

## 관동맥내 스텐트 삽입 후 사용한 Ticlopidine과 저분자헤파린 효과에 대한 전향적 무작위 비교연구

신경덕<sup>1</sup> · 채제건<sup>2</sup> · 문성기<sup>2</sup> · 김원호<sup>2</sup> · 고재기<sup>2</sup>

### Clinical and Angiographic Outcomes :

### Subcutaneous Nadroparin versus Ticlopidine after Coronary Stenting

Kyoung Deok Shin, MD<sup>1</sup>, Jei Keon Chae, MD<sup>2</sup>, Sung Ki Moon, MD<sup>2</sup>,  
Won Ho Kim, MD<sup>2</sup> and Jae Ki Ko, MD<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, <sup>2</sup>Institute of Cardiovascular Research Chonbuk National University,  
College of Medicine, Chonju, Korea

### ABSTRACT

**Background and Objectives :** It was reported that low molecular weight heparin (LMWH) was more effective than unfractionated heparin in patients with acute coronary syndrome. Recent studies have shown that the pathophysiology of restenosis in stented lesions was different from those of nonstented lesions. Treatment strategies designed to limit cellular proliferation that were ineffective in nonstented lesions may be efficacious in reducing in-stent restenosis. This study was aimed to compare the clinical and angiographic results of LMWH (nadroparin) after coronary stenting with those of conventional ticlopidine regimen. **Materials and Methods :** Patients were eligible for inclusion if they had angina and/or objective evidence of myocardial ischemia, and a significant (>50%) stenosis that was documented on a recent coronary angiogram. After stenting, prospective randomized comparison study was performed. Patients were randomly assigned to either nadroparin (200 IU/kg, sc, bid) or ticlopidine (250 mg bid) plus aspirin (200 mg qd) treatment groups. Repeat coronary angiography was performed at 236 ±90 days after stenting, and quantitative coronary angiographic analysis (QCA) was done. **Results :** Intracoronary stent implantation was performed in eighty five lesions in eighty one patients (ticlopidine : 40, nadroparin : 41). There was no significant difference in any baseline clinical/angiographic variables between the two treatment groups. There were no subacute stent thrombosis, infarction and death in both groups. Six-month event-free survival was 36 (90%) in the ticlopidine group and 35 (85.4%) in the nadroparin group. Follow-up quantitative angiographic data such as late loss ( $1.35 \pm 0.70$  vs  $1.32 \pm 0.69$ ), loss index ( $0.53 \pm 0.70$  vs  $0.56 \pm 0.23$ ) and restenosis rate (36% vs 25.8%) were not different between ticlopidine and nadroparin groups. **Conclusion :** Effects of nadroparin were not different from those with ticlopidine therapy in the prevention of restenosis and subacute stent thrombosis after coronary stenting. Clinical outcomes between two strategies were similar. Low molecular weight heparin may be an alternative to ticlopidine in patients that ticlopidine cannot be administered because of severe adverse effects. (**Korean Circulation J 1999;29(3):259-265**)

**KEY WORDS :** Restenosis · Low molecular weight heparin · Ticlopidine.

: 1998 12 14  
: 1999 3 22  
: , 560 - 180 634 - 18  
: (0652) 250 - 1660 · : (0652) 250 - 1680  
E - mail : jaekiko@soback.kornet21.net

## 서 론

## 재료 및 방법

### 대 상

1)2) . (elastic recoil) (pathological arterial remodeling) 가 2

50% , 가 , , 가 2

### 방 법

ISAR Trial 5) (aspirin plus ticlopidine)가 (phenprocoumon with initial overlapping heparin plus aspirin) 가

aspirin 200 mg nadroparin(Fra - xiparine®) ticlopidine . Na - droparin aspirin 200 mg nadroparin 200 IU/kg 1 2 1

6)7) , Hanke 8) Buchwald 9) (low molecular weight heparin) 가 . ERA trial

가 aspirin 200 mg mg bid 1 Ticlopidine ticlopidine 250 nadroparin

10) REDUCE trial 11)

Hoffmann 12)

가 aspirin ticlopidine aspirin

가 1 : 1 (stent optimization) 가 가 1.05 : 1 9 18 13±3

(Table 1)

가

가 . (MLD), (Acute gain), (late loss) .

, Glycoprotein b/ a 50%

. ( <30%, acute gain>20%)

edge detection

system(Siemens Hicor II, Soln, Germany)

on - line system

, angle, rotation gantry position

kilovoltage milliamperes

x - ray setting . 0.1 0.3 mg

. 가 (foreshortening)

, (guiding

(refer - catheter)

ence diamter),

**Table 1.** Types of stent

	Ticlopidine (n = 40)	Nadroparin (n = 45)
Multilink	11 (27.5%)	18 (40.0%)
NIR or Jo	18 (45.0%)	22 (48.9%)
CrossFlex	10 (25.0%)	4 ( 8.9%)
GFX	1 ( 2.5%)	1 ( 2.2%)

**Table 2.** Baseline clinical characteristics

Characteristics	Ticlopidine (n = 40)	Nadroparin (n = 41)
Age	64 ± 9	60 ± 9
Women (%)	18 (45.0)	16 (39.0)
Current smoker (%)	16 (40.0)	28 (68.2)
Hypercholesterolemia (%)	9 (22.5)	5 (12.2)
Diabetes mellitus (%)	7 (17.5)	10 (24.4)
Arterial hypertension (%)	11 (27.5)	20 (48.8)
Clinical diagnosis (%)		
Angina pectoris	2 ( 5.0)	1 ( 2.4)
Unstable angina	16 (40.0)	19 (46.3)
Non-Q MI	2 ( 5.0)	3 ( 7.4)
Acute Q MI	19 (47.5)	17 (41.5)
Old Q MI	1 ( 2.5)	1 ( 2.4)
LVEF(%)	55 ± 9	57 ± 7

Age is expressed as mean ± SD

SPSS(Version 7.5)

±

chi - square test unpaired Student t - test

P 0.05

. cardiac event - free survival Kaplan - Meyer method

## 결 과

1997 9 1998 5 81 , 85

ticlopidine nadroparin

64 ± 9, 60 ± 9 45%, 39%

(Table 2).

가

**Table 3.** Target lesion characteristics

	Ticlopidine (n = 40)	Nadroparin (n = 45)
No. of vessels with lesions (%)		
One vessel	14 (35.0)	24 (53.3)
Two vessel	13 (32.5)	14 (31.1)
Three vessel	13 (32.5)	7 (15.6)
Vessels of target lesions (%)		
LAD	22 (55 )	24 (53.3)
LCX	5 (12.5)	5 (11.1)
RCA	13 (32.5)	16 (35.6)
ACC/AHA lesion classification (%)		
Type A	9 (22.5)	11 (24.4)
Type B1	21 (52.5)	22 (48.9)
Type B2	7 (17.5)	7 (15.6)
Type C	3 ( 7.5)	4 ( 8.9)

LAD : left anterior descending artery

LCX : left circumflex artery, RCA : right coronary artery

ACC/AHA : American College of Cardiology/American Heart Association

**Table 4.** Quantitative angiographic data

	Ticlopidine (n = 40)	Nadroparin (n = 41)
Lesion length (mm)	11.89 ± 6.48	12.07 ± 6.24
Before stenting RD (mm)	3.31 ± 0.52	3.27 ± 0.53
Immediately after stenting MLD (mm)	3.16 ± 0.52	3.10 ± 0.51
At 6-month follow-up (F/U) MLD (mm)	1.88 ± 0.78	1.73 ± 0.65
Acute gain (mm)	2.60 ± 0.59	2.46 ± 0.63
Late loss (mm)	1.35 ± 0.70	1.32 ± 0.69
Loss index	0.53 ± 0.29	0.56 ± 0.23
Restenosis rate (%)	9(36)	8(25.8)
F/U angiogram rate (%)	25(62.5)	31(68.9)

RD : Reference Diameter, MLD : Minimal Lumen Diameter

**Table 5.** In-hospital outcomes

	Ticlopidine (n = 40)	Nadroparin (n = 41)
Non-fatal MI	0	0
Death	0	0
Emergent CABG/re-PTCA	0	0
Subacute stent thrombosis	0	0
UGI bleeding (%)	1 ( 2.5)	0
None (%)	39 (97.5)	41 (100)

CABG : Coronary Artery Bypass Graft

PTCA : Percutaneous Transluminal Coronary Angioplasty

UGI : Upper Gastrointestinal Tract, P = NS

## ACC/AHA

B1 가 .  
가 가

(Table 3).

ticlopidine 3.31 ± 0.52, nadroparin 3.27 ± 0.53  
3.16 ± 0.52, 3.10 ± 0.51  
2.60 ± 0.59, 2.46 ± 0.63  
11.89 ± 6.48, 12.07 ± 6.24  
가 . ticlopidine 25(62.5%)  
, nadroparin 31(68.9%)  
1.88 ± 0.78, 1.73 ± 0.65,  
1.35 ± 0.70, 1.32 ± 0.69, loss index 0.53 ± 0.70, 0.56 ± 0.23  
ticlopidine 9(36%) nadroparin 8(25.8%)

**Table 6.** 6-months clinical outcomes

	Ticlopidine (n = 40)	Nadroparin (n = 41)
Recurrent ischemia (%)	1 ( 2.5)	3 ( 7.3)
Reinfarct (%)	0	0
Death (%)	0	0
TLR (%)	3 ( 7.5)	3 ( 7.3)
Event-free survival (%)	36 (90.0)	35 (85.4)

TLR ; Target Lesion Revascularization, P = NS

(Table 4). nadroparin  
ticlopidine  
, ticlopidine 2  
1 (Table 5). Nadroparin  
2 ticlo-  
pidine nadroparin  
6  
ticlopidine 1 e(2.5%),  
nadroparin 3 (7.3%)  
ticlopidine 3 (7.5%), nadroparin 3 (7.3%)  
. cardiac event free  
survival ticlopidine 90.0%, nadroparin  
85.4% (Table 6).

## 고 찰

aspirin ticlopidine nadroparin

가 .  
. Ticlo-  
pidine aspirin  
13)14)  
가  
. Ticlopidine  
가  
(11%), (4%), 가  
(3%), (3%), (3%), (3%),  
(4%) (1 2%)

가 weight heparin) 가 Lablanche  
 ticlopidine 22) nadroparin ERA trial<sup>10)</sup> RE -  
 가 20 30% DUCE trial<sup>11)</sup>  
 , matrix organization Cairns  
 15)16) 23)  
 (enoxaparine) 가  
 17) ,  
 , , 가  
 가 , 가  
 , 12) (nadro -  
 가 parin) 26% ticlopidine  
 36%  
 ,  
 , ticlopidine  
 가  
 antithrombin  
 antithrombin , ticlopidine  
 가 a, a  
 . Clowes 18)  
 6)7)18)  
 G1  
 19)  
 4000 5000 d  
 antithrombin  
 가  
 가 20)  
 ,  
 21)  
 nadroparin (Fraxiparine®) 4500 d  
 100%  
 ,  
 가 . Hanke 8)  
 Buchwald 9)  
 (low molecular

## 연구의 제한점

ticlopidine 40 , nadroparin 41  
 가  
 66%

## 요 약

### 연구배경 :

가  
 가

ticlopidine

대상 및 방법 :

ticlopidine 81 (85 ) nadroparin

ticlopidine nadroparin

50% . ti -

clopidine aspirin 200 mg/d ticlopidine 250 mg bid 1 nadroparin aspirin 200 mg/d nadroparin 200 IU/kg 1 2 1 6

결 과 :

1997 9 1998 5

81 (85 ) ticlopidine nadroparin

가

. Event - free survival

ticlopidine 36(90%) , nadroparin 35 (85.4%) . Ticlopidine nadroparin (1.35 ± 0.70 ; 1.32 ± 0.69), loss index(0.53 ± 0.70 ; 0.56 ± 0.23), (36%, 25.8%) 가 .

결 론 :

ticlopidine 가

ticlopidine

ticlopidine

중심 단어 : Ticlopidine.

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