

Aspirin Prostaglandin E₁

Abstract

The Effect of Aspirin and Prostaglandin E₁ on the Patency of Microvascular Anastomosis in Rat

Kwang Suk Lee, M.D., Jeong Dae Suh, M.D., Seung Beom Han, M.D.,
Seung Joon Lee, M.D., In Chul Choi, M.D., In Sun Kim, M.D., Seong Jin Cho, M.D.

Department of Orthopedic Surgery and Pathology, Korea University Hospital, Seoul, Korea

In the field of microsurgery, the vascular obstruction of the microvascular anastomosis by thrombus is one of the most important complication. The purpose of this study is to compare the effect between aspirin and prostaglandin E₁(PGE₁) which act as the peripheral vasodilatation and platelet disaggregation.

We have used total 48 white male rats and divided them into three groups(A, B and C group). Each group consists of 16 rats respectively. A group is as control, B group is medicated with aspirin(3.0mg/kg/day) and C group with PGE₁(1.2μg/kg/day). The gross and histopathologic findings at anastomosed site were observed on 3, 5, 10 and 15 days after vascular anastomosis and the results were obtained as the followings.

1. The microvascular patency rate is 81.2% in control group, 93.8% in aspirin group and 100% in PGE₁ group.
2. On the histologic examination, the formation of mural thrombus is decreased both in the aspirin and PGE₁ group as comparing with the control group and also the hypertrophy of the intima forming from media is less formed in PGE₁ group than aspirin group and the degree of thickness is also less.
3. The fibrosis of media is less observed in PGE₁ group than aspirin group.

According to the above results, the application of PGE₁ to the microsurgery is considered to be effective on the prevention of the thrombus formation and on providing high patency rate.

Key Words : Prostaglandin E₁, Patency, Microsurgery

(O brien microvascular clamp)
 straight scissors
 10-0 (Ethilon ,
 UK) (end to end
 가 anastomosis)
 (Adventitia)
 (Adventitia)
 (trimming)
 Aspirin, Warfarin, Heparin, Dextran, Chlorpromazine (suture) 6~8
 Prostaglandin E₁(PGE₁) Arachidonic acid A , B 10 IU heparinized
 polyunsaturated long chain fatty acid saline, C PGE₁ 20mg A, B C
 (platelet disaggregation) 1% lidocaine
¹¹⁾
 PGE₁ 가 가 4-0 3 (Cefmetazole Sodium,
^{4,6,15)} 25mg/kg/day) , A , B
 PGE₁ 가 3.0mg/kg/day Aspirin
 Aspirin , C 1.2μg/kg/day
 PGE₁(Opalmon,)
 가 3 , 5 , 10 15
 4
 1. 10mm 10% formalin
 Hematoxylin-Eosin(H & E) ,
 300g ~ 350g Elastic Van-Gieson(EVG) Masson's
 (Sprague-Dawley rat) 48 Trichrome(MT)
 16 A, B, C 3
 A , B Aspirin , C
 PGE₁
 2. 1.
 Ketamine (12mg/kg)
 Povidone Iodine(Betadine , A
 7.5%) 가 16 13
 (S5, Zeiss , Germany) 81.2% , Aspirin
 (Sternocleidomastoid muscle) B 15 93.8%
 , PGE₁ 100%
 1.0mm (Table 1).

Table 1. Patency rate

group \ exploration(P.O.D)	3	5	10	15	Patency No. / total No.(%)
A	3/4	3/4	4/4	3/4	13/16(81.2)
B	4/4	4/4	4/4	3/4	15/16(93.8)
C	4/4	4/4	4/4	4/4	16/16(100)

2.

1) (Thrombus formation)
A (mural thrombus)

(Fig. 1) 5
, Aspirin PGE₁
(Fig. 2).

2) (Intima)

3 A (endothelial cell) (internal elastic lamina: IEL) 가 B
C 가

(internal elastic lamina)
(PMN cell)

가 A 가
B C 가
5 (flat cell) 15
(lining) ,
(endothelium) 가
(Fig. 4), 3
5 , B
C A 가
(internal elastic lamina) EVG

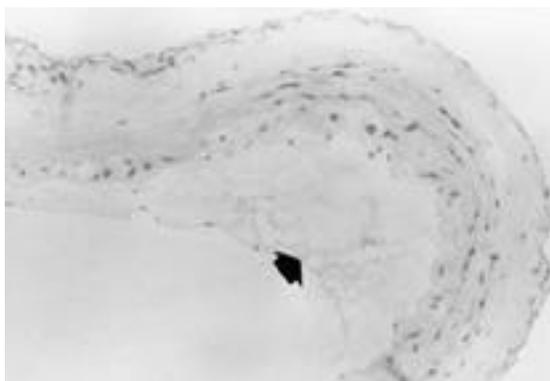


Fig. 1. Subendothelial mural thrombi formation(arrow) around the suture site in postoperative 3 days of A group (H & E, x200).



Fig. 2. Rare mural thrombi formation in postoperative 5 days of C group (H & E, x100).

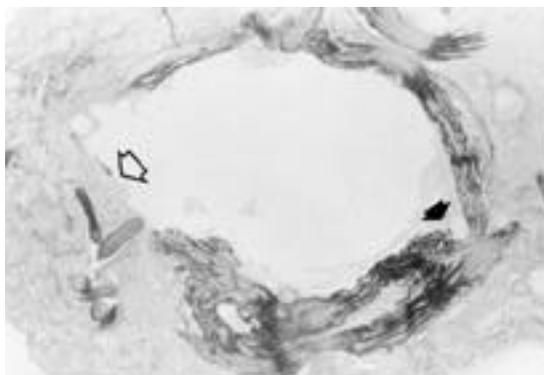


Fig. 3. Severe destruction of intima and media(white arrow) with disruption of internal elastic lamina(black arrow) in postoperative 3 days of A group (Elastic stain, x100).

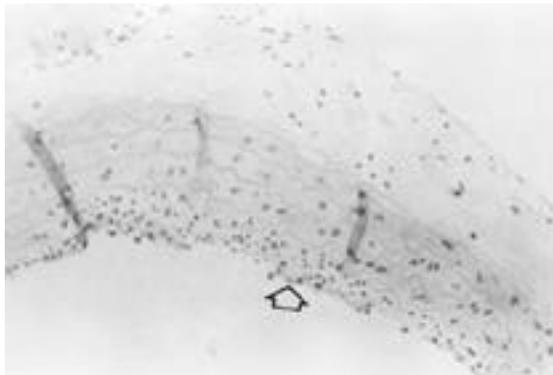


Fig. 4. Plump endothelial proliferation at the well-preserved intimal layer (arrow) in postoperative 5 days of C group (H & E, x 200).

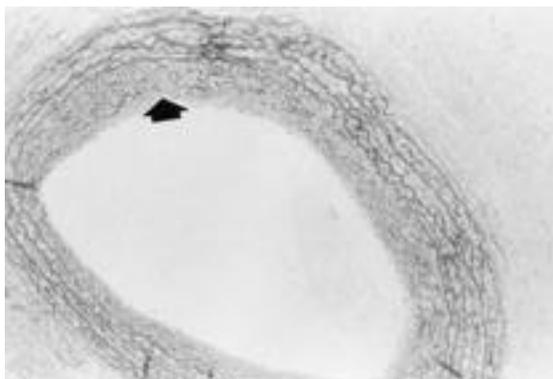


Fig. 5. Prominent intimal hyperplasia (arrow) is noted in postoperative 10 days of A group. The thickness of the intima is equal to that of media (Elastic, x 100).

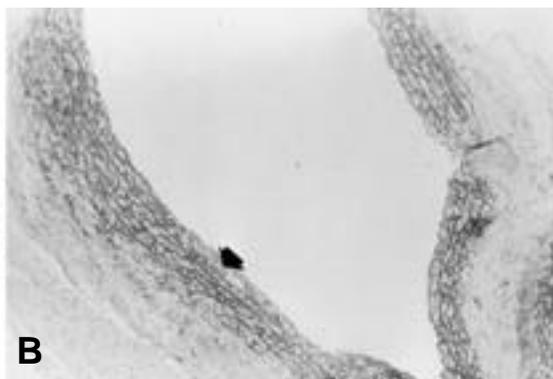


Fig. 6. (A) Intimal thickening (arrow) is more prominent in postoperative 15 days of B group (Elastic, x 200) than (B) C group (arrow) (Elastic, x 100).

가 (Fig. 3), 15
 가 (Fig. 5), B, C
 10 가 (Fig. 6-A, B, Table 2).
 15 B
 3) (Media) 3
 가 가 (Fig. 7-A, B),
 가 (hyaline necrosis)가 (Fig. 8) 15
 . A 3

Table 2. Intimal hyperplasia

group \ exploration(P.O.D)	3	5	10	15
A	-	+	+++	+++
B	-	-	+	++
C	-	-	-	+

- : no fibrosis + : mild
 ++ : moderate +++ : severe

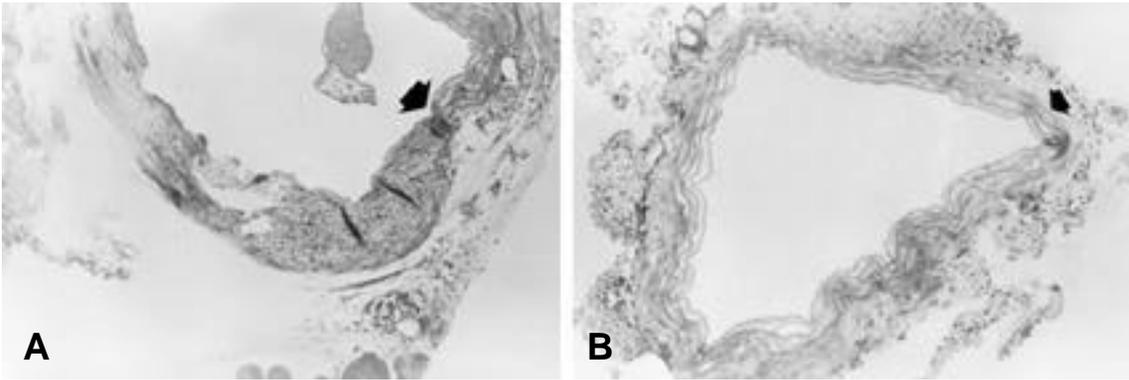


Fig. 7. (A) Multifocal thinning of the tunica media (arrow) is noted around the disruption sites in postoperative 5 days of A group (Masson's Trichrome, $\times 100$) and (B) in postoperative 3 days of B group (arrow) (MT, $\times 100$).

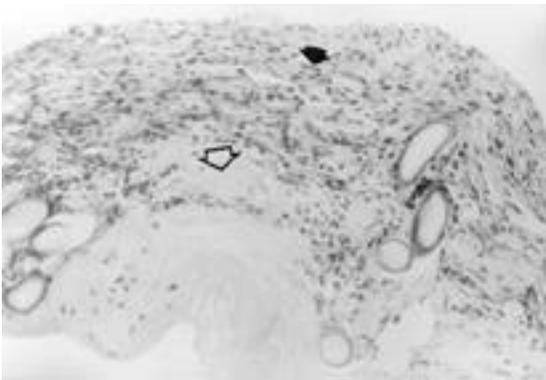


Fig. 8. Hyaline necrosis of the media (white arrow) is associated with severe destruction of intima and media in postoperative 3 days of A group. Also intense neutrophilic inflammation (black arrow) is noted (H & E, $\times 200$).

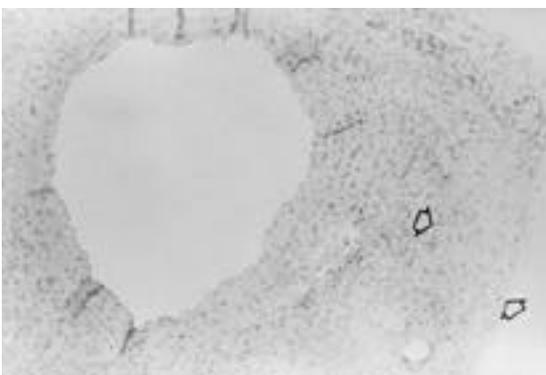


Fig. 9. Granulation tissue formation and the chronic lymphocytic infiltration (arrow) is more pronounced at the media and adventitia in postoperative 15 days of A group (H & E, $\times 200$).

Table 3. Fibrosis of media

group \ exploration(P.O.D)	3	5	10	15
A	-	+	+++	+++
B	-	-	++	++
C	-	-	+	+

- : no fibrosis + : mild
 ++ : moderate +++ : severe

가 , 15
 (granulation tissue)
 가 (Fig. 9), B 10
 가 , C
 10
 가 B
 (Fig. 10-A,B, Table 3).
 .
 ,
 가,
 가 .
 , (endothelium)
 ,
 (internal elastic lamina) ,

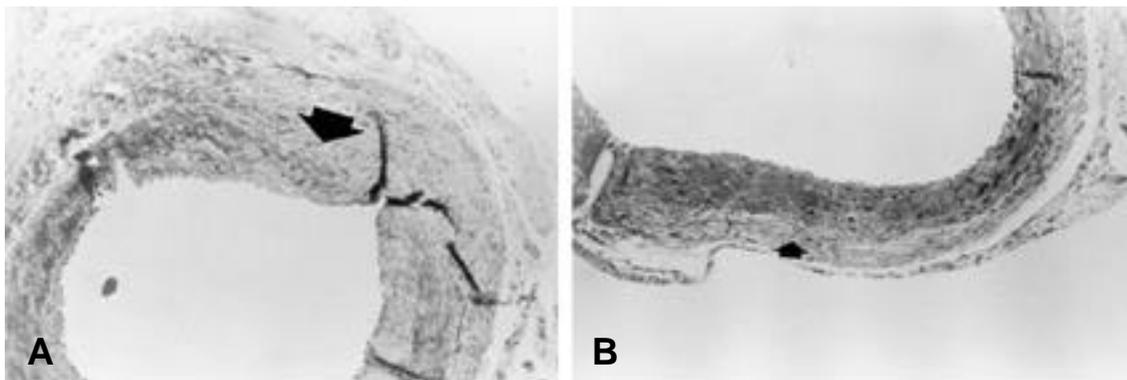


Fig. 10. (A) Fibrosis of the media (arrow) is more severe in postoperative 15 days of B group than **(B)** C group (arrow) (MT, × 100).

(intimal hyperplasia)
 가¹⁶⁾ PGE₁ 가
 가 1,2,12,13) Aspirin
 가 Aspirin
¹⁴⁾ Warfarin, Heparin, Dextran, Chlorpromazine
 . Low molecular weight dextran
 가 Aspirin, PG₁₂ PGE₁
 가 (stable) , -70 PGE₁ PG₁₂
 가 PG₁₂ 가¹⁵⁾
 Chlorpromazine⁸⁾, PGE₁
^{3,7)} Aspirin Prostacycline(PGI₂) Olsson⁴⁾
⁶⁾, Carlson
⁹⁾, PGI₂ 가
 Emmerson PGE₁ 가¹⁵⁾
 Sykes⁵⁾ low-dose PGI₂
 Knight¹⁰⁾ 가
 Prostaglandin Arachidonic acid PGE₁(Opalmon,)
 가
¹¹⁾, PG₁₂ Aspirin
¹⁷⁾ Prostaglandin E₁(PGE₁) 가
 가 PGE₁
¹⁵⁾, (intimal hyperplasia) Aspirin 가

prostacyclin on experimental random pattern flaps in the rat. Br J Plast Surg, 34:264, 1981.

- 6) Ferreira SH, Vane JR : *Prostaglandins: their disappearance from and release into the circulation. Nature, 216:868, 1967.*
- 7) Geter RK, Winters RRW and Puckett CL : *Resolution of experimental microvascular spasm and improvement in anastomotic patency by direct topical agent application. Plast and Reconst Surg, 77(1):105-115, 1986.*
- 8) Humphreys WV, Walker A, Cave FD and Charlesworth D : *The effect of infusion of low molecular weight dextran on peripheral resistance in patients with arteriosclerosis. Br J Surg, 63:691-693, 1976.*
- 9) Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL : *Harrison's principles of internal medicine. 13th ed, New York, Mcgraw-Hill Inc, 431-435, 1994.*
- 10) Knight KR, Crab DJM, Nial M, et al : *Pharmacologic modification of blood flow in the rabbit microvasculature with prostacyclin related drugs. Plast Reconstr Surg, 75:692, 1985.*
- 11) Land WEM : *The biosynthesis and metabolism of prostaglandins. Ann Rev Physiol, 41:633-652, 1979.*
- 12) Lidman D, Daniel RK : *The normal healing process of microvascular anastomoses. Scand J Plast Reconstr Surg, 15:103-110, 1976.*
- 13) Morecraft R, Blair WF and Chang L : *Histopathology of microvenous repair. Microsurgery, 6:219-228, 1985.*
- 14) Pang CY, Neligan PC, Nakatsuka T and Sasaki GH : *Pharmacologic manipulation of the microcirculation in cutaneous and myocutaneous flaps in pigs. Clin Plast Surg, 12:173-184, 1985.*
- 15) Suzuki S, Isshiki N, Ogawa Y, Nishimura R and Kurokawa M : *Effect of intravenous prostaglandin E₁ on experimental flaps. Annals of Plastic Surgery, 19(8):49-53, 1987.*
- 16) Umemura K, Watanabe S, Kondo K, Hashimoto H and Nakashima M : *Inhibitory effect of prostaglandin E₁ on intimal thickening following photochemically induced endothelial injury in the rat femoral artery. Atherosclerosis, 130:11-16, 1997.*
- 17) Whittle BJR, Moncada S, Vane JR : *Comparison of the effects of prostacyclin(PGI₂), prostaglandin E₁ and D₁ on platelet aggregation in different species. Prostaglandins, 16(3):373, 1978.*

REFERENCES

- 1) Acland RD, Trachtenberg L : *The histopathology of small arteries following experimental microvascular anastomoses. Plast Reconstr Surg, 60:868-875, 1977.*
- 2) Baxter TJ, O'Brien BMcC, Henderson PN, Bennett RC : *The histopathology of small vessels following microvascular repair. Brit J Surg, 59:617-622, 1972.*
- 3) Bibi R, Ferder M and Strauch B : *Prevention of flap necrosis by chlorpromazine. Plast and Reconst Surg, 77(6):954-959, 1986.*
- 4) Carlson LA, Olsson AG : *Intravenous prostaglandin E₁ in severe peripheral vascular disease. Lancet, 2:810, 1976.*
- 5) Emmerson DJM and Sykes PJ : *The effect of*