

급성 심근경색증에서 혈전용해제 투여 전후 혈액응고 및 혈전용해능의 비교연구

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The Changes in Coagulation and Fibrinolytic Activities in Acute Myocardial Infarction Patients Treated with Recombinant Tissue Plasminogen Activator and Urokinase

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ABSTRACT

Background : The coagulation and fibrinolytic activities increase in the setting of acute myocardial infarction (AMI) and has been shown to increase further after the administration of thrombolytic agents. The reocclusion rate was slightly higher in patients with recombinant tissue type plasminogen activator (rt-PA) than urokinase (UK). However, there are few studies on serial changes in coagulation and fibrinolytic activities during the thrombolytic therapy. **Methods** : Twenty five AMI patients who visited Yongdong Severance Hospital from August 1996 to August 1997 were recruited. They were randomized two groups either double bolus UK or accelerated rt-PA. Plasma levels of fibrinogen, thrombin-antithrombin complex (TAT), plasmin-2plasmin inhibitor complex (PIC), activities of protein C and protein S were checked before and 3, 12, 24hrs and 7days after the thrombolytic therapy. **Results** : Plasma level of fibrinogen was decreased 3 and 12hrs after the initiation of thrombolytic therapy in both groups ($p < 0.05$) however, the fibrinogen level in UK treated group (59.9 ± 33.5 mg/dl) was decreased than rt-PA treated group (198.2 ± 64.3 mg/dl) at 3hrs after thrombolytic therapy ($p < 0.05$). Activities of protein C and protein S were increased at 3hrs after thrombolytic therapy in both groups and no difference was noticed between UK and rt-PA group. Concentrations of TAT and PIC were increased in both groups even before the thrombolytic therapy was initiated. The increment of TAT level was larger in rt-PA group (21.7 ± 16.1 , 8.9 ± 5.4 ng/mL) compared with UK group (15.0 ± 17.9 , 4.6 ± 1.9 ng/mL) at 3 and 12 hrs after thrombolytic therapy ($p < 0.05$). PIC level was significantly increased at 3 and 12 hrs after the treatment in both groups and no difference was noted between UK and rt-PA group. **Conclusion** : Both coagulation and fibrinolytic activities, activated already before thrombolytic therapy, were further augmented after thrombolytic therapy in AMI patients. The increment of fibrinolytic activity showed no significant difference between UK and rt-PA treated group. However the coagulation activity in rt-PA treated group was increased more than UK treated group. (Korean Circulation J 1998;28(4):700-706)

KEY WORDS : Thrombolysis rt-PA · Urokinase · Thrombin-antithrombin complex(TAT) · Plasmin- 2 plasmin inhibitor complex (PIC) · Protein C · Protein S.

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서 론

대상 및 방법

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(Table 1). cerin 30 , 6

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혈전용해제 치료 aspirin 200 mg Ur -

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30% 가 5)6)

가 ,

urokinase(UK, do -

uble chain form) recombinant tissue type plas -

minogen activator(rt - PA)

fibrinogen, protein C, protein S, thro -

mbin - antithrombin complex(TAT), plasmin -

2 - plasmin inhibitor complex(PIC)

Table 1. Clinical characteristics of the patients

	Urokinase (n = 12)	rt-PA (n = 13)
Age (years)	50.5 ± 7.9	58.2 ± 11.6
Sex (M/F)	11/1	11/2
Smoking (PY)	26.8 ± 16.2	27.9 ± 15.2
Underlying disease		
Hypertension		
DM		
T.cholesterol (mg/dl)	211.3 ± 35.7	200.9 ± 27.7
HDL-chol (mg/dl)	37.4 ± 5.6	39.4 ± 8.3
TG (mg/dl)	151.3 ± 67.5	160.0 ± 60.3
MI location		
Anterior		
Inferior		
Lateral		
Time from onset of chest pain to thrombolytic therapy (min)	137.9 ± 78.6	151.2 ± 93.9

okinase rt - PA Urokinase
 150 Kg 2
 30 300
 rt - PA 15 mg 30
 Kg 0.75 mg 50 mg
 1 Kg 0.5 mg
 100 mg
 heparin 5000
 aPTT 1.5 2 가
 5

(Table 1).

섬유소원의 변화

가 (250.6 ± 100.6, 255.8 ± 128.2 mg/dl)
 3 12
 3 UK 59.9 ± 33.5 mg/dl
 rt - PA 198.2 ± 64.3 mg/dl
 (p<0.05), 24 가 7
 (Table 2, Fig. 1).

혈액채취

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 , 12 , 24 , 7 sodium citrate가
 2 4
 1500 g(3000 rpm) 10
 . fibrinogen Clauss , pro -
 tein C,protein S activity stachrome protein C,
 protein S(Diagnosta Stago, France)
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 . TAT PIC Enzyg -
 nost - TAT(Behringwerke, Marburg, Germany), En -
 zygност - PAP(Behringwerke, Marburg, Germany)

통 계

SPSS/PC(+) program stu -
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결 과

대상환자의 특성

25 (22, 3)
 12 UK (11,
 1, 50.5 ± 7.9), 13 rt - PA
 11, 2, 58.2 ± 11.6).
 UK 137.9 ± 78.6 , rt - PA
 151.2 ± 93.9 7 10
 TIMI flow grade,

Protein C, protein S 활성도의 변화

protein C, protein S
 3 가 (p<0.05),
 protein C, protein S
 (Table 3).

Table 2. Sequential changes in fibrinogen level

Fibrinogen (mg/dl)		
Before	UK	250.6 ± 100.6
	rt-PA	255.8 ± 128.2
3hrs after	UK	59.9 ± 33.5 [†]
	rt-PA	198.2 ± 64.3*
12hrs after	UK	95.7 ± 9.3
	rt-PA	162.3 ± 42.3
24hrs after	UK	175.2 ± 129.4 [†]
	rt-PA	245.9 ± 102.1
7ds after	UK	330.6 ± 115.0
	rt-PA	433.5 ± 210.4 [†]

[†] : p<0.05, compared with UK treated group

* : p<0.05, compared with the level before thrombolytic therapy

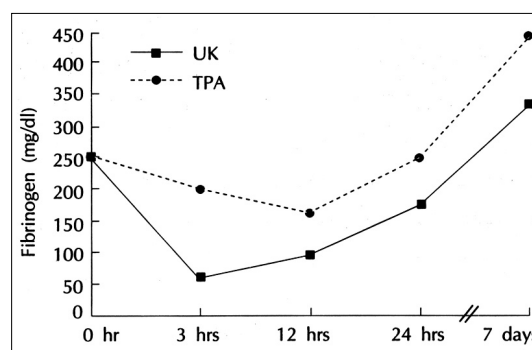


Fig. 1. Sequential changes in fibrinogen level in AMI patients with thrombolytic therapy.

Table 3. Sequential changes in protein C & protein S level

		Protein C (%)	Protein S (%)
Before	UK	102.3 ± 16.7	101.8 ± 27.3
	rt-PA	99.5 ± 19.7	93.6 ± 33.0
3hrs after	UK	129.4 ± 23.6 [†]	131.1 ± 28.3 [†]
	rt-PA	117.0 ± 34.0 [†]	112.2 ± 29.2 [†]
12hrs after	UK	112.0 ± 24.4	116.8 ± 26.1
	rt-PA	91.1 ± 17.5	91.8 ± 20.1
24hrs after	UK	100.3 ± 21.7	97.2 ± 21.0
	rt-PA	92.2 ± 21.8	87.6 ± 20.3
7ds after	UK	95.9 ± 17.4	107.5 ± 17.7
	rt-PA	95.8 ± 11.5	93.8 ± 20.3

[†] : p<0.05, compared with the level before thrombolytic therapy

Table 4. Sequential changes in TAT & PIC level

		TAT (ng/mL)	PIC (ng/mL)
Before	UK	4.8 ± 2.3	2206.3 ± 2137.5
	rt-PA	6.2 ± 4.8	2747.7 ± 2231.6
3hrs after	UK	15.0 ± 17.9 [†]	5073.0 ± 163.8 [†]
	rt-PA	21.7 ± 16.3 ^{*†}	5048.9 ± 145.1 [†]
12hrs after	UK	4.6 ± 1.9	4618.2 ± 955.4 [†]
	rt-PA	8.9 ± 5.4 [*]	3891.6 ± 1563.9
24hrs after	UK	3.5 ± 1.5 [†]	1004.6 ± 1079.0
	rt-PA	6.9 ± 5.8	648.6 ± 391.2 [†]
7ds after	UK	3.8 ± 1.0	536.4 ± 275.7
	rt-PA	4.8 ± 2.1	738.7 ± 337.6 [†]

^{*} : p<0.05, compared with UK treated group

[†] : p<0.05, compared with the level before thrombolytic therapy

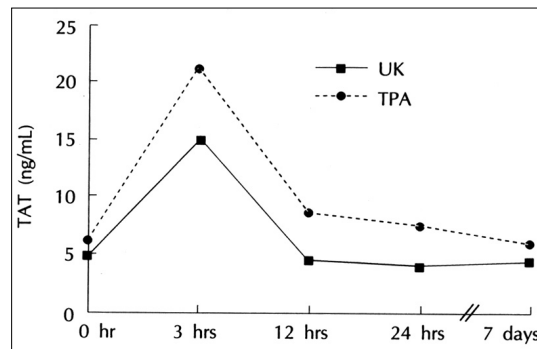


Fig. 2. Sequential changes in TAT level in AMI patients with thrombolytic therapy.

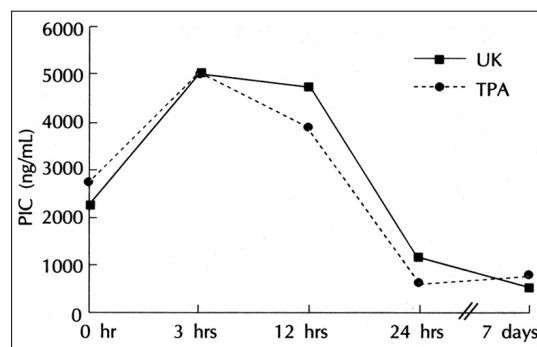


Fig. 3. Sequential changes in PIC level in AMI patients with thrombolytic therapy.

4 6

TAT와 PIC 농도의 변화

TAT PIC
가 (Table 4) TAT
3 가
(p<0.05), 3 12 UK (15.0 ± 17.9, 4.6 ± 1.9 ng/mL)
8.9 ± 5.4 ng/mL) rt - PA (21.7 ± 16.3, 8.9 ± 5.4 ng/mL)
2). PIC 가 (p<0.05),
(Fig. 3).

고 안

Dewood 7)

8)9)

가

1, 2, 3
streptoki -
nase urokinase(UK) 1
rt - PA single chain urokinase
type plasminogen activator(scu - PA) 2
anisoyla -
ted plasminogen - streptokinase activator complex
(APSAC) 3 10)
UK rt - PA UK pla -
sminogen plasmin
가 rt - PA cofactor

plasminogen 3 가 24

plasmin 11)

protein C, protein S (Table 3).

UK 가 3 UK rt - PA 12) (Table 2, Fig. 1).

plasminogen activator inhibitor 1(PAI - 1) 13)

가 t - PA 가

2 가

가 ,

14)15)

3 6 가

16) 가

24 48 17)

16)17) 가 3 7

24 , 25)

protein C vitamin K - thrombin - C thrombin 27 - 33)

thrombomodulin complex (activated protein C) , 25%, 15 5 15%

C protein S 33)

18) plasminogen activator inhibitor Goto 22)

19 - 21) TAT PIC 가 (Table 4)

thrombin 가 , plasmin TAT

가 protein C, protein S 22) PIC 가 3 UK rt - PA 가 ,

1
27-33)

3

TAT

가 15

1

TAT

3

PIC 12

plasmin

12

3

(Figs. 2

PIC

and 3).

가 plasmin

가 rt-PA TAT

가 3 12

thrombin

prothrombin

plasmin

thrombin

UK

thrombin

rt-PA

heparin aspirin

7 10

TAT, PIC

요 약

연구배경 :

가 , .

가

방 법 :

1996 8 1997 8

(Urokinase or rt-PA)

25

3 , 12 , 24 , 7 fibrin -
ogen, protein C, protein S, thrombin - antithrombin
complex(TAT), plasmin - plasmin inhibitor
complex(PIC)

결 과 :

1)

가 (250.6 ± 100.6, 255.8 ± 128.2 mg/
dl) 3 12

3

UK 59.9 ± 33.5 mg/dl

rt-PA

198.2 ± 64.3 mg/dl

7

(p<0.05), 24 가

2)

protein C, protein S

3 가 가

(p<0.05),

3) TAT PIC

가 TAT 3

가 (p<0.05),

UK (15.0 ± 17.9, 4.6 ±

1.9 ng/mL) rt-PA (21.7 ± 16.3, 8.9 ± 5.4

ng/mL) 가 (p<0.05). PIC

3 12

가 (p<0.05),

결 론 :

가 (UK rt-PA)

, rt-PA

UK

thrombin 가

UK

중심 단어 : Urokinase · rt-PA · TAT ·

PIC · Protein C · Protein S.

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