation or cryopexy has been performed to increase adhesion between the retina and choroid, and intraocular tamponade with gas or silicone oil is necessary to prevent vitreous fluid from flowing into subretinal space through retinal breaks. Major failures in vitreous surgery for rhegmatogenous retinal detachment frequently result from inability to keep retinal breaks closed and proliferative vitreoretinopathy (PVR) caused by migration of retinal pigment epithelium (RPE) cells through retinal breaks. Patching retinal breaks appears to be a logical approach to prevent vitreous fluid from flowing through retinal breaks into the subretinal space and to prevent the dispersion of RPE cells into the vitreous cavity.¹ Therefore some intraocular adhesive glue such as cyanoacrylate, fibrin glue, or others, have been utilized to patch retinal breaks in experimental retinal detachment models or in clinical cases.^{2–13} However, each glue has disadvantages and is not ideal to close retinal breaks.^{2–13} Sueda *et al*¹⁴ previously demonstrated that Seprafilm[®] adhered to the retina *in vitro* and had no toxicity *in vivo* study and the possibility that Seprafilm[®] could be utilized in the treatment of rhegmatogenous retinal detachment. We evaluated the short-term efficacy of Seprafilm[®] for patching retinal breaks in vitreous surgery for experimental rhegmatogenous retinal detachment in rabbit eyes.

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Materials and methods

Ten male pigmented rabbits (Dutch, postnatal 10 weeks, weighing from 3.0 to 4.5 kg) were used in our study. We certify that all applicable institutional and governmental regulations concerning the ethical use of animals were followed during this research. All procedures were carried out in right eyes with sterile techniques. The animals were anesthetized with intramuscular injection of 1.0 ml of ketamine hydrochloride (10 mg/ml) and 1.0 ml of xylazine (10 mg/ml). Pupils were dilated with topical 0.5% phenylephrine hydrochloride, 0.5% tropicamide, and 1% atropine. Each rabbit underwent the following procedures. A conjunctival peritomy for 180° (from 0800 to 1400 hours) was carried out at corneoscleral limbus. After lens removal (phacoemulsification technique) from approximately 3 mm sclerocorneal incision, the wound was sutured with 10-0 nylon. An infusion port was made 1 mm posterior to the sclerocorneal limbus in the inferotemporal quadrant with a vitreoretinal knife. A 20-gauge infusion cannula delivering balanced salt solution (BSS®) was secured with a preplaced 8-0 Vicryl® mattress suture. Similar ports were created in superotemporal and superonasal quadrants. The lens capsule was removed with a vitreous cutter. Core vitrectomy was performed under three-port technique with a vitreous cutter and an illumination. The vitreous was detached from posterior retina by aspirating cortical vitreous visualized with triamcinolone acetonide. After removal of posterior vitreous as much as possible, a retinal break, approximately 1/3 of disc diameter (DD) in size, was made 2 DD inferiorly from the optic disc with an extrusion needle. An infusion stream of BSS® was directed under the retinal break and a localized retinal detachment, which was approximately 2 DD in size, was made. Fluid–air exchange with internal drainage of subretinal fluid through the original break was performed. After fluid–air exchange procedure, a sheet of Seprafilm®, which was approximately 2 × 4 mm in size, was delivered to cover the breaks entirely in seven eyes (study group). The same procedures without Seprafilm® application were carried out in three eyes (control group). All scleral ports were closed with 8-0 Vicryl® suture. As the globes were apt to be hypotonic after removal of an infusion cannula, intraocular pressure was regulated by injecting air into the anterior chamber. Conjunctival wounds were closed with 8-0 Vicryl® suture and antibiotics ointment was applied. Operation was finished, leaving eyes filled with air in both groups. Indirect ophthalmoscopy and slit-lamp examinations were performed on 1st, 3rd, 7th, and 14th postoperative day. Optical coherence tomography (OCT) was used to evaluate the adhesion of Seprafilm® on the retinal breaks in study group on 7th and 14th postoperative day. Four

rabbits in study group were killed with an overdose of pentobarbital and the globes were enucleated for histological evaluation on 7th postoperative day and the other three rabbits were also killed and the globes were enucleated on 14th postoperative day. Enucleated globes were fixed in 3% glutaraldehyde in 0.1 M cacodylate buffer for 1 day. Then the globes were bisected and the sections of tissues were stained with haematoxylin and eosin and the photographs were taken under the light microscope to evaluate local reactions of the retina.

Results

In all eyes of study group, the retina was reattached when observed through the air bubbles on 3rd postoperative day. On 7th postoperative day, the air bubbles were replaced with aqueous. The fundus was hardly seen but Seprafilm® attaching to the retina was observed. Seprafilm® dissolved within 14 days postoperatively (Figure 1a). OCT showed that Seprafilm® adhered to the retina tightly and the edge of the break was indistinct on 7th postoperative day (Figure 1b). The retina was reattached without any coagulation around retinal breaks in study group on 14th postoperative day. Atrophic change was observed at the site of retinal breaks, where the site was touched with an extrusion needle during fluid–air exchange procedure. All eyes of control group showed retinal redetachment when observed through air bubbles on 3rd postoperative day. Total retinal detachment was observed on 7th postoperative day and resulted in PVR on 14th postoperative day. Histological examination revealed that Seprafilm® adhered to the retina tightly around the break on 7th postoperative day and there is no invasion of inflammatory cells in the retinal layers under Seprafilm® around retinal breaks (Figure 1c). On 14th day, Seprafilm® had dissolved and the structure of the retina was normal.

Conclusion

In vitreous surgery of retinal detachment, gas or silicone oil tamponade requires maintaining postoperative prone position or face-down position, which is a major discomfort for patients, and inferior breaks are often difficult to be closed because of gas absorption.

These problems of vitreous surgery for retinal detachment have led many surgeons to attempt to patch retinal breaks with tissue adhesive to prevent fluid from flowing through retinal breaks into subretinal space. Some intraocular glue have been tried to be utilized to patch retinal breaks in the treatment of retinal detachment for many years.^{2–13} Methyl-2-cyanoacrylate monomer was examined with a large number of

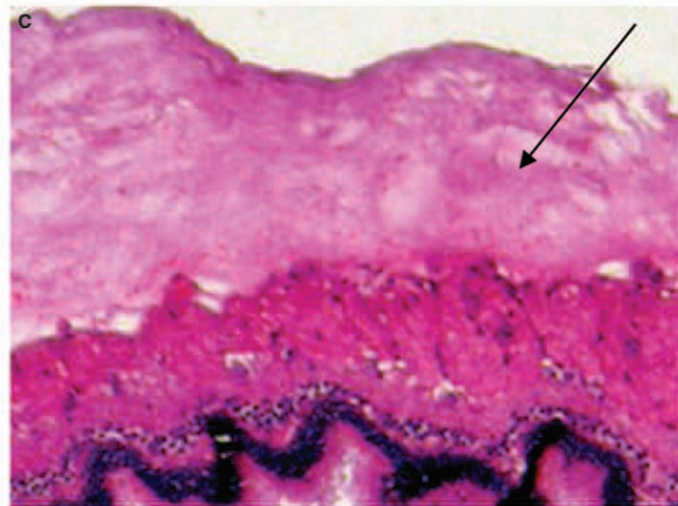
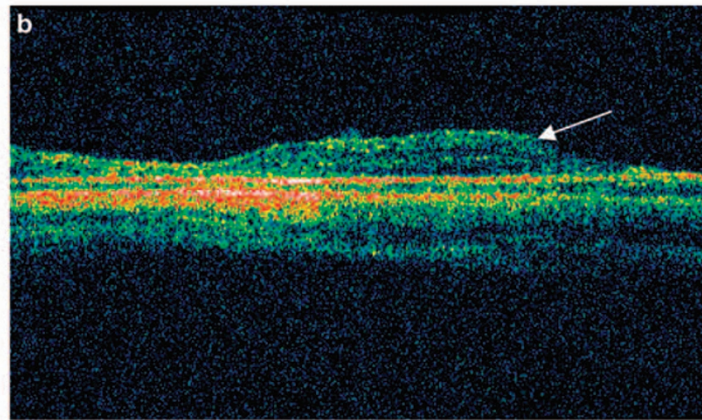
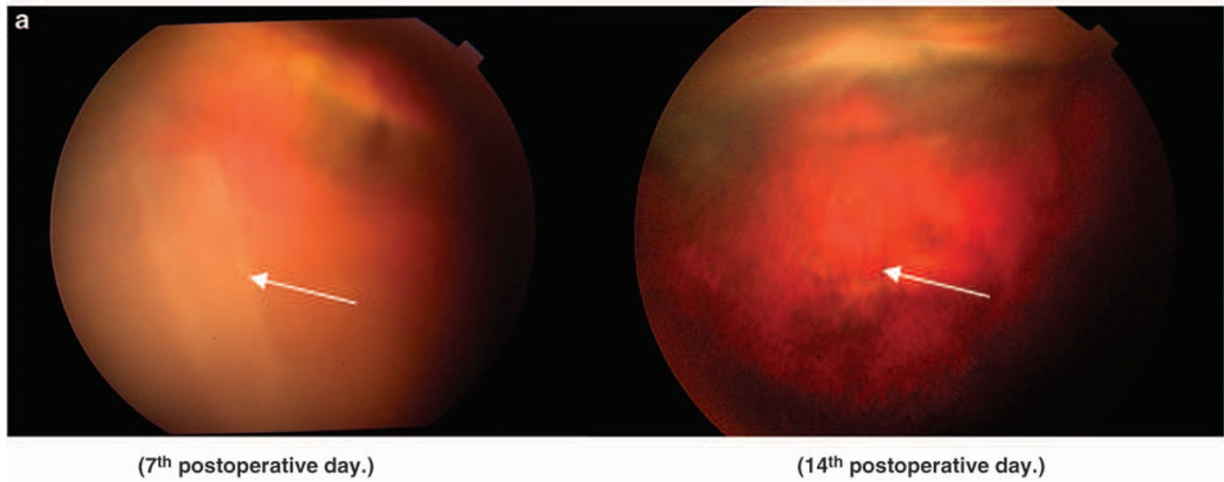


Figure 1 (a) Funduscopy examination (study group). Seprafilm[®] was observed (→) on the retina with funduscopy on seventh postoperative day. An original retinal break was covered with Seprafilm[®]. Seprafilm[®] resolved on 14th postoperative day. Retina was reattached. The retinal break (→) was indistinct. (b) OCT finding on seventh postoperative day. Membranous object (Seprafilm[®]) was observed (→) on the retina and the surface was smooth. The edge of the break was indistinct. (c) Histologic examination of Seprafilm[®] on the retina. Seprafilm[®] (→) adhered to the retina tightly and there is no invasion of inflammatory cells in the retinal layers under the Seprafilm[®].

experimental and clinical studies.^{2–8} The advantages of cyanoacrylate are to patch retinal breaks and to remain on the breaks permanently. However, its delivery is difficult because of rapid polymerization on contact with fluid and this substance is significantly cytotoxic and reactive to the retina.^{5–7} Fibrin glue,⁹ which was made from bovine blood or human autologous serum, is one of adhesive glue that has been utilized to patch retinal breaks. It is non-toxic and non-inflammatory but major disadvantage of fibrin glue is weak adhesive effect lasting only 4–6 days and retinal redetachment easily occurs. Other intraocular adhesive glue to patch retinal breaks has been evaluated,^{10–13} but some are toxic or reactive to the retina, some are lack of adequate adhesion, and some are difficult to deliver. No ideal adhesive glue has been detected as a sealant. Sueda *et al*¹⁴ previously described that Seprafilm[®] adhered to the retina in bovine eye cup and was non-toxic in rabbit eyes *in vivo*. Seprafilm[®] (Genzyme Corporation, Cambridge, MA, USA) is a bioresorbable translucent membrane composed of sodium hyaluronic acid and carboxymethylcellulose. Seprafilm[®] is non-toxic, non-immunogenic, and biocompatible and frequently used during abdominal or pelvic surgery¹⁵ to reduce postoperative adhesion. This membrane strongly adheres to moist surfaces of tissues.^{15,16}

In our small series of seven eyes in animal models, Seprafilm[®] was found to be beneficial to patch retinal breaks in a short term. Histological results revealed that Seprafilm[®] was non-toxic and non-inflammatory and had strong adhesion to the retina in early phase (7th postoperative day). Seprafilm[®] remained and adhered to the retina for at least 1 week and resolved within 2 weeks after application.

We encountered some technical difficulties associated with Seprafilm[®] delivery in vitreous surgery. Seprafilm[®] needed to be delivered in dry condition and only a small piece of Seprafilm[®] could be applied into the vitreous cavities. It means that Seprafilm[®] application is difficult to patch peripheral and large breaks and it is only suitable for a small and posteriorly located retinal breaks. In a small series of seven eyes in an animal model with a short-term follow-up, Seprafilm[®] was found to be beneficial to patch retinal breaks. Further studies with more cases should be needed to evaluate the safety and long-term effect of Seprafilm[®].

References

- 1 Gilbert CE, Grierson I, McLeod D. Retinal patching: a new approach to the management of selected retinal breaks. *Eye* 1989; **3**: 19–26.
- 2 McCuen II BW, Hida T, Sheta SM, Isbey III EK, Hahn DK, Hickingbotham D. Experimental transvitreal cyanoacrylate retinopexy. *Am J Ophthalmol* 1986; **102**: 199–207.
- 3 Hida T, Sheta SM, Proia AD, McCuen II BW. Retinal toxicity of cyanoacrylate tissue adhesive in the rabbit. *Retina* 1988; **8**: 148–153.
- 4 McCuen II BW, Hida T, Sheta SM. Transvitreal cyanoacrylate retinopexy in the management of complicated retinal detachment. *Am J Ophthalmol* 1987; **104**: 127–132.
- 5 Hartnett EM, Hirose T. Cyanoacrylate glue in the repair of retinal detachment associated with posterior retinal breaks in infants and children. *Retina* 1998; **18**: 125–129.
- 6 Hotta K, Hiraoka A, Hida T. The management of retinal detachments associated with choroidal colobomas by vitrectomy with cyanoacrylate retinopexy. *Jpn J Ophthalmol* 1998; **42**: 323–326.
- 7 Sheta SM, Hida T, McCuen II BW. Cyanoacrylate tissue adhesive in the management of recurrent retinal detachment caused by macular hole. *Am J Ophthalmol* 1990; **109**: 28–32.
- 8 Faulborn J, Witschel H. Intraocular application of tissue adhesive (Histoacryl) in retinal detachment surgery. *Graefes Arch Klin Exp Ophthalmol* 1978; **207**: 15–20.
- 9 Nasaduke I, Peyman GA. The use of autologous rabbit fibrin sealant to plug retinal holes in experimental detachments. *Ann Ophthalmol* 1986; **18**: 324–327.
- 10 Coleman DJ, Lucas BC, Fleischman JA, Dennis Jr PH, Chang S, Iwamoto T *et al*. A biologic tissue adhesive for vitreoretinal surgery. *Retina* 1988; **8**: 250–256.
- 11 Liggett PE, Cano M, Robin JB, Green RL, Lean JS. Intraocular biocompatibility of mussel adhesive protein. *Retina* 1990; **10**: 144–147.
- 12 Smiddy WE, Glaser BM, Green WR, Connor TB, Roberts AB, Lucas R *et al*. Transforming growth factor beta. A biologic chorioretinal glue. *Arch Ophthalmol* 1989; **107**: 577–580.
- 13 Sueda J, Fukuchi T, Usumoto N, Okuno T, Arai M, Hirose T. Intraocular use of hydrogel tissue adhesive in rabbit eyes. *Jpn J Ophthalmol* 2007; **51**: 89–95.
- 14 Sueda J, Sakuma T, Nakamura H, Usumoto N, Okuno T, Arai M *et al*. *In vivo* and *in vitro* feasibility studies of intraocular Seprafilm to close retinal breaks in bovine and rabbit eyes. *Invest Ophthalmol Vis Sci* 2006; **47**: 1142–1148.
- 15 Peck LS, Quigg JM, Fossum GT, Goldberg EP. Evaluation of carboxymethylcellulose and hyaluronic acid solutions for adhesiolysis. *J Invest Surg* 1995; **8**: 337–348.
- 16 Burns JW, Colt MJ, Burgess LS, Skinner KC. Preclinical evaluation of Seprafilm[™] bioresorbable membrane. *Eur J Surg* 1997; **577**(Suppl): 40–48.