

고혈압 흰쥐에서 Nifedipine과 Bay K 8644의 정맥내 주입이 혈압에 미치는 영향

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= Abstract =

Cardiovascular Effects of Nifedipine and Bay K 8644 in Hypertensive Rats

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Background : Calcium plays a key role in vascular contraction and regulates receptor sensitivity to certain neurotransmitters. Calcium channel blockers are useful in the treatment of both clinical and experimental hypertension. The present study was designed to examine whether there is an alteration of the activity of calcium channels in association with the development of hypertension.

Methods : Deoxycorticosterone acetate(DOCA)-salt hypertension was made by subcutaneous implantation of DOCA(200mg/kg) strip plus saline drinking(1%) and 2-kidney, 1 clip(2K1C) hypertension by clipping the left renal artery with a silver clip(internal gap of 0.2mm). They were used 4 weeks later. Age-matched normal rats served as a control. Mean arterial pressure(MAP) and heart rate(HR) were continuously recorded from the right femoral artery. The drugs were administered intravenously.

Results : Vehicle alone was without effect on MAP or HR. In normotensive rats, nifedipine infusion(5 and 10 μ g/kg/min) caused a dose-dependent decrease in MAP without significant changes in HR, while Bay k 8644(Bay K, 5 and 10 μ g/kg/min) increased MAP transiently. Both the depressor response to nifedipine and the pressor response to Bay k were more marked in DOCA-salt hypertensive rats than in normotensive rats. The maximal changes in MAP induced by nifedipine(5 and 50 μ g/kg) or Bay K(5 and 50 μ g/kg) were also enhanced in 2K1C hypertensive rats as compared with control rats.

Conclusion : These results indicate that calcium channel inhibitors and activators can affect on

the regulation of blood pressure in an opposite fashion. It is also suggested that the activity of calcium channels might be altered in the development of experimental hypertension.

KEY WORDS : Cardiovascular · Nifedipine · Bay K 8644 · Hypertension.

서론

Ca²⁺ channel (sa - rcoplasmic reticulum) Ca²⁺ channel 가 가 Ca²⁺ Ca²⁺ channel 가 1) slow Ca²⁺ influx Ca²⁺ 2) Nifedipine Ca²⁺ dihydropyridine(DHP) 3). Garthoff 4) Ca²⁺ 가 nifedipine nitrendipine DHP (salt - sensitive) 가 Ca²⁺ 5) nitrendi - pine deoxycorticosterone acetate(DOCA) - salt 6,7) nif - edipine 8) 가 Ca²⁺ 9) DOCA - salt renin 가 nifedipine DHP

Bay K 8644 (Bay K) Ca²⁺ Ca²⁺ channel 10) nifedipine 11) Ca²⁺ channel DOCA - salt 2 - kidney, 1 clip(2K1C) 가 nifedipine Bay K

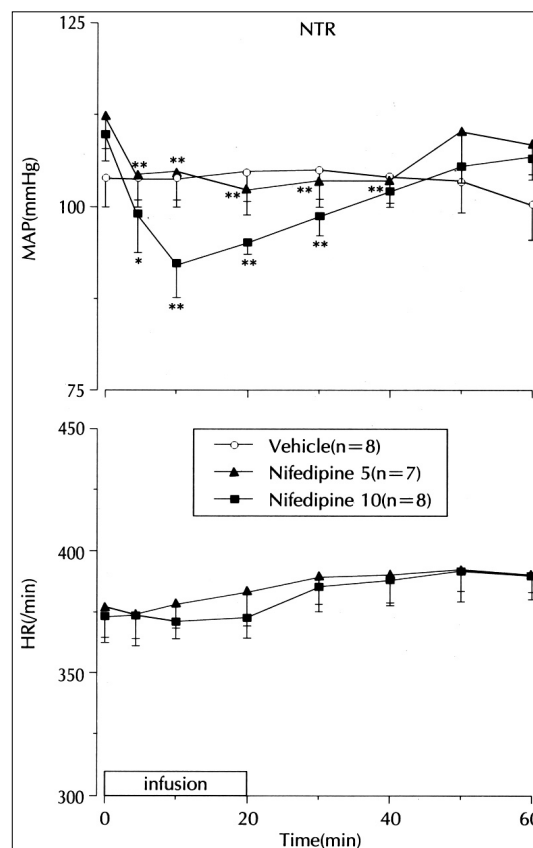


Fig. 1. Effects of intravenous infusion of nifedipine (5 and 10 μ g/kg/min) on the mean arterial pressure (MAP) and heart rate (HR) in normotensive rats (NTR). Nifedipine was infused for 20 min. Vehicle alone was without effect. Each point represents mean \pm SE. * p <0.05, ** p <0.01 compared to the 0 time value in each group.

tachyphylaxis

대상 및 방법

1. 실험동물

1) DOCA-salt 고혈압의 유발
130 180g (Sprague - Dawley,)
thiopental(50mg/kg, IP)
1 DOCA(Si -
gma, 200mg/kg) silastic strip
(implantation) 1% 0.2% KCl
4 1

2) 2K1C 신성고혈압의 유발
150 200g thiopental
0.2mm silver clip
4

3) 정상혈압쥐

2. 혈압 및 심박수 기록
Thiopental cannula
heparin(3
00IU/ml) polyethylene tube(PE 60)
pressure transducer(Gould, P23Db)
polygraph(Beckman, R511A)
(mean arterial pressure, MAP) (dia-
stolic pressure + pulse pressure/3)

3. 약물투여

1
DOCA - salt nifedipine(5, 10 μ g/kg
/min, Sigma) Bay K(5, 10 μ g/kg/min, Bayer)
20
2K1C 5 μ g/kg 50 μ g/kg
99% ethanol

4. 통 계

mean \pm SE
Student t - test(paired unpaired)
p<0.05 가

결 과

1. 정상혈압쥐에서 nifedipine이 혈압 및 심
박수에 미치는 영향
Nifedipine 5 μ g/kg/min 5
20

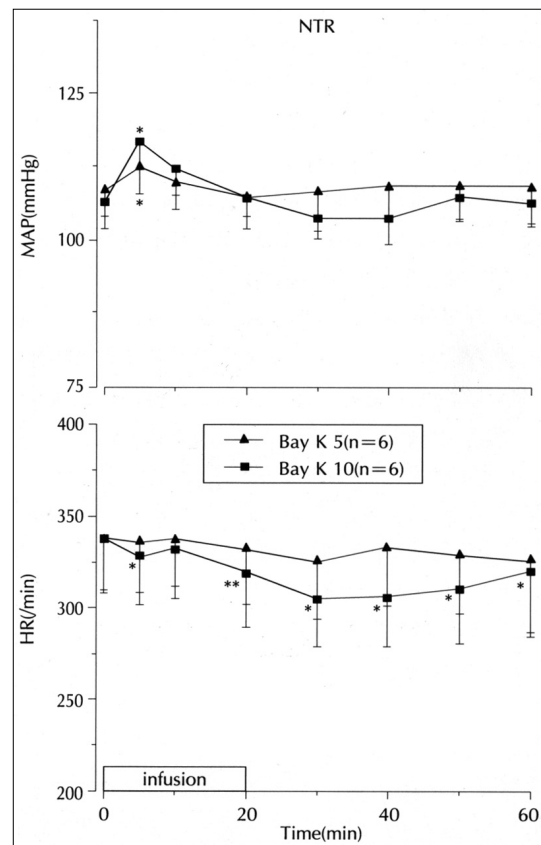


Fig. 2. Effects of intravenous infusion of Bay K 8644(Bay K, 5 and 10 μ g/kg/min) on the mean arterial pressure(MAP) and heart rate(HR) in normotensive rats (NTR). Bay K was infused for 20 min. *p<0.05, **p<0.01 compared to the 0 time value in each group.

40
10 µg
가
Ve -
hicle(99% ethanol)
1
(Fig. 1).

2. 정상혈압쥐에서 혈압 및 심박수에 미치는
Bay K의 영향
Bay K 5 µg/kg/min
1
10 µg
10 µg
1
(Fig. 2).

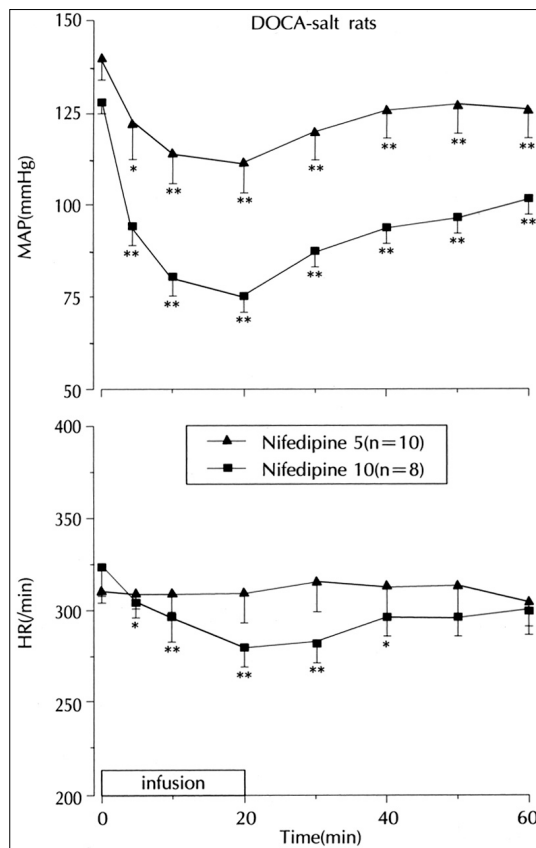


Fig. 3. Effects of intravenous infusion of nifedipine (5 and 10 µg/kg/min) on the mean arterial pressure (MAP) and heart rate (HR) in DOCA-salt hypertensive rats. Nifedipine was infused for 20 min. *p<0.05, **p<0.01 compared to the 0 time value in each group.

3. DOCA-salt 고혈압쥐에서 nifedipine이
혈압 및 심박수에 미치는 영향
DOCA - salt 135 ± 3.2mmHg
(n=33) (109 ± 1.7, n=64)
(p<0.01) Nifedipine 5 µg/kg/min
5
20
1
10 µg
5 µg
10 µg
1
(Fig. 3).

4. DOCA-salt 고혈압쥐에서 혈압 및 심박
수에 미치는 Bay K의 영향
Bay K 5 µg/kg/min 5
20
50
10 µg
가
5 µg
(Fig. 4).

5. DOCA-salt 및 2K1C 고혈압쥐에서 nifed-
ipine과 Bay K에 의한 최대혈압 변동치 비교
DOCA nifedipine
Bay K
nifedipine
Bay K 가
(Table. 1). 2K1C
163 ± 8.9mmHg(n=28) nifedipine(5, 50 µ
g/kg) Bay K(5, 50 µg/kg)
(Table 2).

고 안

nifedipine
가 Ca^{2+}
12)
13)
DHP

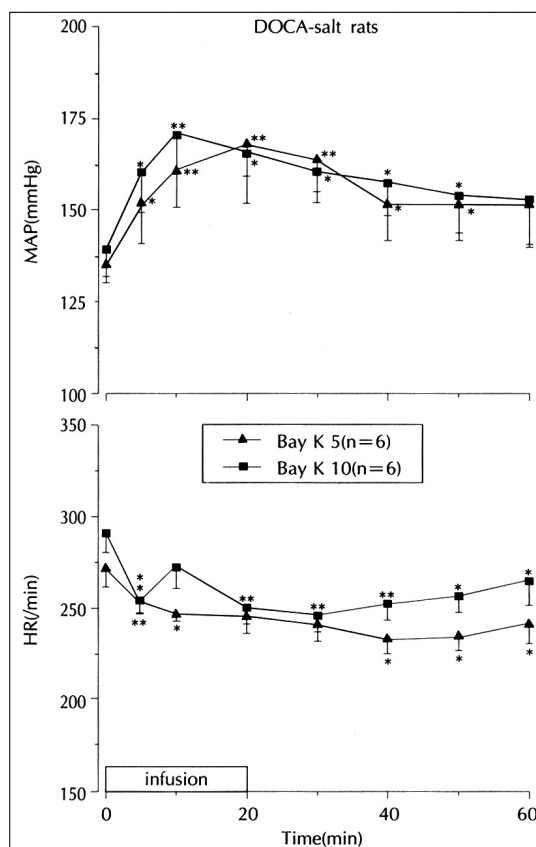


Fig. 4. Effects of intravenous infusion of Bay k 8644(Bay K, 5 and 10 μ g/kg/min) on the mean arterial pressure (MAP) and heart rate(HR) in DOCA-salt hypertensive rats. Bay K was infused for 20 min. * $p < 0.05$, ** $p < 0.01$ compared to the 0 time value in each group.

Table 1. Maximal changes in mean arterial pressure(mmHg) during the intravenous infusion of nifedipine and Bay K 8644(Bay K) in normotensive and DOCA-salt hypertensive rats

Drug	Dose	NTR	DOCA-salt rats
Nifedipine	5 μ g/kg/min	- 11.4 \pm 1.7(n=7)	- 31.9 \pm 5.8(n=8)**
	10 μ g/kg/min	- 17.8 \pm 4.4(n=8)	- 55.1 \pm 5.8(n=8)**
Bay K	5 μ g/kg/min	+ 2.5 \pm 3.0(n=6)	+ 35.5 \pm 4.5(n=6)**
	10 μ g/kg/min	+ 5.8 \pm 4.9(n=6)	+ 33.0 \pm 5.2(n=6)**

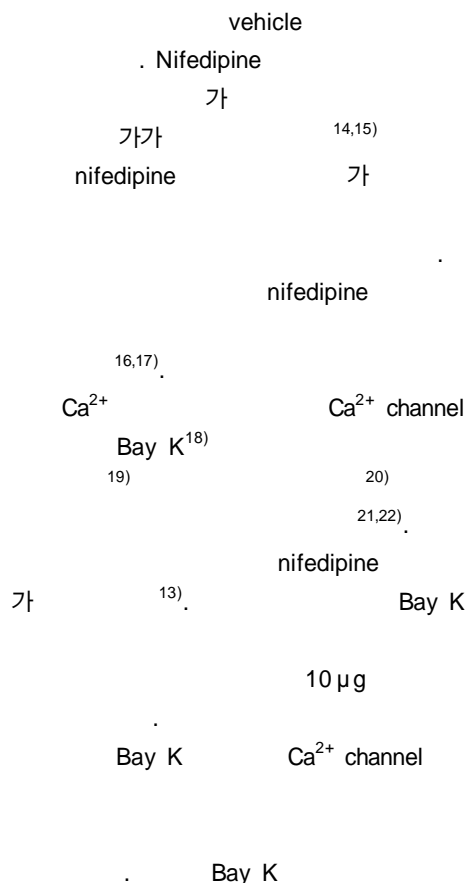
** $p < 0.05$; compared with NTR(normotensive rats) responses to the same dose of the drug.

Table 2. Maximal changes in mean arterial pressure(mmHg) following the intravenous injection of nifedipine and Bay K 8644(Bay K) in normotensive and 2K1C hypertensive rats

Drug	Dose	NTR	2K1C
Nifedipine	5 μ g/kg	- 28.5 \pm 6.8(n=8)	- 46.3 \pm 6.2(n=8)*
	50 μ g/kg	- 43.7 \pm 5.0(n=7)	- 73.5 \pm 7.8(n=5)*
Bay K	5 μ g/kg	+ 7.5 \pm 6.2(n=6)	+ 51.0 \pm 8.6(n=7)**
	50 μ g/kg	+ 13.4 \pm 5.8(n=5)	+ 99.2 \pm 3.1(n=5)**

2K1C, 2-kidney, 1 clip hypertensive rats. The maxial responses were always within the first one minute following the intravenous administration of the drug. * $p < 0.05$, ** $p < 0.01$; compared with NTR(normotensive rats) responses to the same dose of the drug.

5)



- 1315 -

channel
Bay K
nifedipine
nitrendipine
Ca²⁺
34,35)
36)

가
Ca²⁺ channel
가

References

Bay K
DOCA
2K1C
Ca²⁺ channel
가
DOCA - salt
Ca²⁺ channel
가
요 약
연구배경 :
Ca²⁺
nifedipine
Bay K 8644(Bay K)가
가
방 법 :
deoxy -
corticosterone acetate(DOCA) - salt
clip 2 - kidney, 1 clip(2K1C)

결 과 :
1) nifedipine
Bay K
2) DOCA nifedipine
Bay K
가
3) DOCA 2K1C ni -
fedipine Bay K
결 론 :
Ca²⁺ channel

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