

경피적 관동맥 풍선확장 성형술후 재협착에 관한 Sulodexide의 효과에 대한 전향적, 무작위 비교연구

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= Abstract =

A Prospective, Randomized, Comparative Clinical Investigation of the Effects of Sulodexide on Restenosis after Percutaneous Transluminal Coronary Balloon Angioplasty

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Background : Restenosis remains as the major limitation of percutaneous transluminal coronary balloon angioplasty (PTCA). Although its mechanism remains incompletely understood, proliferative action of arterial smooth muscle cells has been found to play an important role on restenosis by neointimal formation after PTCA. Glycosaminoglycan-containing compounds, including Sulodexide (Vessel Due, ALFA, Wasserman, S.p.A., Italy), inhibit the proliferation and migration of vascular smooth muscle cells in vitro.

Objectives : This study was performed to assess the efficacy of Sulodexide, a glycosaminoglycan compound with antithrombotic and antiproliferative properties, in preventing restenosis after PTCA.

Method : Two hundred eighty-four patients with ischemic heart disease were randomized to receive either the standard PTCA without Sulodexide in 144 patients (control group, M : F = 99 : 45, Age = 58 ± 9), 160 lesions or the standard PTCA with Sulodexide in 140 patients (treated group, M : F = 89 : 51, Age = 58 ± 10), 158 lesions. Successful angioplasties were performed in 258 atheromatous coronary lesions in 224 patients for whom follow-up angiographic data were obtained 6 months later. Quantitative coronary angiographic analysis (QCA) was performed before, immediate after PTCA and 6-months later. Angiographic restenosis ($>50\%$ diameter stenosis at follow-up) was the primary end point ; minimal luminal diameter at follow-up angiogram was the secondary end point.

Results : Successful PTCA was 97.6% and 97.5% in the standard PTCA with Sulodexide and the standard PTCA without Sulodexide, respectively. Although reference vessel size and minimal luminal

diameter after PTCA were larger in the control group than in the Sulodexide group (2.94 ± 0.11 vs 2.83 ± 0.13 mm and 2.26 ± 0.12 vs 2.18 ± 0.08 mm, respectively, $p=NS$), there was a increased tendency of minimal lumen diameter at 6 months angiogram in the Sulodexide group than in the control group (1.12 ± 0.50 vs 1.07 ± 0.53 mm, respectively, $p=NS$). Angiographic restenosis occurred in 42% of lesions in the Sulodexide group and 52% of the control group ($p=NS$).

Conclusions : Sulodexide treatment had a tendency to reduce restenosis rate in 6 months after coronary angioplasty. However, further study is necessary to verify the antiproliferative effect of Sulodexide with much larger number of patients.

KEY WORDS : Sulodexide · Restenosis · Percutaneous transluminal coronary balloon angioplasty.

가 7-8)

서 론

가

9). Sulodexide heparin -

(percutaneous tran - like compounds

sluminal coronary balloon angioplasty, PTCA

) 2가

10).

PTCA (media)

(neointima formation) 1), (intimal

(pathologic remodeling), PTCA hyperplasia) Sulodexide

(adventitia) 가 .

2).

Sulodexide(Vessel Due®, ALFA, Wasserman, S. 연구대상 및 방법

p.A., Italy)

glycosaminoglycan de -

rmatan sulfate heparin fraction 1 : 4

8,000 daltons

1994 7

Sulodexide (lipoprotein -

1995 12 PTCA

lipase) (very 284 Sulodexide

low density lipoprotein, low density lipoprotein) 140 (M : F=89 : 51, Age=58 ± 10), 158

가 3), Sulodexide 144 (M : F=99 :

activated partial thromboplastin time 45, Age=58 ± 9), 160 6

thrombin time Xa (minimal luminal diameter, MLD)

antithrombin III heparin cofactor II . 70%

가 4). - PTCA

(tissue - plasminogen activator) PTCA

(plasminogen 50%

activator inhibitor - 1)

(profibrinolysis) 5-6). Sulodexide

가 PTCA .

2. 방 법

cholesterol 240mg/dL

Sulodexide

600 lipoprotein - lipase - releasing units(LRU)

PTCA 450LRU

2 450

LRU 2 . Aspirin 200mg/day

(percent reference

diameter stenosis) ,

vessel

가

on - line quantitative coronary angiographic system(ANCOR V2.0, Siemens)

(guiding catheter) 2

가 PTCA

50% . PTCA

American College of Car - diology/American Heart Association type A, B, C lesion

가 1 : 1

heparin

10,000U activated clotting

time 250 hep -

arin 5,000U

284 224 (79%)가 6

+ / -

two - tailed T test

chi - square

test

3. 결 과

284 , 318

5±2 , 29 (10.2%)

3 (1.2%),5

PTCA

3 (1.2%),

2 (0.7%)

284 , 318

PTCA

242 , 276 224 (92.6%), 258(93.4%)

6

6 224

Table 1 . 258

Table 2 .

47%(122/258) , Sulodexide

42%(54/128), 52%(68/130)

Sulodexide

Table 1. Baseline clinical characteristics of PTCA patients (n=224)

	Sulodexide	
	(n=110)	(n=114)
Age(years)	58±10	58±9
Male gender	74(67%)	84(74%)
Risk factors		
Hypertension	43(39%)	27(24%)
Diabetes m ellitus	25(23%)	18(16%)
Hyperlipidemia	8(7%)	5(4%)
Current smoker	48(44%)	55(48%)
Myocardial infarction		
Previous	8(7%)	18(16%)
Acute	20(18%)	32(28%)
Unstable angina	51(46%)	36(32%)
Number of disease vessel		
1	96(87%)	100(88%)
2	11(10%)	11(10%)
3	3(3%)	3(2%)

Table 2. Angiographic and procedural characteristics of PTCA lesion(n=258)

	Sulodexide (n=128)	(n=130)
Modified AHA/ACC lesion type		
A	9(7%)	21(16%)
B ₁	36(28%)	27(21%)
B ₂	2(41%)	52(40%)
C	31(24%)	30(23%)
Stenosis site		
LAD	72(56%)	70(54%)
LCX	31(24%)	39(30%)
RCA	25(20%)	21(16%)

AHA = American Heart Association
ACC = American College of Cardiology
LAD = Left anterior descending artery
LCX = Left circumflex artery, RCA = Right coronary artery

Table 3. The restenosis rate for clinical characteristics of patients

	Sulodexide (n=110)	(n=114)	P value
Risk factors			
Diabetes mellitus	14(56%)	10(55%)	NS
Hypertension	18(42%)	12(44%)	NS
Hyperlipidemia	3(38%)	2(40%)	NS
Current smoking	21(44%)	28(51%)	NS
Clinical diagnosis			
Unstable angina	20(39%)	16(44%)	NS
Myocardial infarction			
Old	3(38%)	8(44%)	NS
Acute	9(45%)	16(50%)	NS
Number of diseased vessel			
2 vessel disease	3(27%)	4(36%)	NS
3 vessel disease	2(67%)	2(67%)	NS

(Table 3)

(Table 4)

PTCA	PTCA
(diameter stenosis)	가 Sulodexide
74.6 ± 9.6%	23.0 ± 9.0%, 73.2 ±
8.9%	21.0 ± 10%
Sulodexide	PTCA
2.18 ± 0.08mm,	
2.26 ± 0.12mm	, 6
Sulodexide	1.12 ± 0.50mm
1.07 ± 0.53mm	가

(Table 5).

Table 4. The restenosis rate of PTCA lesions
*Total restenosis rate = 47%

	Sulodexide (n=128)	(n=130)	P value
Restenosis rate	54(42%)	68(52%)	NS
Modified AHA/ACC lesion type			
A	15(60%)	11(56%)	NS
B ₁	12(30%)	12(42%)	NS
B ₂	23(45%)	32(61%)	NS
C	14(47%)	13(46%)	NS
Stenosis site			
LAD	34(41%)	41(32%)	NS
LCX	8(29%)	13(11%)	NS
RCA	12(43%)	14(11%)	NS

AHA = American Heart Association
ACC = American College of Cardiology
LAD = Left anterior descending artery
LCX = Left circumflex artery
RCA = Right coronary Artery

Table 5. Quantitative angiographic measurement

	Sulodexide (n=128)	(n=130)	P value
Diameter stenosis(%)	74.6 ± 9.6	73.2 ± 8.9	NS
Reference vessel diameter(mm)	2.83 ± 0.13	2.94 ± 0.11	NS
Post MLD(mm)	2.18 ± 0.08	2.26 ± 0.12	NS
Follow up MLD(mm)	1.12 ± 0.50	1.07 ± 0.53	NS
Late loss(mm)	1.07 ± 0.10	1.18 ± 0.15	NS

MLD = Minimal luminal diameter

6

Sulodexide

고 안

heparin	11)
heparin sulfate	
(con -	
tractile phenotype)	가
platelet	
factor 4, heparitinase	
(synthetic	
phenotype)	12)
Sulodexide	

glycosaminoglycan dermatan sulfate heparin PTCA (elastic recoil) 가

arin 1 : 4 . Heparin 가 . Heparin 19),

8,000 daltons medium molecular weight heparin Mauro derma - 20)

. Heparin glycosaminoglycan (heparinoid) Hirshfeld 19,21)

¹³⁾ . Sulodexide antithrombin III 22)

Xa heparin - like substances(80%) he Low molecular weight heparin

parin cofactor II dermatan fraction(20%) 가 heparin - like subs -

tance 가 (ERA Trial, EMPAR 23 - 25)

^{10,14,15)} . 1989 Trial and FACT) 가

4

(5ug/ml)

300ug/ml 32%, 48% , 100ug/ml, ¹⁰⁾ . Sulo -

dexide (potency)

Sulodexide heparin

16 90 PTCA ²⁶⁾

5 가 15 가

^{16,17)} .

(elapsing time)

600LRU 120 , 1200LRU 300 (2 3) ²⁷⁾

48 (platelet - derived growth factor, PDGF)

¹⁸⁾ . Sulodexide (30 40%) 2

4 6 (mitogen) PDGF

12 4 (steady state) ¹⁸⁾ .

PTCA 6 (balloon injury) 2 3

가 6 7

²⁹⁾ . 가

(diameter sten - (migration) 14 가

osis)가 50% balloon injury 1

가 , 47% Sulodexide ³⁰⁾ . Balloon injury 14

42%, 52% 가 (volume)

			Sulodexide	가	
		대상 및 방법 :			
	가	1994	7	1995	12
(hyperplasia)	가	284		Sulodexide	140
	PTCA	(M : F=89 : 51, age=58±10),	158	Sulode -	
		xide	144	(M : F=99 : 45, age=58	
	PTCA	Sulode -	± 9), 160	Sulodexide	
xide	diameter stenosis가	6			
	, reference vessel diameter			(minimal luminal diam -	
PTCA	6	eter)			
	Sul -	Sulodexide			
odexide		600 lipoprotein - lipase - releasing units(LRU)			
Sulodexide가		1 /	PTCA		
		450LRU	2 /		
		450LRU	2 /	as -	
PTCA	Sulodexide	pirin 200mg/	diltiazem 180mg/		
		6			
		chi - square test	t - test		
가					
	요 약	결 과 :			
		284	, 318	PTCA가	
		29	(10.2%)		
연구배경 :					
Sulodexide	heparin - like compound	medium	3	(1.2%), 5	(1.8%)
molecular weight glycosaminoglycans(80%)	der -		PTCA		
matan sulfate(20%)	Xa	3	(1.2%), 2	(0.7%)	
, antithrombin III	heparin cofa -				
ctor II	가				
	가				
	가				47%(122/
	Sulodexide	heparin -	258)	Sulodexide	42%(54/
like compounds			124),	52%(68/130)	Sulodexide
		PTCA		PTCA	
(media)		(diameter stenosis)가	Sulodexide	74.6 ±	
		9.6%	PTCA	23.0 ± 9.0%, B	73.2 ± 8.9%
		21.0 ± 10%			

PTCA			
		2.18 ± 0.08mm	
Sulodexide	2.26 ± 0.12mm		
, 6			Sulo -
dexide	1.12 ± 0.50mm	1.07 ± 0.53mm	
.		Sulodexide	

결 론 :

PTCA Sulodexide

가

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