

협심증 환자에서 관상동맥 풍선확장술 후 재협착에 대한 Tranilast의 임상 효과

정우곤 · 정명호 · 김계훈 · 주임관 · 이상록 · 박옥영 · 염주협 · 김 원
김주한 · 류제영 · 안영근 · 김영철 · 조정관 · 박종춘 · 강정채

The Clinical Effects of Tranilast on Restenosis after Percutaneous Transluminal Coronary Angioplasty

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ABSTRACT

Background and Objectives : Tranilast is an anti-allergic drug that suppresses the release of cytokines, such as platelet-derived growth factor, transforming growth factor- and interleukin-1 . It has recently become known to be effective in the prevention of restenosis following PTCA (percutaneous transluminal coronary angioplasty). **Subjects and Methods :** One hundred forty two consecutive patients with angina who underwent PTCA between Jan 1999 and Jul 2000 at Chonnam National University Hospital were analyzed prospectively. Thirty patients (Tranilast group : 60.8 ± 7.7 years, M : F = 22 : 8, 41 lesions) out of 48 who received 300 mg tranilast for 3 months following PTCA and who underwent follow-up CAG (coronary angiogram), were compared with 61 patients (Control group : 58.1 ± 11.0 years, M : F = 52 : 9, 82 lesions) out of 94, 94 who did not receive tranilast but did undergo follow-up CAG. **Results :** The restenosis rate per lesion was significantly lower in the Tranilast group than in the Control group on the 6-month follow-up CAG (Tranilast vs. Control group : 19.5% vs. 40.2%, $p = 0.021$). The minimal luminal diameter was significantly larger in the Tranilast group as compared to the Control group (1.99 ± 0.76 vs. 1.50 ± 0.83 mm $p = 0.002$). One patient of the Tranilast group suffered from liver dysfunction and stopped medication. **Conclusion :** The oral administration of tranilast is safe and effective in the prevention of restenosis following PTCA in patients with angina. (**Korean Circulation J 2001;31(12):1274-1280**)

KEY WORDS : Tranilast ; Restenosis ; Coronary disease ; Angioplasty, transluminal, percutaneous coronary.

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서 론

(PTCA : percutaneous transluminal coronary angioplasty)

¹⁾²⁾ PTCA

growth factor cytokine

³⁻⁵⁾

가

⁶⁾

Tranilast

가

(keloid)

⁷⁻⁹⁾

TREAT (Tranilast Restenosis Following Angioplasty Trial) study
tranilast가 platelet - derived growth factor (PDGF) transforming growth factor - TGF -

PTCA directional coronary atherectomy

¹⁰⁾¹¹⁾

TREAT study

255

nilast 3

14.7%,

tra -

acebo group)

46.5%

tranilast

tranilast PTCA

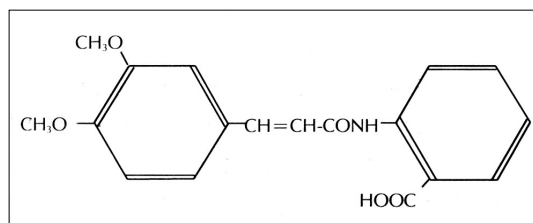


Fig. 1. Chemical structure of tranilast : N-(3,4-dimethoxycinnamoyl) anthranilic acid.

PTCA

tranilast

대상 및 방법

대상 환자 및 투약

1999 1

2000 7

American college of cardiology/American heart association (ACC/AHA)⁶⁾ type A B, Thrombolysis in Myocardial Infarction (TIMI) flow¹²⁾ grade 2 3, 50%

(PTCA)

142

(Fig. 2).

48

12

Tr -

anilast 300 mg

100 mg

(Tranilast group), 94

Tranilast

(Control group).

Tranilast

가

가

Tranilast

N - (3,4 - dimethoxycinnamoyl) anthranilic acid

327.34

(Fig. 1).

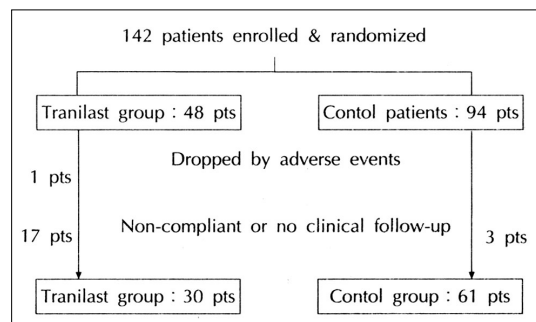


Fig. 2. Flow chart for study design.

관상동맥 풍선확장술 및 추적 관상동맥 조영술

통계 분석 방법

() Seldinger
6 French sheath
, ACC/
AHA , TIMI flow
edge detection 가 on-line quantit-
ative coronary angiogram(Philips H5000, Nether-
lands)

MS Windows® SPSS - PC 10.0(Statisti-
cal package for the Social Sciences, SPSS Inc. Ch-
icago, IL, USA) Student's t test Chi-
square test , p 0.05

결 과

대상 환자 및 병변의 특징

50%
PT -
CA heparin 7,
500 10,000 U
가
TIMI 가 2
25%

142
91 (64.0%) Tranilast 30
(60.8±7.7 , ; 22 , 41) 61
(58.1±11.0 , ; 52 , 82)
Tranilast 62.5%(30/48), 64.9%
(61/94)
ilast 48
1 (2%),
7 (14.9%) 12
10 (20.8%)

¹²⁾
6

94

추적 관찰

4
가

33 (35.1%)

(Table 1).

1
(33.3%),
45 (73.8%),
5 (8.2%)

Tranilast
19 (55.6%), 11
0 (0%)
11 (18.0%),
5 (8.2%)

일차 종결점 및 이차 종결점

12
(MACE : major adverse cardiac events)
(repeated reperfusion
therapy),
50%
50%

Tranilast
18 (43.9%), 13 (31.7%),
10 (24.4%), 35 (42.
7%), 22 (26.8%), 25 (30.5%)

PTCA
AHA Tranilast A 6 (14.6%), B1
29 (70.7%), B2 6 (14.6%), A 15

ACC/
AHA Tranilast A 6 (14.6%), B1
29 (70.7%), B2 6 (14.6%), A 15

(2.2%), B1 54 (54.1%), B2 13 (27.6%)
(Table 2).

PTCA TIMI I II
가 10 (24.4%), III가 31 (75.6%), II II
가 23 (28.0%), III가 59 (72.0%)

재협착률 및 최소혈관 내경

PTCA (reference diameter) Tr -
anilast 2.92 ± 0.50 mm, 2.85 ± 0.49
mm . PTCA
(minimal lumen diameter) Tra -
nilast 0.60 ± 0.35 mm, 2.66 ± 0.46 mm,
0.51 ± 0.37 mm, 2.52 ± 0.46 mm
Tranilast 41
8 (19.5%) 82
33 (40.2%) Tra -
nilast (p = 0.021, Fig.
2). Tra -

Table 1. Baseline clinical characteristics of tranilast group and control group

	Tranilast	Control	p
Number	30	61	
Age (years)	60.8 ± 7.7	58.1 ± 11.0	NS
Sex (%)			NS
Male	22 (73.3)	52 (85.2)	
Female	8 (26.7)	9 (14.8)	
Clinical diagnosis (%)			NS
Stable angina pectoris	7 (23.3)	21 (34.4)	
Unstable angina pectoris	23 (76.7)	40 (65.6)	
Risk factors (%)			
Smoking	13 (43.3)	32 (56.1)	NS
Hypertension	9 (30.0)	23 (40.4)	NS
Diabetes mellitus	7 (23.3)	14 (24.6)	NS
Dyslipidemia	6 (20.0)	13 (22.8)	NS
Ejection fraction (%)	63.05 ± 6.09	60.82 ± 7.39	NS
Concomitant medications (%)			NS
Nitrates	69	73.8	
Calcium channel blockers	73.3	68.9	
-Blockers	63.3	70.5	
Antiplatelets	90	93.4	

NS : not significant

nilast 1.99 ± 0.76 mm, 1.50 ± 0.83
mm Tranilast (p = 0.002,

Fig. 3, Table 3).

Initial gain Tranilast 2.05 ± 0.55 mm,
2.00 ± 0.63 mm
Late loss Tranilast 0.66 ± 0.68 mm,
1.01 ± 0.96 mm Tranilast
(p = 0.020), loss index Tranilast
0.32 ± 0.31, 0.47 ± 0.40 Tranilast

Table 2. Angiographic characteristics

	Tranilast	Control	p
Number	41	82	
Target lesion (%)			NS
Left anterior descending artery	18 (43.9)	35 (42.7)	
Right coronary artery	13 (31.7)	22 (26.8)	
Left circumflex artery	10 (24.4)	25 (30.5)	
Number of involved vessel (%)			NS
One vessel disease	19 (63.3)	45 (73.8)	
Two vessel disease	11 (36.7)	11 (18.0)	
Three vessel disease	0 (0)	5 (8.2)	
ACC/AHA types (%)			NS
A	6 (14.6)	15 (18.3)	
B ₁	29 (70.7)	54 (65.9)	
B ₂	6 (14.6)	13 (15.9)	
C	0 (0)	0 (0)	
Thrombolysis In Myocardial Infarction flow grade (%)			NS
II	10 (24.4)	23 (28.0)	
III	31 (75.6)	59 (72.0)	

ACC/AHA : American college of cardiology/American heart association, NS : not significant

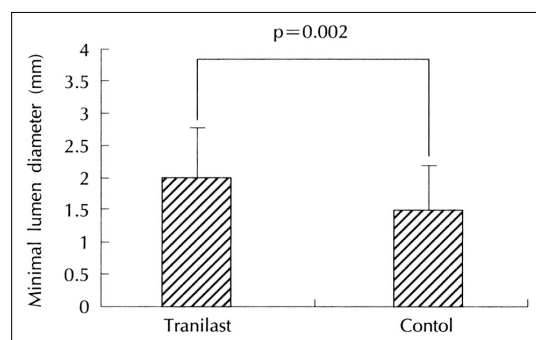


Fig. 3. Minimal lumen diameter at 6-month follow up was significantly larger in Tranilast group than that in Control group (1.99 ± 0.76 mm vs. 1.50 ± 0.83 mm, respectively).

Table 3. Quantitative coronary dimensions

	Tranilast	Control	p
Reference diameter (mm)	2.92 ± 0.50	2.85 ± 0.49	NS
Minimal lumen diameter (mm)			
Before PTCA	0.60 ± 0.35	0.51 ± 0.37	NS
After PTCA	2.66 ± 0.46	2.52 ± 0.46	NS
6-month follow-up	1.99 ± 0.76	1.50 ± 0.83	0.002
Initial gain (mm)	2.05 ± 0.55	2.00 ± 0.63	NS
Late loss (mm)	0.66 ± 0.68	1.01 ± 0.96	0.020
Loss index	0.32 ± 0.31	0.47 ± 0.40	0.024
Restenosis rate (%)	19.5	40.2	0.021
Lesion length (mm)	7.92 ± 1.66	8.33 ± 1.82	NS

PTCA : percutaneous transluminal coronary angioplasty, NS : not significant

Table 4. Major adverse cardiac events (MACE)

	Tranilast	Control	p
Patients (lesions)	30 (41)	61 (82)	
MACE at 12 months			
Myocardial infarction	1 (3.3%)	2 (6.6%)	NS
Repeated intervention	1 (2.4%)	3 (3.6%)	NS
Death	0	0	

NS : not significant

(p=0.024). (lesion length) (Table 3).

임상적 추적 결과

Tranilast 1 (3.3%), 2 (6.6%)가 Tranilast 1 (2.4%), 3 (3.6%), MA - CE Tranilast 2 (5.7%), 5 (10.2%) (Table 4).

부작용

Tranilast 48 1 (2.0%), 2 (4.1%) 12

고 찰

PTCA

Tranilast

free radical oxygen, keloid collagen, Tranilast, interleukin - 1, cyclooxy - genase - 2, tranilast cytokine - induced nitric oxide, Tranilast

cy - tokine PDGF, TGF - , interleukin - 1, trapidil, angiotensin

Takahashi tranilast, p21, waf1/cip1/sdi1, p53, retinoblastoma gene product(pRb) phosphorylation, pRb phosphorylation, cyclin - dependent kinases(CDK), p21, CDK, p21, CDK2/CDK4

Dzau, myointimal hyperplasia, angiotensin(ANG) I, Shiota, (conn - ective tissue - type mast cell), chy - mase, tranilast, chymase gene expression

Tranilast, PTCA, 600 mg, Tosuga, directional coronary atherectomy

300 mg

tranilast

가

가

tranilast

Prevention

of Restenosis with Tranilast and its Outcomes(PR-ESTO) trial

25) PRESTO trial

tranilast

Tranilast

26)

last 48 1 (2.0%)

, tranilast PTCA

가

■ 본 연구의 제한점

tranilast가

가

stent

가 가

요 약

배경 및 목적 :

Tranilast

가 (keloid)

, Percutaneous Transluminal Coronary Angio-plasty(PTCA)

Tranilast PTCA

방 법 :

1999 9 2000 7 PTCA

142

12 Tranilast(300 mg/

d) 48

30 (Tranilast , 41 , 60.8 ± 7.7 , :

=22 : 8) Tranilast 94

61 (, 82 ,

58.1 ± 11.0 , : =52 : 9)

PTCA Tranilast

결 과 :

PTCA 6 Tranilast

(1.99 ± 0.76 mm vs. 1.50 ± 0.83 mm, $p=0.002$).

Tranilast 19.5%, 40.2%

Tranilast

($p=0.021$). Tranilast 48

1 (2.0%),

7 (14.9%)

12

결 론 :

PTCA 12 300 mg Tranilast

중심 단어 : Tranilast ; ;

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