

급성 심근경색증 환자 혈액에서 분리 배양한 단핵구의 Tumor Necrosis Factor- α 및 Interferon- γ 의 분비 기능에 관한 연구

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Tumor Necrosis Factor- α and Interferon- γ Secretory Capacity of Mononuclear Leukocytes after Incubation in Patient with Acute Myocardial Infarction

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ABSTRACT

Background : Studies of human coronary plaque specimens have shown that T lymphocytes and macrophages are present in all types of lesions, from fatty streaks to advanced plaques. There is growing evidence for a pathogenic role for immune response in progression of atherosclerosis. This study was designed to investigate cytokine production by mononuclear leukocytes from patients with myocardial infarction. **Method** : We measured the kinetics of secretion of tumor necrosis factor- α (TNF- α) and interferon- γ (IFN- γ) by mononuclear leukocytes from 8 control subjects and 12 patients with acute myocardial infarction. Mononuclear leukocytes were isolated and incubated with plant lectin mitogen concanavalin-A for 24 and 48 hours. TNF- α and IFN- γ secretions were measured by ELISA. **Results** : There were no significant differences between TNF- α and IFN- γ secretions by mononuclear leukocytes at and before 24 hours of incubation from both patients and control subjects, but TNF- α and IFN- γ secretions at 48 hours of incubation were higher ($p < 0.005$, $p < 0.05$) in patients when compared with control subjects. TNF- α and IFN- γ secretions by mononuclear leukocytes after incubation correlated with the peak level of creatine phosphokinase (CK) and CK-MB. **Conclusion** : Increased cytokine secretory capacity of mononuclear leukocytes may be due to the acute inflammatory response of myocardial infarction. Further trials may be needed to determine the effects of increase in secretory capacity of mononuclear leukocytes before myocardial infarction. (*Korean Circulation J* 1998;28(4):586-591)

KEY WORDS : Myocardial infarction · Cytokine · TNF- α · IFN- γ

서 론

1

1)

: 1997 11 8

: 1998 4 27

: , 657

T 가 T (subtype)

2-4) recombinant DNA

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1)

가
T 1
cytokine
1-4)
Judkin's
cytokine tumor necrosis
factor - (TNF -) interferon - (IFN -)
interleukin - 1(IL - 1) . TNF -
가,
5) IFN - TNF -
T
class II MHC 2 2.5%
intracellular adhesion molecule(ICAM -
1) T (ad - herburg, MD) RPMI 1640(Sigma, St.L -
hesion) 가 ,
6)
가 cyt - nicillin, Stepromycin)가 Tc199 ml 2 x
okine 가 10⁶ Concanavalin A(Con A)
가 7) 5% CO₂, 37 48
Con A(100 µg/ml) 가 24
24 , 48 TNF - 48
IFN - 400 g 10
70

대상 및 방법

대 상
12 (8, 4)
8 (3, 5)
2가
심장검사
3
(fractional shortening)
nm
TNF - IFN - 2
TNF -
15.6 pg/ml 4.4 pg/ml
E - toxoate
assay system(Sigma)
면역혈청학적 검사
TNF - IFN - EL -
ISA kit(Quantikine, R&D system, USA)
TNF -
20 INF - 40
2 2
kit
450

Table 1. Clinical characteristics

	Control (n = 8)	MI (n = 12)	p value
Age (yrs, mean \pm SD)	57.2 \pm 4.7	56.3 \pm 5.2	NS
Sex (Male/Female)	3/5	9/3	NS
Smoking (%)	1 (12.5)	7 (58.3)	NS
Hypertension (%)	2 (25.0)	5 (41.7)	NS
Total cholesterol (mg/dl)	197.5 \pm 30.6	184.2 \pm 29.7	NS
Diabetes mellitus (%)	2 (25.0)	3 (25.0)	NS
Peak CK-MB (IU/L, mean \pm SD)		297 \pm 255.3	
Peak CK (IU/L, mean \pm SD)		1055.2 \pm 965.3	

MI : myocardial infarction

Table 2. M-mode echocardiographic findings in study groups

	Control (n = 8)	Myocardial infarction (n = 12)	p value
LVDs (Cm)	2.68 \pm 0.65	3.52 \pm 0.73	<0.01
LVDd (Cm)	4.58 \pm 0.60	4.68 \pm 0.63	NS
FS (%)	41.1 \pm 8.18	28.1 \pm 11.62	<0.005

LVDs : left ventricular systolic dimension, LVDd : left ventricular diastolic dimension
FS : fractional shortening

, IFN - 15.6 pg/ml
3.0 pg/ml .

통계처리

\pm
SPSS PC⁺ (version 3.0)
unpaired t - test, Chi - square
method Person corr -
elation . p 0.05

결 과

임상적 소견

, , cholesterol
가
(p<0.001, p<
0.05)(Table 1). creatinine
phosphokinase(CK) - MB 297 \pm 255.3 IU/L
CK 1055.2 \pm 965.3 IU/L .
12 11 (Urokinase 7 , tPA
4) .

Table 3. Cardiac catheterization findings in study groups

	Control (n = 8)	Myocardial infarction (n = 12)	p value
Pulmonary artery (mean mmHg)	15.5 \pm 3.52	15.5 \pm 3.27	NS
PCWP (mmHg)	10.4 \pm 4.27	9.52 \pm 2.93	NS
Aorta (mmHg)	128.7 \pm 30.21	117.8 \pm 30.12	NS
Cardiac index (L/min/m ²)	2.82 \pm 0.47	2.92 \pm 0.44	NS

PCWP : pulmonary capillary wedge pressure

Table 4. TNF- level after incubation of mononuclear leukocytes

	Control (n = 8)	Myocardial infarction (n = 12)
Without Con.A (pg/mL)	5.27 \pm 1.73	6.45 \pm 1.81
24 hr (pg/mL)	702.8 \pm 793.2	928.8 \pm 1251.7
48 hr (pg/mL)	115.1 \pm 91.5	1746.4 \pm 1100.5*

*p<0.005

심초음파도 소견 및 심도자 소견

M
3.52 \pm 0.73 cm 2.68 \pm 0.65
cm (p<0.01),
28.1 \pm 11.62% 41.1 \pm 8.18%
(p<0.005),
가 (Table 2).

, 가
(Table 3).

Con.A 투여유무와 시간경과에 따른 배양액의 TNF- α
치 및 INF- γ 치
Con.A TNF - Con.A

Table 5. IFN- γ level after incubation of mononuclear leukocytes

	Control (n = 8)	Myocardial infarction (n = 12)
Without Con.A (pg/mL)	10.47 \pm 2.75	11.68 \pm 3.25
24 hr (pg/mL)	691.9 \pm 988.4	1926.0 \pm 1547.7
48 hr (pg/mL)	275.3 \pm 199.4	1967.3 \pm 1842.0*

*p<0.05

Table 6. Correlation between TNF- α level after 24 hour incubation and clinical and hemodynamic data

	Correlation coefficient	P value
Peak CK-MB	0.77	0.02
Peak CK	0.47	NS
Pulmonary capillary wedge	0.15	NS
Fractional shortening	- 0.28	NS
Cardiac index	0.04	NS

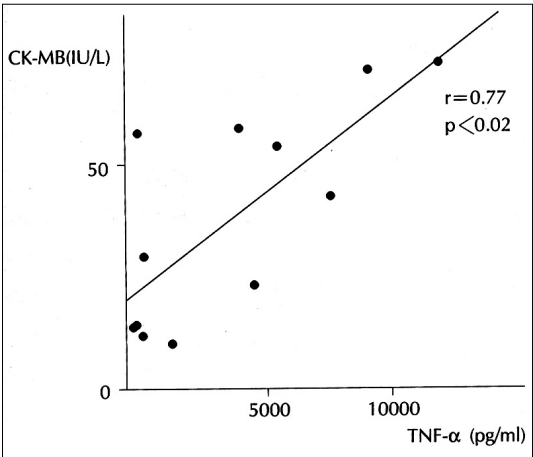


Fig. 1. Correlation between TNF- α level after 24 hour incubation and peak CK-MB level.

24 TNF - α 가
Con.A 48
115.1 \pm 91.5 pg/ml, 1746.4 \pm
1100.5 pg/ml
(p<0.005)(Table 4). Con.A
IFN - γ Con.A 24 IFN - γ
가 . Con.A
48 275.3 \pm 199.4 pg/ml,
1967.3 \pm 1842.0 pg/ml
(p<0.05)(Table 5).

Table 7. Correlation between IFN- γ level after 24 hour incubation and clinical and hemodynamic data

	Correlation coefficient	P value
Peak CK-MB	0.74	0.03
Peak CK	0.81	0.009
Pulmonary capillary wedge	0.26	NS
Fractional shortening	- 0.15	NS
Cardiac index	0.19	NS

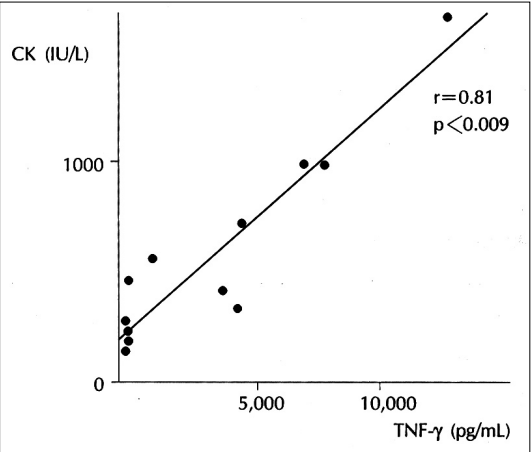


Fig. 2. Correlation between IFN- γ level after 24 hour incubation and peak CK level.

Table 8. Correlation between IFN- γ level after 48 hour incubation and clinical and hemodynamic data

	Correlation coefficient	P value
Peak CK-MB	0.72	0.03
Peak CK	0.89	0.001
Pulmonary capillary wedge	0.32	NS
Fractional shortening	- 0.11	NS
Cardiac index	0.17	NS

단핵구 배양 후 TNF- α 측정치 및 IFN- γ 측정치와 임상적 검사소견과의 상관관계

Con.A 24
TNF - α CK - MB
0.77(p<0.02) 가 (Table 6)
(Fig. 1). Con.A 24 IFN - γ
CK - MB 0.74(p<0.03),
CK 0.81(p<0.09)
가 (Table 7)(Fig. 2), Con.A 48

IFN - CK - MB CK cytokine molecule
0.72(p<0.03), 0.89(p<0.001)
가 (Table 8). Barath 5) TNF - 가 65 TNF -
고 찰 TNF -
가 TNF -
recombinant DNA TNF - 7)11) TNF -
1 - 4) IL - 1 TNF -
8) T T cytokine TNF -
1 - 10) plasminogen activator inhibitor(PAI)
cholesterol , , , 가
prostaglandin I 2 가
2) Jonasson 4) procoagulant 6)12) T
(molecule) TNF -
가 fibrous 가 6)7) TNF -
cap T T₃ 가 IFN - 가
Hansson 2) T CD₃ cluster cytokine T
가 fibrous cap fibrous cap TNF -
T 가 6) T
class II MHC 2)7) CD₄⁺⁺T -
ICAM T 가
cell substrate 6)7) nitric oxide
T (epitheloid cell) 6)
T 2가 가 1) T cyt - cytokine
가 T okine 가
LDL 가 LDL 가 13)
1) cytokine TNF - ,
가 IL - 1 7) IFN - 24 48 TNF -
cytokine cytokine target Con.A 24

cytokine 가 48 , cytokine cytokine
 24 48 cytokine 가
 가 , 48 cytokine 가
 Con.A cytokine 가

결 론 : cytokine cytokine
 가 ,
 가

cytokine CK - MB CK
 가 T

중심 단어 : Cytokine · TNF - · IFN -

가 cyt -
 okine 가
 cytokine 가
 가
 요 약

연구배경 :

cytokine cytok -
 ine TNF - IFN -
 cytokine 가
 가
 방 법 :

12 (8, 4)
 8 (3, 5)

concanavalin A 가 24 , 48
 TNF - IFN - ELISA kit

결 과 :

Con.A Con.A
 24 TNF - IFN -
 가 Con.A 48
 TNF - IFN -
 TNF - IFN - CK
 CK - MB 가

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