

## 저산소증의 조건여부가 재관류 부정맥에 미치는 영향

정 남 식

\*

, 나홍식 · 남숙현 · 오동주\*

= Abstract =

**The Effect of Hypoxic-Preconditioning on the Reperfusion-Induced Arrhythmias in the Cat Hearts****Namsik Chung, M.D.***Cardiology Division, Yonsei Cardiovascular Center, College of Medicine, Yonsei University, Seoul, Korea***Heung-Sik Na, M.D., Sook-Hyun Nahm, M.D., Dong-Joo Oh, M.D.\****Departments of Physiology, Internal Medicine, \* Korea University, College of Medicine, Seoul, Korea*

**Background** : Ischemic preconditioning(a prior short period of coronary artery occlusion) has been known to have protective effects on ischemia-induced myocardial injury. The purpose of this study was to investigate the effects of hypoxic preconditioning or ischemic preconditioning on the reperfusion-induced ventricular arrhythmias after a prolonged period of coronary artery occlusion in the cat hearts.

**Method** : Thirty-six cats were anesthetized with a -chloralose(60mg/kg, I.P.) and prepared for left anterior descending coronary artery(LAD) occlusion after thoracotomy.

A 10minute occlusion of LAD was used with a subsequent 3minute reperfusion period as ischemic-preconditioning before a 20minute occlusion of LAD and subsequent reperfusion in 10cats. Hypoxic-preconditioning was done according to the identical procedure as ischemic-preconditioning but using hypoventilation and normal ventilation instead of occlusion and reperfusion, respectively, in 12 cats. The remaining 14 were used as controls following occlusion of LAD for 20minutes and subsequent reperfusion.

**Results** : Two preconditionings significantly reduced the severity of ventricular arrhythmias during the reperfusion period following a 20 minute occlusion of LAD compared with controls.

Ischemic-proeconditioning reduced the frequency of ventricular premature beats(VPBs) during a 20minute occlusion of LAD with absence of significant fatal ventricular arrhythmias such as ventricular tachycardia or fibrillation compared with controls. Hypoxic-preconditioning failed to reduced the frequency of VPBs during a 20minute occlusion of LAD where as ventricular fibrillation

was totally suppressed and ventricular tachycardia occurred in one cat.

**Conclusion :** These data suggest that 1) not only ischemic-preconditioning but also hypoxic-preconditioning alleviates the reperfusion-induced arrhythmias : 2) the mechanism of the reperfusion-induced arrhythmias is different from that of the ischemia-induced arrhythmias : 3) hypoxic-preconditioning allows one to perform further studies regarding the mechanisms of preconditioning.

**KEY WORDS :** Preconditioning · Hypoxia · Reperfusion arrhythmia.

# 서 론

가

## 실 험 방 법

1-4),  
 1970 (oxygen paradox) (2.5 4kg) 36  
 가  
 Rosenkranz 가 5) 1983 - chloralose 60mg/kg  
 Buckberg<sup>6)</sup> 가  
 (Physiography 7P4J, Grass)  
 lead  
 가  
 7-9) (Respirator, Model645, Harvard  
 apparatus)  
 pancuronium bromide(Miobloc<sup>®</sup>) 0.5  
 2.0mg  
 10-13)  
 14-16)  
 (Capnometer, Model 2200, TMM)  
 17) 29 36mmHg가

### 1. 실험조작

가

2 5

가

가

### 1) 대조군

가

18-22)

5

6 0 silk 20

14

2) 허혈 조건부여군

10 3  
20 5  
10 (Fig. 1).

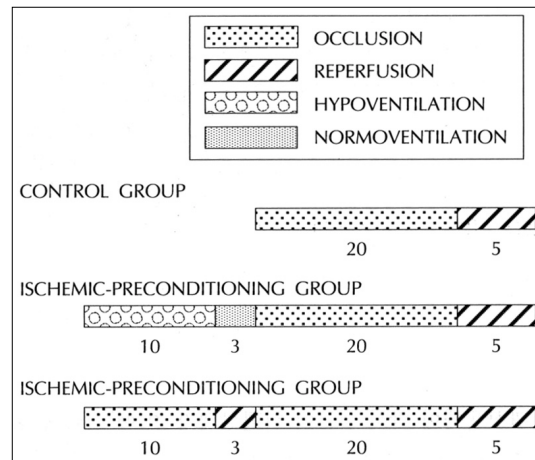
3) 저산소증 보건의부여군

3 5 10  
20 5  
12 4 ( , 10  
, 3  
20 )  
(Fig. 1).

2. 부정맥의 평가

1)  
2) 3)  
4) Lam -  
beth convention 23)

3. 통계적 처리



**Fig. 1.** Experimental design for preconditioning studies. In the ischemic-preconditioning group, animals consecutively underwent as following : A 10 minute occlusion of left anterior descending coronary artery for preconditioning, 3 minutes of reperfusion, a sustained 20 minute occlusion, and 5 minutes of reperfusion. In the hypoxic-preconditioning group, the same time-course as to the ischemic-preconditioning group was used as followings : A 10 minute hypoventilation, 3 minutes of normal respiration, a sustained 20 minute occlusion, and 5 minutes of reperfusion. A 20 minute occlusion followed by reperfusion was used as controls for comparison with preconditioning groups.

**Table 1.** The effect of ischemic-preconditioning and hypoxic-preconditioning on the severity of ischemia-induced arrhythmias during a 20 minute occlusion of left anterior descending coronary artery and that of reperfusion-induced arrhythmias

No. of animals	Ischemia (20min)		Reperfusion			
	No. of VPBs	Duration of VT(sec)	No. of VPBs	Duration of VT(sec)	Onset of VF(sec)	Mortality
1	58	15	13	15	34	DEAD
2	156	70	1	4	17	ALIVE
3	184	29	20	7	20	ALIVE
4	132	32	42	3	-	ALIVE
5	19	-	8	-	15	DEAD
6	220	-	21	39	56	DEAD
7	3	-	12	47	-	ALIVE
8	5	-	2	8	30	DEAD
9	-	-	24	4	26	DEAD
10	-	-	2	19	32	DEAD
11	53	-	30	11	31	DEAD
12	217	-	18	8	19	DEAD
13	122	58	6	-	24	DEAD
14	125	24	-	-	12	DEAD
Mean	92.5	15.6	14.2	11.8	22.6	71%
S.E.	22.1	6.0	3.3	3.9	3.9	

Table 1. Continued

		Ischemic-preconditioning (10min)		Ischemia(20min)		Reperfusion			Mortality
No. of animals		No. of VPBs	Duration of VT(sec)	No. of VPBs	Duration of VT(sec)	No. of VPBs	Duration of VT(sec)	Onset of VF(sec)	
1		329	-	8	-	17	-	9	DEAD
2		-	-	-	-	-	-	-	ALIVE
3		13	12	6	-	-	4	5	DEAD
4		-	-	39	-	-	5	20	DAED
5		270	20	36	-	8	17	-	ALIVE
6		49	-	3	-	-	-	-	ALIVE
7		2	-	11	-	13	90	-	ALIVE
8		100	24	4	-	13	-	-	ALIVE
9		2	-	4	-	43	3	-	ALIVE
10		2	-	9	-	2	-	-	ALIVE
Mean		76.6	5.6	12.0	0	9.6	11.9	3.4	
S.E.		38.7	3.0	4.4	0.0	4.2	8.8	2.1	30%

C.

		Hypoxic-preconditioning(10min)		Ischemia(20min)		Reperfusion			Mortality
No. of animals		No. of VPBs	Duration of VT(sec)	No. of VPBs	Duration of VT(sec)	No. of VPBs	Duration of VT(sec)	Onset of VF(sec)	
1		106	-	3	-	-	3	-	ALIVE
2		16	-	270	32	4	39	-	ALIVE
3		60	54	6	-	-	-	6	DAED
4		7	2	442	-	258	10	-	ALIVE
5		9	-	96	-	5	-	-	ALIVE
6		2	-	3	-	-	-	1	ALIVE
7		2	-	48	-	48	120	-	ALIVE
8		4	-	4	-	2	-	-	ALIVE
9		38	-	140	-	12	22	-	ALIVE
10		54	-	-	-	-	-	-	ALIVE
		10	-	89	-	-	-	4	DAED
		18	-	65	-	18	-	-	ALIVE
Mean		27.2	4.7	97.2	3.3	28.9	16.2	0.9	
S.E.		9.2	4.5	38.8	2.7	21.2	10.1	0.6	25%

A : control group

VPBs : ventricular premature beats

B : ischemic-preconditioning group

VT : Ventricular tachycardia

C : hypoxic-preconditioning group

VF : ventricular fibrillation

±  
Mann - Whitney U  
2

12  
92.5 ± 22.1 (Table 1A, Fig. 2).

6  
15.6 ± 6.0 (Table 1A).

실험 결과

1. 대조군

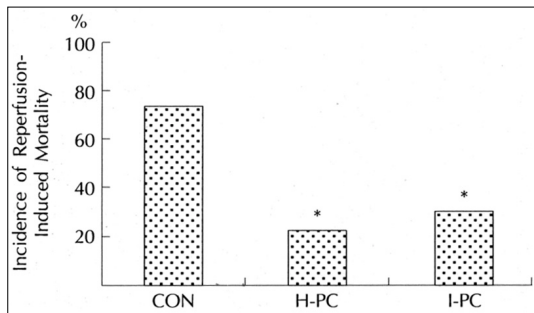
14  
20  
3.9  
12

13  
14.2 ± 3.3 (Table 1A, Fig. 3).

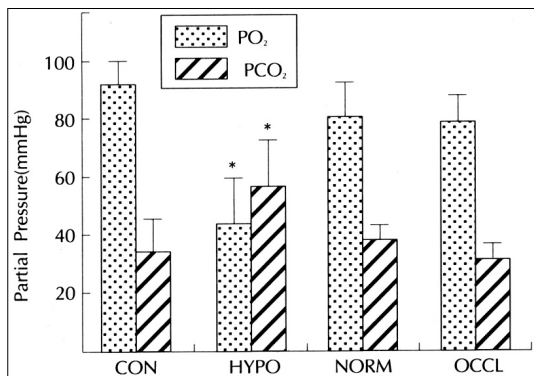
11  
11.8 ± 3.9 (Table 1A, Fig. 3).

10  
22.6 ± 3.9





**Fig. 4.** Relation between preconditioning and incidence of mortality occurring during 5minutes of reperfusion following a20minute occlusion of left anterior descending coronary artery. Both ischemic-preconditioning and hypoxic-preconditioning reduced the incidence of mortality significantly. CON : control group, I-PC : Ischemic-preconditioning grop, H-PC : hypoxic-preconditioning group \*p<.05 for preconditioning vs control group.



**Fig. 5.** The change of partial pressure of oxygen and carbon dioxide according to the hypoventilation and subsequent normal respiration followed by prolonged occlusion or left anterior descending coronary artery. The partial pressure of oxygen was significantly decreased by hypoventilation, where as the partial pressure of carbon dioxide was significantly increased. However, partial pressure of carbon dioxide was recovered after normal respiration for 3minutes. CON : control group. HYPO : hypoventilation for 5minutes. NORM : normal respiration for 3minutes. OCCL : A 20minute occlusion of left anterior descending coronary artery. \*p<.05 for hypoventilation vs control.

#### 4. 저산소증 조건부여군의 산소와 이산화탄소 분압

PO<sub>2</sub> 93.8 ± 6.3  
 mmHg, PCO<sub>2</sub> 33.6 ± 3.9mmHg 10  
 5 / PO<sub>2</sub> 42.3 ± 12.8  
 mmHg, PCO<sub>2</sub> 55.7 ± 9.0mmHg ,  
 3 PO<sub>2</sub> 79.7 ± 4.8  
 mmHg, PCO<sub>2</sub> 39.5 ± 3.6mmHg . 20  
 PO<sub>2</sub>  
 85 ± 4.5mmHg, PCO<sub>2</sub> 30.2 ± 2.5mmHg(Fig. 5).

#### 고찰

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24),  
 26,27)

25),

가

28.9 ± 21.2

(Table 1C, Fig. 3).

5

16.2 ± 10.1

3

28 - 30)

0.9 ± 0.6

5

(p<0.05, Table

20

1C, Fig. 3, 4).

가 5 5 4 ATP가

가 37) Murry 41) 15 가

가 , Mac Donald 42) 5 가

가 가 가 pH Na<sup>+</sup> - K<sup>+</sup> pump가 10

가 Na<sup>+</sup> Na<sup>+</sup> - Ca<sup>++</sup> Ca<sup>++</sup> 가 가 Donnelly 43)

가 pH가 Na<sup>+</sup> - Ca<sup>++</sup> 5 5 4 45

가 pH가 Ca<sup>++</sup> 가 phosphocreati -

가 (oxygen free radical) 가 nine ATP (high - energy

phospholipase<sup>33)</sup> protease<sup>34)</sup> phosphate)

superoxide dismutase, glutathione pero -

oxidase, catalase (free radical)

가 가 가

xanthine dehydrogenase xanthine oxidase

(oxygen free radical)가 35)

가 (lipid peroxidation) 가 가 (heat shock

36) protein) 가 가 44,45)

가 46 - 48)

37,38) 9), 20), 21,39) mRNA 가 49)

가 mRNA 가 가

90 가 50 - 52)

가 40) 10

가 가 90 120

가

49,53)

가

가

1)

2)

가

3)

4)

Lambeth convention

결 과 :

가

(p<0.05).

20

(p<0.05).

### 요 약

연구배경 :

결 론 :

(isch -

emia - induced ventricular arrhythmia)

(reperfusion injury)

(preconditioning)

가

(hypoxic preconditioning)

(ischemic preconditioning)가

20

가

방 법 :

36 - chloralose

14

20

가

10

10

3

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12

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