Yonsei Medical Journal
Vol. 32, No. 1, 1991

Neurosurgical Application of Fibrin Adhesive

Kyu-Chang Lee, Sang-Keun Park and Kyu-Sung Lee

We have tried fibrin adhesive, which mimics the end stage of plasmatic coagulation, in 26 patients with various neurosurgical problems such as: repair of cerebrospinal fluid (CSF) leaks, sealing of the vascular anastomosis sites, reinforcements of aneurysmal clippings, and hemostasis after resection of brain tumors. Presented in this report are 11 intracranial aneurysms, 11 brain tumors, 2 lipomyelo-meningoceles, and one each of cerebral arteriovenous malformation and torn dura resulting from a mastoidectomy. Procedures which seemed to be impossible or very difficult by conventional neurosurgical techniques could be accomplished in all cases without any complication. Our experience with fibrin adhesive suggests that it is a valuable adjuvant to various microneurosurgical procedures, and it may be potentially useful for protection of major cerebral veins and venous sinuses during cerebral retraction.

Key Words: Fibrin adhesive, biological glue. reinforcement, reconstruction

Synthetic chemical adhesives have been used for reinforcement of intracranial aneurysms, the closure of vascular incisions, vascular anastomosis, and the sealing of CSF leaks. The chemical substances include methyl meta-acrylate, synthetic resins, silicone polymer, EDH-adhesive and cyano-acrylate glues (Albin *et al.* 1962; Carton *et al.* 1962; Sachs *et al.* 1966; Hayes and Leaver 1966; Lee *et al.* 1976).

Isobutyl 2-cyanoacrylate and n-butyl 2-cyanoacrylate are most widely used because of their lesser tissue toxicity, shorter polymerization time and slower hydrolytic degradation than the shorter chain ethyl homologue (Lehamn and Hayes 1967), while effectively maintaining the adhesive properties (Matsumoto *et al.* 1968). However, because of their carcinogenic potential in laboratory animals (Giunta and Shklar 1972; Barbalinardo *et al.* 1986), cyanoacrylates are approved only for emergency uses by the Federal Drug Administration (FDA) of the U.S.A.

Recently, a fibrin adhesive material which reproduces the final phase of blood coagulation was introduced in Europe. It is a biological product that can be tolerated well and absorbed readily (Barbalinardo *et al.* 1986). The value of fibrin adhesive was documented confidently in the surgical management of cut surfaces exposed by the resection of parenchymatous structures. The strong sealing forces of fibrin adhesive without adverse effects endorse its usefulness as an adjunct in neurosurgery for vessel sutures, dural closures and bipolar coagulation (Maxwell and Goldwarl 1973; Klein and Schafer 1983; Schafer *et al.* 1985). Our recent experience of clinical application of fibrin glue, Beriplast (Behring, Behringwerke AG, D-3350, Marburg, FRD), for various neurosurgical procedures is presented in this paper.

Received July 5, 1990
Accepted December 3, 1990

Department of Neurosurgery, Yonsei University College of Medicine, Seoul, Korea

Address reprint requests to Dr. K-C Lee, Department of Neurosurgery, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul, Korea, 120-752

MATERIALS AND METHOD

Fibrin adhesive (Beriplast) was utilized in 26 patients who underwent microneurosurgical operations from January 1987 through December 1988 at the Department of Neurosurgery at Yonsei University College of Medicine. Among the 26 patients, 11 had brain tumors, 11 had cerebral aneurysms, 2 had lipomyelomeningoceles, and there was one each of arteriovenous malformation and dural tear as a complication of a mastoidectomy. Indications

Table 1. Summary of 20 cases using fibrin adhesive

Case	Age	Sex	Diagnosis	Indication	Efficacy
1	64	F	ACOA aenurysm	Reinforcement	Effective
2	13	F	AV malformation	Hemostasis	Effective
3	46	M	Metastatic tumor	CSF leak	Effective
4	47	M	Oligodendroglioma	CSF leak	Effective
5	36	M	MCA aneurysm	Reinforcement	Effective
6	43	M	MCA aneurysm	Reinforcement	Effective
7	32	M	MCA aneurysm	Reinforcement	Effective
8	51	M	MCA aneurysm	Reinforcement	Effective
9	32	F	MCA aneurysm	Reinforcement	Effective
10	62	F	ACOM aneurysm	Reinforcement	Effective
11	4	F	Lipomeningocele	CSF leak	Failed
12	4	F	Lipomeningocele	CSF leak	Reduced leak
13	41	F	MCA aneurysm	Hemostasis	Effective
14	31	M	Pituitary tumor	CSF leak prevention	Effective
15	31	F	Torn dura	CSF leak	Reduced leak
16	64	M	Pituitary tumor	CSF leak prevention	Failed
17	32	F	Orbital tumor	Hemostasis	Effective
18	47	M	Oligodendroglioma	Hemostasis	Effective
19	38	M	Astrocytoma	Protection of vein	Effective
20	44	M	ACOM aneurysm	Reinforcement	Effective
21	59	F	ACOM aneurysm	Reinforcement	Effective
22	62	F	Meningioma	Hemostasis	Effective
23	42	M	CSF rhinorrhea	CSF leak	Minimal leak
24	56	F	Meningioma	Protection of vein	Effective
25	34	M	Pituitary tumor	CSF leak prevention	Effective
26	54	F	Ophthalmic aneurysm	Hemostasis	Effective

ACOA: Anterior communicating artery
AV: Arteriovenous
CSF: Cerebrospinal fluid
MCA: Middle cerabral artery

for applying the fibrin adhesive include reinforcing aneurysmal clippings, local hemostasis, protection of cerebral veins and sealing CSF fistulae. During the reinforcement of aneurysmal clip, the thin vascular portion proximal to the clip was wrapped with teflon, cotton or muslin pieces and fixed by fibrin glue. For hemostasis after the resection of brain tumors or vascular malformation, the fibrin glue was applied directly to the cut surface. In several cases, oxidized cellulose (Surgicel) or ultra-thin strips of collagen felt were used in conjunction with fibrin adhesives.

The fibrin adhesive was used along with muscle and fascia for reconstruction of the sellar floor to prevent possible CSF leakage after the transsphenoidal approach (TSA) for pituitary tumors (Table 1).

The mechanism of fibrin glue mimics the last step of blood clotting, in which thrombin is the solidifier of the system and causes fibrinogen to coagulate. Solidification of the clot occurs within 10-20 seconds. The fibrin adhesive (Beriplast) is a combination

of two solutions - one solution contains fibrinogen (65-115 mg) and aprotinin (100 Kininogenin inactivator unit), and the other contains thrombin (400-600 I.U.) and calcium choride(40 mmol/l). Forty to eighty units of factor XIII, which stabilizes the fibrin monomers, are added to the first solution. The two solutions are placed in two separate syringes and are connected to a Y-piece. The Y-piece dispenser has two openings at the tip through which the solutions flow separately. The two solutions are mixed in a needle attached to the Y-piece dispenser and then exit through the needle. It is necessary to replace the needle after each application due to the clotting of the solution within the needle a few sec-

onds after blending of the two solutions. The dosage per use depends on the extent of the surface to be covered or on the volume of the defect to be filled, ranging from 0.5ml to 3ml. The tissues to be fixed should be held in position for several minutes until a preliminary adhesion takes place. The fixed tissue has maximum firmness about 2 hours after the application.

RESULTS

Reinforcement of aneurysmal clipping

Nine patients needed the reinforcement either because of the regional thinning of the vascular wall proximal to the clip or the remnant of the aneurysmal neck after clipping. The encasement of the rest of the aneurysm was done effectively by using fibrin adhesive in conjunction with teflon, cotton, or muslin pieces. Neither recurrent bleeding of the aneurysm nor adverse reaction from the glue was observed in these nine cases for a follow-up period of 25 months.

Local hemostasis

Fibrin adhesive was used in 8 patients for the purpose of local hemostasis. Among these patients, 5 had brain tumors, 2 had cerebral aneurysms, and 1 had a cerebral arteriovenous malformation. Fibrin adhesive was used to control oozing from parenchymal resection surfaces in 6 cases. Two cases of cerebral aneurysms required fibrin glue; one for sealing of a needle hole on the parent arterial wall, the other for bleeding control from the cavernous sinus. The opened cavernous sinus was repaired by packing small pieces of surgical soaked in fibrin glue while maintaining gentle pressure until complete hemostasis was achieved. Under the operating microscope, the gelation of the fibrin adhesive followed by local hemostasis was observed within a minute. Postoperative follow-up by computerized tomography showed no evidence of hemorrhage in these eight patients.

Protection of cerebral veins

Fibrin adhesive was also used for the protection and preservation of the vein of Labbe which had to be retracted during a subtemporal approach. Immediately after opening the dura, the vein of Labbe was dissected out from the arachnoid covering near the drainage junction to the lateral sinus. The vein of Labbe was protected from tear during temporal lobe retraction by applying the fibrin adhesive over the surgicel-covered vein. With this technique, the vein of Labbe was well preserved in two cases.

Sealing CSF leakage

CSF leaks were treated with fibrin adhesives in 11 cases. Six cases showed satisfactory results, while the treatment was ineffective in 5 cases. The fibrin adhesives were used as an adjunct for incomplete dural closure in 3 patients, and all of these patients developed CSF leakage subsequently. Two cases of CSF rhinorrhea developed among 5 pituitary tumors where fibrin glue was used to reconstruct the sellar floor after a transsphenoidal approach(TSA). However, all of the leakages were controlled eventually by lumbar drainage and strict bed rest.

DISCUSSION

Currently, fibrin glue is extensively used for cardiac surgery, microvascular anastomosis, ocular surgery, bone grafts, and skin grafts (Hjortrup *et al.* 1986; Margarit *et al.* 1987; Zaubermand and Hemo; 1988). Fibrin glue is also useful in neurosurgery. Principal application of this bilological glue may be the control of diffuse oozing of blood that cannot be controlled by conventional means, because it has a strong hemostatic effect. It may be particulary helpful in cavernous sinus surgery, since bleeding from the sinus is very difficult to halt by conventional surgical techniques. Hasegawa(1985) successfully closed carotid cavernous fistula using fibrin glue intravascularly. Our experience on the application of fibrin glue during cavernous sinus surgery is limited to only one case. The cavernous sinus was opened to dissect the neck of an ophthalmic artery aneurysm. Bleeding from the sinus was easily controlled by surgicel soaked in fibrin glue.

The incidence of evacuo-rebleeding could be reduced, because the hemostasis achieved by surgicel or collagen fleece is further fortified by the effect of fibrin glue. Another beneficial effect may be the additional adhesion of dural seams or duraplasties. In extra-intracranial arterial anastomosis operations, even the minimal bleeding from the side branches of the superficial temporal artery could be avoided by applying fibrin adhesive, while preserving sufficient blood flow within the artery. Schafer(1985) reported that he could limit the use of sutures to six to eight by the application of fibrin glue onto actual vascular anastomosis. By doing so, the danger of vascular stenosis caused by additional

seams, and the duration of the temporary clipping of the cerebral recipient artery could be reduced. Haase (1986) reported the use of fibrin adhesives in cases of muscle wrapping of giant aneurysms or broad-based, unclippable aneurysms. Auer (1985) used fibrin glue and septal bone to reconstruct the sellar floor and the wall of the sphenoid sinus after transsphenoidal approach for pituitary adenomas in a series of 108 patients. And he found out that only one patient developed CSF fistula, a very low rate when compared to the 3.5% incidence of CSF leakage from conventional reconstruction technique. In animal experiments the fibrin adhesive was absorbed within 7 days with simultaneous formation of granulation tissue(Scheele and Pesch, 1983). Once the granulation tissue is formed, the fibrin adhesive is no longer needed.

We have observed the effect of fibrin adhesives in four different situations: reinforcement of aneurysmal clipping, local hemostasis, sealing CSF space, and protection of the cerebral veins. We could not estimate the efficacy of fibrin glue for reinforcing the aneurysmal clip, because no patients have taken the follow-up angiography. The drawback for applying fibrin glue around the aneurysms is that circulation of CSF around the major cerebral vessels, where the aneurysms arise, may facilitate absorption of the glue. Fibrin glue is effective in controlling the bleeding from the resection margins of brain tumors or arteriovenous malformations. However, it should be stressed from our experience that fibrin glue could not be used as a substitute for meticulous surgical technique, especially closing the dura mater water-tight to prevent CSF leaks. CSF leakage from the tiny gap could be sealed easily by fibrin glue. But the leakage cannot be controlled by fibrin glue alone if the dural defect of incision is large. It was reported that fibrin glue works well on wet surfaces (Zauberman and Hemo 1988), unlike the synthetic tissue glues which can only be used on the dry surfaces. However, it has been our experience that fibrin adhesive also requires a dry surface to be effective. Another indication of using fibrin adhesives in neurosurgery is the protection of large veins. Fibrin glue is useful in protection of large veins and venous sinuses during microsurgery, especially when they require retraction. Preservation of the vein of Labbe is critical in subtemporal approaches because damage to the vein of Labbe results in catastrophic venous infarction of the temporal lobe which jeopardizes the patient's life. Our technique of protecting the critical vein described in this article, which has not yet been published in neurosurgical literatures, should be one of the most useful application of fibrin glue in neurosurgical field.

In conclusion, fibrin glue is effective in many neurosurgical procedures such as: control of oozing from the cut surface of parenchymal lesions, during cavernous sinus surgery, sealing of small dural openings or CSF leakage sites, protection of important cerebral veins, thus contributing to the improvement of micro-neurosurgical techniques.

ACKNOWLEDGEMENT

The authors wish to express their appreciation to Behringwerke, Marburg, Federal Republic of Germany for supplying fibrin glue (Beriplast).

REFEREMCES

Albin MS, Dagostino AN, White RJ, Grindlay JH: Nonsuture sealing of a dural substitute urilizing a plastic adhesive, Methyl 2-Cyanoacrylate. *J Neurosurg 19: 545-550, 1962*

Auer LM, Clarici G: The first 100 transsphenoidally operated pituitary adenomas in a non-specialised centre: surgical results and tumor recurence. *Neurol Res 7: 153-160, 1985*

Barbalinardo RJ, Citrin P, Franco CD, Hobson RW: A comparison of isobutyl 2-cyanoacrylate glue, fibrin adhesive, and oxidized regenerated cellulose for control of needle hole bleeding from polytetrafluoroethylene vascular prostheses. *J Vasc Surg 4(3): 220-223, 1986*

Carton CA, Heifetz MD, Kessler LA: Patching of intracranial internal carotid artery in man using a plastic adhesive(East-man 910 adhesive). *J Neurosurg 19: 887-895, 1962*

Giunta J, Shklar G: Studies on tongue carcinogenesis in rats using DMBA with and without cyanoacrylate adhesive. *Arch Oral Biol 17: 617-622, 1972*

Haase J, Falk E, Firdmadsen F, Teglbjaerg PS: *Experimental and clinical use of Tissel(Tissucol) and muscle to reinforce rat arteries and human cerebral saccular aneurysms.* In Schlag G, Red IH eds. *Fibrin sealant in operative medical Ophthalmology-Neurosurgery. Vol. 2* Springer-Verlag Berlin Heidelberg *1986, 172-175*

Hasegawa H, Bitoh S, Obashi J, Maruno M: Closure of carotid-cavernous fistulae by use of a fibrin adhesive system. *Surg Neurol 24: 23-26, 1985*

Hayes GJ, Leaver RC: Methyl methacrylate investment of intracranial aneurysms. *J Neurosurg 25: 79-80, 1966*

Hjortrup A, Nordkild P, Kiaergaard J, Sjontoft E, Olesen

HP: Fibrin adhesive versus sutured anastomosis: A comparative intra-individual study in the small intestine of pigs. *Br J Surg 73: 760-761, 1986*

Klein HJ, Schafer M: Arrest of haemorrhage by sealing: Fibrin adhesives in neurosurgery. *Die Gelben Hefte 23: 155-159, 1983*

Kline DG, Hayes GJ: An experimental evaluation of the effect of a plastic adhesive, Methyl 2-Cyanoacrylate, on neural tissue. *J Neurosurg 20: 647-654, 1963*

Lee KC, Lee KS, Chung SS, Kim YS, Choi JU: Surgical treatment of anterior communicating artery aneurysms. *Yonsei Med J 23: 131-145, 1976*

Lehman RA, Hayes GJ: The toxicity of alkyl 2-cyanoacrylate tissue adhesives. Brain and blood vessels. *Surgery 61: 915-922, 1967*

Margarit E, Martinez-Ibanex V, Lloret J, Ventura H, Broto J, Isnard R, Banco J, Allende H: Segmental liver transplantation in pigs: Use of a fibrin sealant and collagen as hemostatic agents. *Transplant Proc 19: 3835-3837, 1987*

Matsumoto T, Pani KC, Hamit HF: Use of tissue adhesive for arterial anastomosis. *Arch Surg 96: 405-409, 1968*

Maxwell JA, Goldware SI: Use of tissue adhesive in the surgical treatment of cerebrospinal fluid leaks. *J Neurosurg 39: 332-336, 1973*

Messer HD, Strenger L, McVeety H: Use of plastic adhesive for reinforcement of a ruptured intracranial aneurysm. *J Neurosurg 20: 360-362, 1962*

Sachs E, Erbengi A, Margolis G: Fatality from ruptured intracranial aneurysm after coating with methyl-2-Cyanoacrylate (Eastman 910 Monomer, M2C-1). *J Neurosurg 24: 889-891, 1966*

Schafer M, Klein HJ, Richter HP: Fibrin adhesives in neurosurgery uses and results. *Fortschritte der Medizin 103: 545-547, 1985*

Scheele J, Pesch HJ : *Morphologische Aspekte des Fibrinkleberabbaus im Tierexperiment.* In Cotta Braun eds, *Fibrinklebung in Orthopadie und Traumatologie,* Thieme Verlag, Stuttgart, New York, *1982. 35-43.*

Sugar O, Tsuchiya G: Plastic coating of intracranial aneurysms with "EDH-adhesive". *J Neurosurg 21: 114-117, 1964*

Zauberman H, Hemo I: Use of fibrin glue in ocular surgery. *Ophthal Surg 19(2): 132-133, 1988*