

혈관이완제의 전처치가 토끼의 상완동맥과 복강동맥의 혈관수축에 미치는 효과; Nitroglycerin, Nicardipine, Verapamil과 Papaverine의 비교

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***In Vitro* Effects of Nitroglycerin, Nicardipine, Verapamil, and Papaverine on Rabbit Brachial and Celiac Arterial Tone**

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Background: Vasoconstrictor-induced reduction in arterial graft diameter can cause significant flow deprivation. The aim of this study was to evaluate the effect of vasodilator pretreatment on vasoconstrictor-induced blood vessel spasm *in vitro*. **Material and Method:** Rabbit brachial arteries (BA) and celiac arteries (CA) were cut into rings (3-4 mm) and suspended with a force displacement transducer (TSD 125C, Biopac Inc. USA) in a tissue bath filled with 5 mL modified Krebs solution bubbled with 5% CO₂ and 95% O₂ at 38°C. The rings were contracted with vasoconstrictors, and the developed tension changes were considered control values. The rings were then pretreated with 30 μM nitroglycerin, nicardipine, verapamil, and papaverine, respectively, for 40 minutes and rinsed with the physiologic buffered salt solution three times every 15 min. The vasoconstrictor-induced tension changes after the previous procedure were considered experimental values. Data are expressed as the percentage tension induced by vasoconstrictors before and after pretreatment with vasodilators. **Result:** Nicardipine depressed vasoconstriction induced by norepinephrine, angiotensin II (All), and U46619 in both the BA and the CA more significantly than did nitroglycerin (p < 0.01) and verapamil (p < 0.05). Verapamil depressed vasoconstriction induced by 5-hydroxytryptamine (5HT), All, and U46619 in the BA and by 5HT in the CA more significantly than did nitroglycerin (p < 0.01). **Conclusion:** These findings suggest that both nicardipine and verapamil effectively depressed vasoconstrictor action. Nicardipine is thought to be more effective than verapamil for the prevention of vasoconstrictor action.

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Key words: 1. Nitroglycerin
2. Nicardipine
3. Verapamil

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- 4. Papaverine
- 5. Vascular tone

(donor vessel)

(donor vessel)

nitroglycerin (NTG), nocardipine (Nica), verapamil (Vera), papaverine (Papa), norepinephrine (NE), 5-hydroxytryptamine (5HT), angiotensin II (AII), U46619 (thromboxane A₂ analogues)

1)

(2 2.5 kg Male N=28) 97% 3% enflurane heparin 600 900 IU

3

CO₂ 4°C modified Krebs (NaCl 120.0, NaHCO₃ 25.0, KCl 5.0, MgSO₄ 1.2, CaCl₂ 2.5, NaH₂PO₄ 1.4, glucose 11.0 mM) petri dish

95% O₂ 5%

3 4 mm

(ring segment)

38±0.5°C 5% CO₂ 95% O₂ 5 mL modified Krebs tissue bath

force displacement transducer (TSD

125C, Biopac Inc. USA)

90



Fig. 1. Experimental field.

15 modified Krebs 2.0 g
 1.5 g
 (DA100C, Biopac Inc. USA) data acquisition system (MP100, Biopac Inc. USA) PC
 NE 10⁻⁶ M acetylcholine (ACh)
 10⁻⁶ M 60%

(Fig. 1).

norepinephrine (NE, 10⁻⁷, 10⁻⁶, 10⁻⁵ M), 5HT (10⁻⁷, 10⁻⁶, 10⁻⁵ M, 10⁻⁶, 10⁻⁵, 10⁻⁴ M), AII (3×10⁻⁹, 10⁻⁸, 3×10⁻⁸ M) U46619 (3×10⁻⁸, 10⁻⁷, 3×10⁻⁷ M) 5 10

Krebs

NTG, Nica, Vera Papa 30μ M

40

Krebs

2)

NE, ACh, 5HT, AII, U46619, NTG, Vera, Papa Sigma Co. (USA), Nica (Perdipine) (Korea)

Table 1. Percentage changes of rabbit brachial arterial tension induced by vasoconstrictors Before and after pretreatment with vasodilators (30µ M)

Agent (M)	NTG	Nica	Vera	Papa
NE (n)	6	6	6	6
10 ⁻⁷	96.7±19.8	36.2±3.4*	67.9±19.3	65.2±8.8*
10 ⁻⁶	89.0±6.3	34.8±3.3*	72.9±6.0*	75.5±7.9*
10 ⁻⁵	97.1±2.7	63.7±5.0* ^{bV}	87.1±5.0 ^a	87.1±3.5 ^a
5HT (n)	16	16	16	16
10 ⁻⁷	130.4±11.1	77.1±6.4*	40.5±7.0*	125.4±12.5
10 ⁻⁶	112.8±3.1	90.2±3.5*	52.9±5.3*	111.6±2.9
10 ⁻⁵	111.2±2.9	94.0±3.5	89.0±4.3* ^b	107.6±2.5
AII (n)	16	16	15	16
3×10 ⁻⁹	79.0±11.4	62.0±8.0	71.0±7.7	95.4±17.1
10 ⁻⁸	99.0±12.9	70.5±3.6*	75.5±6.1*	84.9±3.3*
3×10 ⁻⁸	83.9±2.9	75.1±2.7* ^{bP}	75.4±2.6* ^{bP}	89.4±3.0
U46619 (n)	12	12	14	13
3×10 ⁻⁸	77.0±8.6	47.6±4.5*	52.6±3.9*	72.2±6.1
10 ⁻⁷	87.2±3.5	68.6±4.2*	69.5±3.0*	83.1±3.5
3×10 ⁻⁷	92.5±2.4	76.0±4.0* ^b	77.5±2.9* ^b	87.5±2.0

Values are expressed as Mean±SEM. N=Number of samples; NTG=Nitroglycerin; Nica=Nicardipine; Vera=Verapamil; Papa=Papaverine; NE=Norepinephrine; 5HT=5-hydroxytryptamine; AII=Angiotensin II; U46619=Thromboxane A₂ analogues. *p < 0.05 compared with control values; ^ap < 0.05 compared with NTG group; ^bp < 0.01 compared with NTG group; ^Pp < 0.05 compared with Papa group; ^Vp < 0.05 compared with Vera group.

3)

± Prism 2.0 (Graphpad software, USA) non-linear regression analysis
paired Student's t test
one way ANOVA
NTG Papa
Bonferoni (compare with selected group) test
p < 0.05

1)

(1) NE

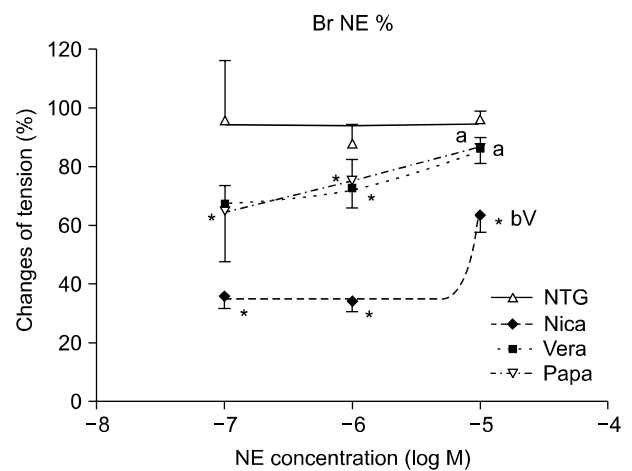


Fig. 2. The effects of vasodilators on the vascular tones induced by NE in rabbit brachial artery. The Nica, Vera, and Papa groups decreased the degrees of vasoconstriction more potently than the NTG group. The Nica group was vasoconstricted less than the Vera group by NE. Values are expressed as Mean±SEM. NTG=Nitroglycerin 30µ M; Nica=Nicardipine 30µ M; Vera=Verapamil 30µ M; Papa=Papaverine 30µ M; NE=Norepinephrine. *p < 0.05 compared with control values; ^ap < 0.05 compared with NTG group; ^bp < 0.01 compared with NTG group; ^Vp < 0.05 compared with Vera group.

(5HT p 0.01, AII p 0.01, U46619 p 0.01). NE NTG [4]. Norepinephrine (p 0.05). 5HT NTG (p 0.01). NE NTG Papa (p 0.05). (4) Papa : NE NTG (87.1±3.5% vs 97.1±2.7%, p 0.05).



(endothelium) (vascular tone) endothelium-derived relaxing factor (EDRF (NO)) EDRF (NO) [1]. endothelin I EDCF (endothelium-derived contracting factor), thromboxane A₂ prostaglandin F₂ prostanoid, norepinephrine circulating sympathomimetic substances (α-adrenoceptor agonists) synthetic α₁-adrenoceptor agonists (methoxamine, phenylephrine), 5-HT thromboxane A₂ platelet-derived contracting substances, histamine mast cell basophil muscarinic receptor agonist, angiotensin II renin-angiotensin system related substances, [2].

norepinephrine, 5-HT, angiotensin II, thromboxane A₂ mimetic U46619 . 5-HT 5-HT₂ [3], 5-HT_{1D} EDRF(NO) 5-HT, thromboxane A₂ 5-HT

[4]. Norepinephrine [5], norepinephrine . Angiotensin II voltage-depend- ent Ca²⁺ channel Ca²⁺ [6]. Thromboxane A₂ EDCF [7], thromboxane A₂ [8], Thromboxane A₂ mimetics U46619 endothelin I [9]. (catecholamine) Reeves nor- epinephrine 200 pg/mL (1.2×10⁻⁹ 10⁻⁸) 4,500 pg/mL (2.7×10⁻⁸) [10]. Nitroglycerin nitric oxide (NO) guanylate cyclase cGMP

nitrates, verapamil
 (Thromboxane A₂ , endo- . He verapamil
 thelin) nitroglycerin (VG solution; 30μ mol/L verapamil
 30μ mol/L nitroglycerin)
 [11]. Chavanon nitroglycerin
 10
 25.5±2 mL/min 50±
 [18]. Ali verapamil
 6.1 mL/min nitroglycerin
 [12]. [16]. VG
 verapamil
 40 15 2 modified Krebs
 nitroglycerin nicardipine
 . Organic nitrates nitrates (nonspecific vaso-
 nitroglycerin dilator) phosphodiesterase inhibitor
 cGMP [19]. Papaverine
 [13]. [20]. He
 [14,15]. Verapa- papaverine
 mil nicardipine [18]. Papa
 voltage-operated calcium channel (L-type calcium chan-
 nel) NTG
 . NTG Papa
 receptor-operated calcium channel
 [11]. Nicardipine 2 di- Nica Vera
 hydroxyridine endo-
 thelin
 diltiazem endothelium-
 15 [11]. Ali ni- dependant relaxation, endothelium-independent relaxation, re-
 cardipine nifedipine norepinephrine ceptor-mediated contraction
 [21]. papaverine nitroglycerin
 [16], endothelin
 [17] voltage-operated calcium channel
 nicardipine
 . Nicardipine

1. Nica	Vera		
2. Nica		NE	
		NE, 5HT, AII	U46619
	Vera		
		Nica	Vera
3. NTG	Papa		
			Nica
	Vera		

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=국문 초록=

배경:

. 대상 및 방법: 3 4 mm
5% CO₂ 95% O₂ modified Krebs (38±0.5°C) tissue bath
force displacement transducer (TSD 125C , Biopac Inc. USA)
(NTG), (Nica), (Vera) (Papa) 30 μ M
40 , Krebs 15 3

. 결과: Nica norepine-
phrine (NE), angiotensin II (AII), U46619 NTG Vera
(Nica vs NTG, p 0.01; Nica vs Vera, p 0.05). Vera NTG
5HT (5-hydroxytryptamine), AII, U46619 ,
5HT (p 0.01). 결론: Nica Vera
Nica Vera

- 중심 단어 1.
2.
3.
4.
5.