# CHAPTER 4

# RESULTS

All dogs in this experiment were clinically normal based on physical examinations. Some of baseline data recorded on the beginning of experimental day are shown in table 4.1.

**Table 4.1** - Physical and laboratory examination-variables of all 10 dogs in the beginning of the experiment.

| | *Hct (%)* | *Cr (mg%)* | *Bl glucose (mg%)* | *HR (mean±SD) (beats/min)* | *RT (°F)* | *RR (breaths/ min)* | *MAP (mean±SD) (mmHg)* |
|---|---|---|---|---|---|---|---|
| Low-dose | | | | | | | |
| Dog 1 | 30 | 0.53 | 56 | 92.66±9.55 | 102 | 36 | 124.03±11.28 |
| Dog 2 | 39 | 0.47 | 51 | 79.51±10.34 | 102.2 | 41 | 91.19±6.47 |
| Dog 3 | 41 | 0.73 | 66 | 108.50±18.99 | 101 | 36 | 86.15±5.46 |
| Dog 4 | 33 | 0.94 | 73 | 112.16±5.43 | 102 | 38 | 110.26±4.1 |
| Dog 5 | 34 | 0.84 | 95 | 120.65±10.77 | 101.7 | 60 | 126.76±3.93 |
| High-dose | | | | | | | |
| Dog 6 | 34 | 0.60 | 71 | 95.22±7.36 | 103 | 56 | 90.94±3.91 |
| Dog 7 | 45 | 0.60 | 73 | 86.14±9.68 | 102 | 36 | 101.52±3.82 |
| Dog 8 | 32 | 0.60 | 64 | 88.29±6.93 | 100.8 | 22 | 92.52±3.97 |
| Dog 9 | 38 | 0.70 | 66 | 87.71±10.28 | 102.7 | 28 | 88.97±4.32 |
| Dog 10 | 46 | 0.70 | 74 | 125.74±5.48 | 102.5 | 64 | 114.07±6.24 |

Hct = hematocrit; Cr = plasma creatinine concentration; HR = heart rate; RT = rectal temperature; RR = respiratory rate; MAP = mean arterial pressure; bpm = beats per minute.

## Cardiovascular effects of brimonidine

### 1. Effects of brimonidine on mean arterial pressure (MAP) and R-R interval

**Table 4.2** - Mean arterial pressure (MAP), and R-R interval of low and high-doses of brimonidine, and yohimbine administrations in 5 dogs of each group.

| | *MAP (mmHg)* | *R-R interval (second)* |
|---|---|---|
| Low-dose | | |
| Baseline | 106.53±5.80 | 0.61±0.07 |
| B1 | 93.19±2.83 | 0.74±0.09 |
| B2 | 81.61±4.23 * | 0.92±0.08 * |
| B3 | 86.57±3.08 * | 0.91±0.08 * |
| B4 | 88.32±2.44 * | 0.88±0.10 * |
| B5 | 83.52±2.30 * | 0.85±0.10 * |
| Yohimbine | 108.41±6.33 | 0.57±0.06 |
| High-dose | | |
| Baseline | 89.85±3.73 | 0.73±0.07 |
| B1 | 81.25±4.94 | 0.92±0.06 |
| B2 | 72.17±3.98 * | 1.07±0.06 * |
| B3 | 70.61±3.64 * | 1.03±0.10 * |
| B4 | 72.63±3.36 * | 0.92±0.10 |
| B5 | 69.83±2.96 * | 0.83±0.14 |
| Yohimbine | 97.67±5.65 | 0.56±0.05 |

The data were shown as mean ± SE.

*, $P < 0.05$, significant difference from corresponding baseline value.

B1-B5 = first to fifth hour after brimonidine administration.

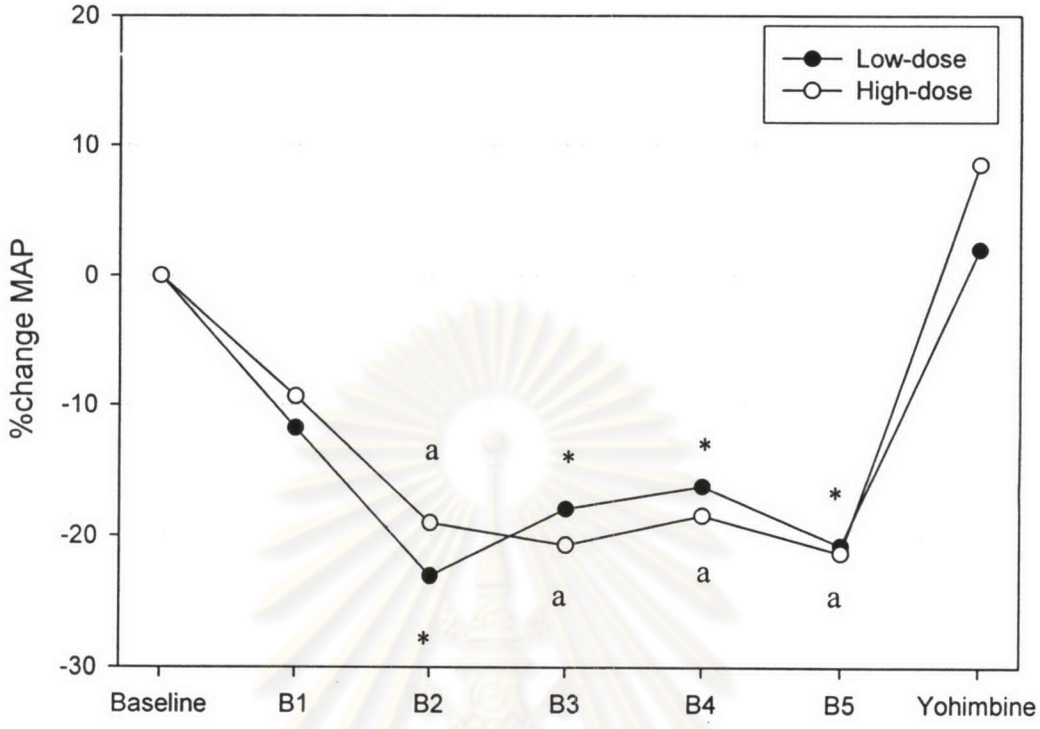


**Figure 4.1** – Percent changes of MAP after low and high-dose of brimonidine administrations and yohimbine intravenous injection in 5 dogs of each group.
Data were present as percent change of mean.
* and [a] $P < 0.05$, significant difference from corresponding baseline value in low- and high-dose groups respectively.
B1-B5 = first to fifth hour after brimonidine administration.

The mean arterial pressure (MAP) declined significantly after either low or high dose of brimonidine administration and it was reversed after yohimbine administration. In a low dose of brimonidine administration (0.2 mg/kg *per os)*, mean value of MAP decreased in all recording periods, the first to fifth hour, after brimonidine administration but statistical significances were detected only in second to fifth hour and it could be reversed completely after intravenous injection of yohimbine, specific antidote,. In a higher dose (0.5 mg/kg brimonidine *per os*), MAP

declined in the first to fifth hour after brimonidine ingestion but significant differences were detected only in the second to fifth hour and it was also completely reversed and tended to be higher after yohimbine administration as compared with baseline value. (Table 4.2 and fig. 4.1)

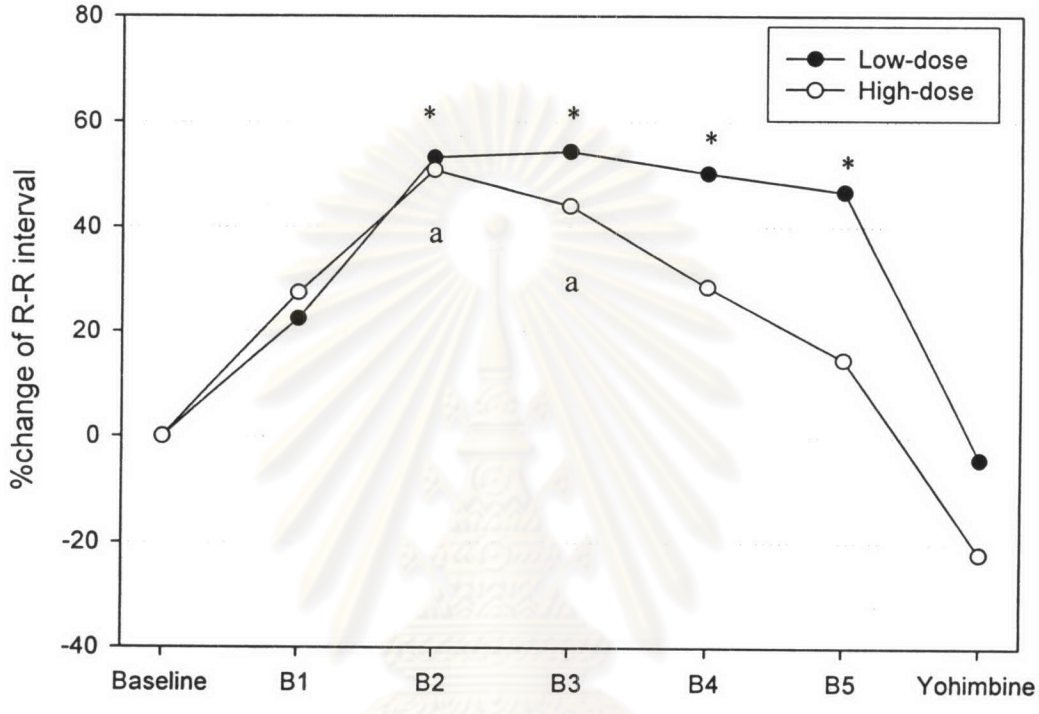


**Figure 4.2** – Percent changes of R-R interval after low and high-dose of brimonidine administrations and yohimbine injection in 5 dogs of each group.
Data were present as percent change of mean.
* and [a] $P < 0.05$, significant difference from corresponding baseline value in low- and high-dose groups respectively.
B1-B5 = first to fifth hour after brimonidine administration.

The R-R intervals were increased in all recording periods after either low or high dose of brimonidine administration. The significant differences were detected in the second to fifth hour after 0.2 mg/kg brimonidine administration and the second and third hour in 0.5 mg/kg brimonidine administration of brimonidine. As well as

MAP and HR, R-R intervals were returned and slightly shorter than baseline levels after administration of yohimbine. (Table 4.2 and figure 4.2)

**2. Effects of brimonidine on ratio between MAP and R-R interval, standard deviation of MAP and standard deviation of HR**

**Table 4.3** – Ratio between MAP and R-R interval (MAP/R-R), standard deviation of MAP (SDMAP) and HR (SDHR) of low- and high-dose groups of brimonidine administration and yohimbine intravenous injection in 5 dogs of each group.

| | ***MAP/R-R*** ***(mmHg/sec)*** | ***SDMAP*** ***(mmHg)*** | ***SDHR*** ***(mmHg)*** |
|---|---|---|---|
| Low-dose | | | |
| Baseline | 185.38±25.68 | 4.197±0.744 | 8.601±2.445 |
| B1 | 133.87±17.24 | 11.665±1.748$^{\pi}$ | 17.350±2.945 |
| B2 | 93.44±13.61 | 5.536±0.879 | 6.831±1.659 |
| B3 | 98.49±10.63 | 4.001±0.799 | 6.514±1.409 |
| B4 | 106.50±15.55 | 6.093±0.799 | 7.364±1.254 |
| B5 | 104.13±13.09 | 5.437±1.054 | 8.142±1.052 |
| Yohimbine | 200.60±26.21 | 11.586±1.639$^{\pi}$ | 14.937±3.828 |
| High-dose | | | |
| Baseline | 127.46±14.34 | 5.536±1.207 | 6.913±1.728 |
| B1 | 91.25±10.98 | 11.651±1.554* | 15.746±3.940 |
| B2 | 69.45±8.65* | 5.727±1.002 | 7.026±0.941 |
| B3 | 72.80±11.89* | 4.347±0.711 | 6.706±1.427 |
| B4 | 83.80±11.84 | 5.314±0.763 | 8.293±1.325 |
| B5 | 93.47±14.14 | 5.552±1.474 | 7.759±3.115 |
| Yohimbine | 178.54±17.28* | 14.125±1.288* | 11.932±1.626 |

The data were shown as mean ± SE.

*, $P < 0.05$, significant difference from corresponding baseline value.

$^{\pi}$ significant difference in non-parametric method ($P < 0.05$).

B1-B5 = first to fifth hour after brimonidine administration.

MAP/R-R appeared to be reduced in all recording periods, first to fifth hour after administration of brimonidine, nevertheless the statistical significances were

detected in only the second and third hour following 0.5 mg/kg of brimonidine administration. The reverse effects of these variables after yohimbine administration were also observed in both groups. The values after yohimbine administration were higher than those of the baseline values. (Table 4.3)

When compared with baseline values, SDMAP and SDHR were higher in the first hour after brimonidine administration and after yohimbine intravenous injection. These changes were observed in both dose-groups. An hour after brimonidine administration, SDMAP values were doubled from the baseline levels, and then they became decrease to the baseline levels observed on next hour and stable until the administration of yohimbine. These observations occurred similarly in both groups. These trends were also observed in SDHR, although the significant differences were not detected as compared with the baseline levels. (Table 4.3)

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### 3. Effects of brimonidine on electrocardiogram

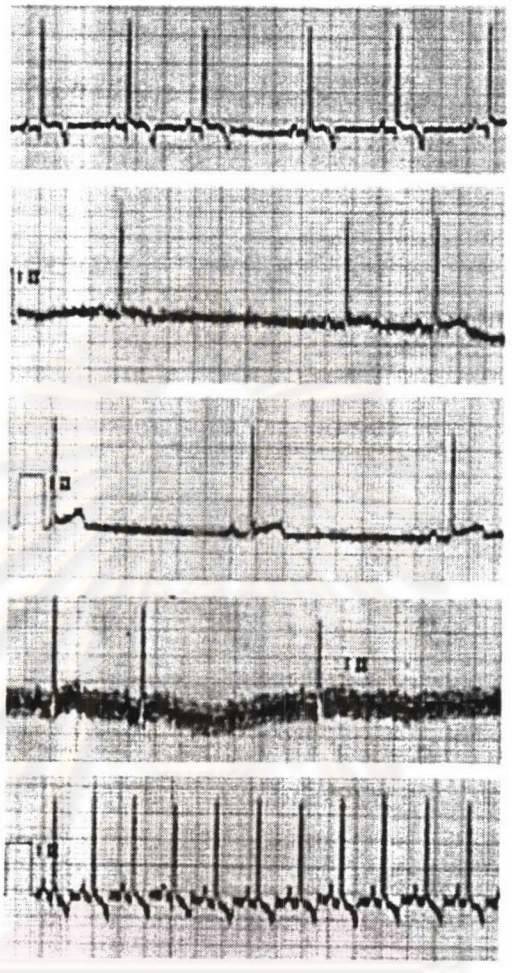


**Figure 4.3** – Lead II electrocardiograph tracing obtained from one dog before and after high dose of brimonidine, and after yohimbine administrations.
B1-B3 = first to third hour after brimonidine administration.

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**Table 4.4** - P-R interval, P duration, Q-T intervals, and QRS duration of low and high-doses of brimonidine and yohimbine administrations in 5 dogs of each group.

| | *P-R interval (second)* | *P duration (second)* | *Q-T interval (second)* | *QRS duration (sec)* |
|---|---|---|---|---|
| Low-dose | | | | |
| Baseline | 0.118±0.009 | 0.050±0.004 | 0.212±0.008 | 0.060±0.003 |
| B1 | 0.134±0.011 | 0.062±0.002 | 0.234±0.010 | 0.064±0.004 |
| B2 | 0.140±0.010 * | 0.060±0.000 | 0.232±0.007 | 0.058±0.074 |
| B3 | 0.126±0.012 | 0.056±0.005 | 0.228±0.013 | 0.062±0.074 |
| Yohimbine | 0.110±0.013 | 0.054±0.005 | 0.202±0.007 | 0.058±0.007 |
| High-dose | | | | |
| Baseline | 0.124±0.005 | 0.058±0.002 | 0.228±0.009 | 0.056±0.050 |
| B1 | 0.148±0.007 * | 0.060±0.000 | 0.240±0.009 | 0.048±0.002 |
| B2 | 0.138±0.006 | 0.052±0.005 | 0.250±0.010 | 0.054±0.004 |
| B3) | 0.134±0.004 | 0.052±0.004 | 0.246±0.009 | 0.048±0.004 |
| Yohimbine | 0.106±0.006 * | 0.054±0.004 | 0.198±0.012 * | 0.060±0.000 |

The data were shown as mean ± SE.

*, $P < 0.05$, significant difference from corresponding baseline value.

B1-B3 = first to fifth hour after brimonidine administration.

From the ECG recording, P-R intervals increased in all periods after brimonidine administration. These changes were significantly different in second hour of low-dose and first hour of high-dose after administration. The P-R intervals were reversed after administration of yohimbine in both groups. In the high-dose group, after yohimbine injection, P-R interval became shorter than baseline value significantly.

There were no significant alterations after brimonidine and yohimbine administrations for P wave and QRS durations in the present study.

Q-T intervals in both groups were widening following the administration of brimonidine. However, these changes were not statistically significant difference. Interestingly, after yohimbine injection, Q-T intervals decreased significantly as compared with baseline values.

**Table 4.5** – P and R amplitude of low and high-doses of brimonidine and yohimbine administrations in 5 dogs of each group.

| | *P amplitude (mV)* | *R amplitude (mV)* |
|---|---|---|
| Low-dose | | |
| Baseline | 0.22±0.02 | 1.49±0.13 |
| B1 | 0.18±0.03 | 1.40±0.14 |
| B2 | 0.22±0.04 | 1.43±0.18 |
| B3 | 0.19±0.04 | 1.43±0.13 |
| Yohimbine | 0.23±0.02 | 1.58±0.19 |
| High-dose | | |
| Baseline | 0.20±0.00 | 1.71±0.16 |
| B1 | 0.16±0.02 | 1.70±0.13 |
| B2 | 0.16±0.02 | 1.65±0.25 |
| B3 | 0.18±0.01 | 1.58±0.23 |
| Yohimbine | 0.19±0.01 | 1.71±0.14 |

The data were shown as mean ± SE.

B1-B3 = first to fifth hour after brimonidine administration.

Comparing to baseline levels, no significant changes in P and R amplitudes were observed after administration of brimonidine and yohimbine. These observations occurred in both groups.

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## Effects of brimonidine on renal function.

### 1. Effects of brimonidine on renal hemodynamics

#### 1.1. Effects of brimonidine on glomerular filtration rate

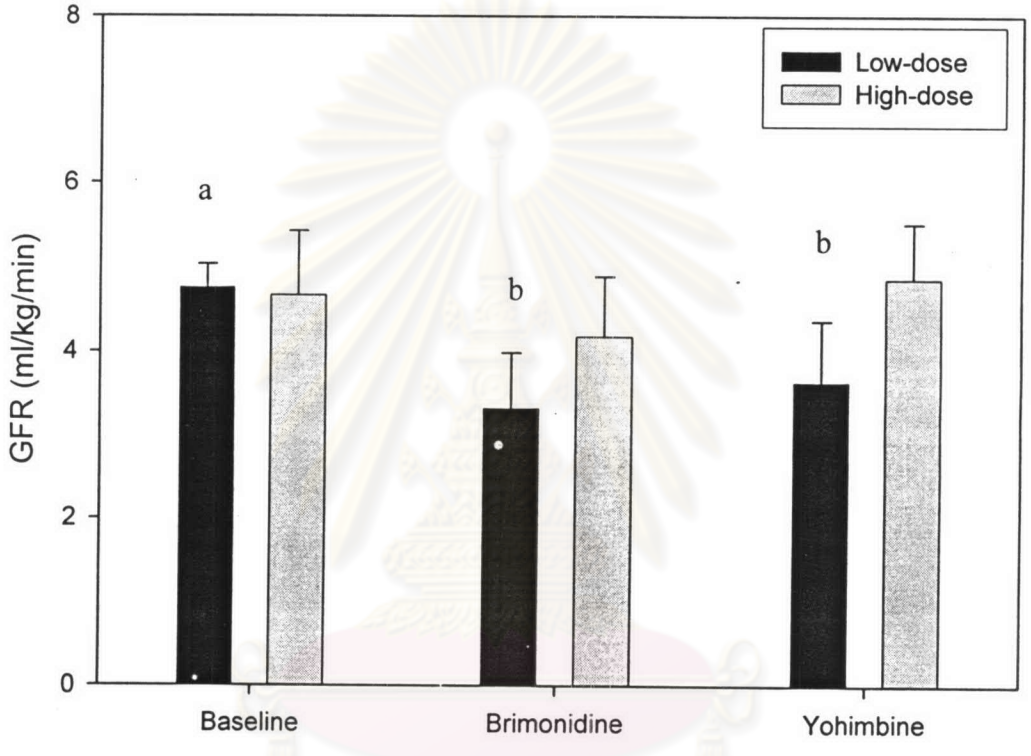


**Figure 4.4** –The glomerular filtration rate of either low or high-dose groups of brimonidine administration and the effects after administration of yohimbine in 5 dogs of each group.

The data were shown as mean ± SE.

[a,b] means with different superscripts differ significantly ($p<0.05$).

Glomerular filtration rates (GFR) decreased after whether low or high dose of brimonidine administration and was reversed after yohimbine injection. The decreases of GFR following brimonidine administration occurred in both dose-groups but

statistical significances were detected only in low-dose group (from 4.752±0.280 to 3.322±0.666 ml/kg/min and 4.668±0.759 to 4.178±0.715 ml/kg/min in low- and high-dose groups, respectively). After yohimbine injection, the GFRs were elevated in both groups (3.642±0.725 and 4.868±0.654 ml/kg/min, low- and high-dose groups, respectively). However, in low-dose group, the reversal effect of yohimbine was not complete. (Figure 4.4)

### 1.2. Effects of brimonidine on effective renal plasma flow, renal blood flow, renal vascular resistance and filtration fraction

**Table 4.6** – Effective renal plasma flow (ERPF), renal blood flow (RBF), calculated renal vascular resistance (RVR) and filtration fraction (FF) of low and high doses of brimonidine, and yohimbine administrations in 5 dogs of each group.

| | *ERPF (ml/kg/min)* | *RBF (ml/kg/min)* | *RVR (mmHg/ $ml*kg^{-1}*min^{-1}$ )* | *FF (%)* |
|---|---|---|---|---|
| Low-dose | | | | |
| Baseline | 14.16±0.66 | 21.94±0.83 [a] | 5.08±0.34 | 33.51±1.15 |
| Brimonidine | 10.76±2.21 | 15.09±2.82 [b] | 6.98±2.08 | 31.46±1.77 |
| Yohimbine | 11.48±2.03 | 18.34±2.96 [ab] | 6.46±0.94 | 31.43±1.30 |
| High-dose | | | | |
| Baseline | 18.97±2.74 [a] | 31.39±5.17 [a] | 2.86±0.37 | 24.24±1.40 |
| Brimonidine | 15.20±2.18 [b] | 23.02±3.71 [b] | 3.53±0.72 | 26.32±2.25 |
| Yohimbine | 17.89±2.58 [a] | 32.33±5.20 [a] | 3.37±0.66 | 26.19±1.44 |

The data were shown as mean ± SE.

[a,b] means with different superscripts differ significantly ($p<0.05$).

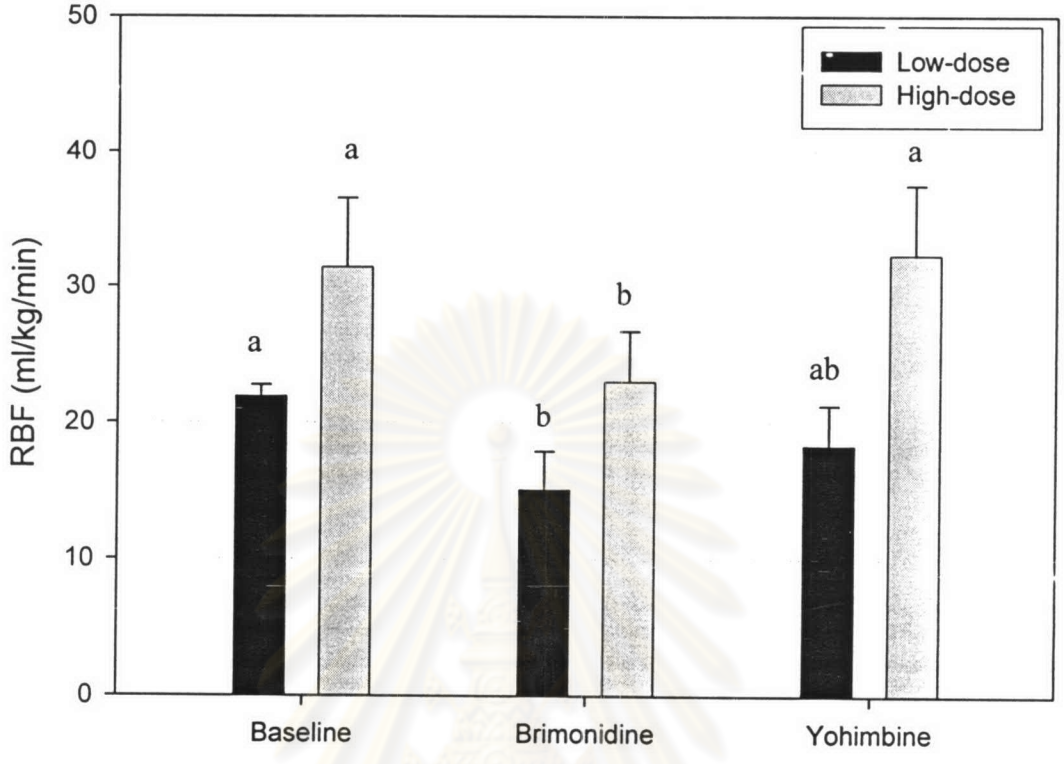


**Figure 4.5** – Renal blood flow (RBF) of low- and high-dose groups of brimonidine administration and reversed effects after administration of yohimbine in 5 dogs of each group.

Data were present as mean ± SE.

[a,b] means with different superscripts differ significantly ($p<0.05$).

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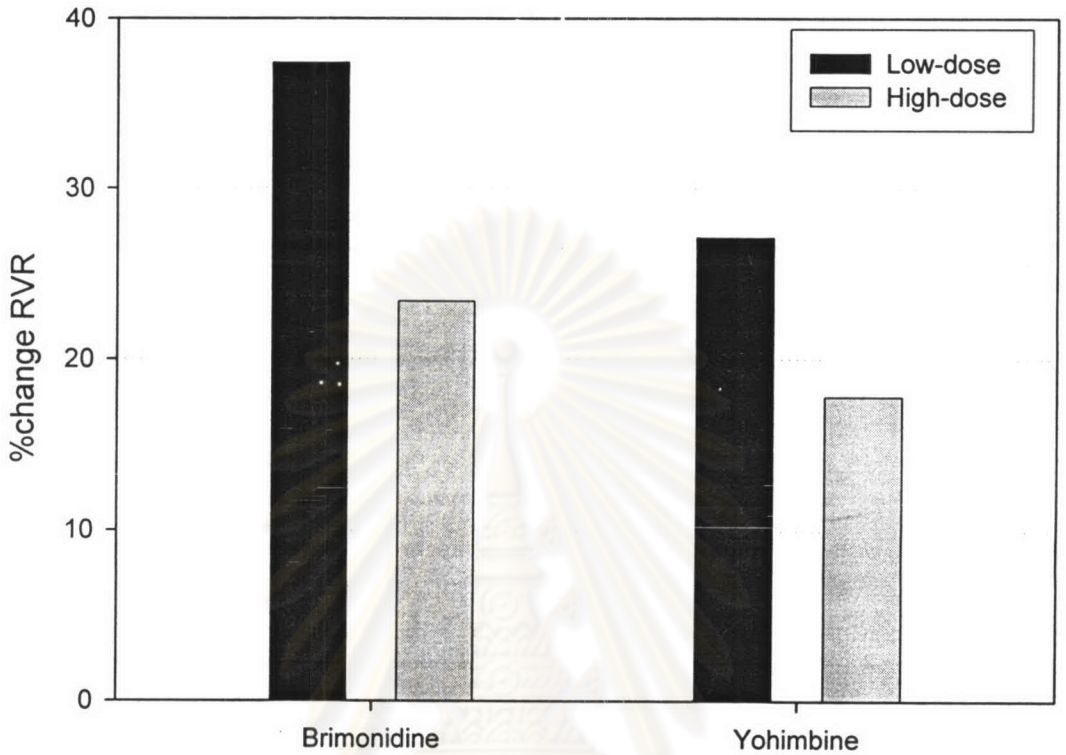


**Figure 4.6** — Percent changes of renal vascular resistance (RVR) of low- and high-dose groups of brimonidine administration and also reversed effects after administration of yohimbine in 5 dogs of each group.
Data were present as percent change of mean.

Effective renal plasma flow (ERPF) and renal blood flow (RBF) were decreased after the administration of brimonidine.The significant differences were all detected except ERPF in the low-dose group. The reversal effects of yohimbine were also noted in these two variables even though this effect on ERPF and RBF in low-dose group was not apparent. (Table 4.6 and figure 4.5)

There were no significant differences for renal vascular resistance (RVR) between the value of baseline and the value after brimonidine ingestion and also value after yohimbine injection. Although there were no statistically significant changes,

RVR had a tendency to increase after brimonidine and reverse after yohimbine administration. (Table 4.6 and figure 4.6)

Regarding to filtation fraction (FF), no significant differences were detected among baseline values and values after brimonidine and yohimbine administrations in both low and high-dose groups. (Table 4.6)

## 2. Effects of brimonidine on fractional excretion of the electrolytes

**Table 4.7**- Fractional excretion (FE) of the electrolytes, sodium, potassium, chloride, calcium and phosphorus of low and high-dose groups of brimonidine administration in 5 dogs of each group.

| | *FENa* (%) | *FEK* (%) | *FECl* (%) | *FECa* (%) | *FEP* (%) |
|---|---|---|---|---|---|
| Low-dose | | | | | |
| Baseline | 0.597±0.060[a] | 8.56±1.19 | 0.130±0.036 | 0.190±0.032 | 3.51±2.66 |
| Brimonidine | 1.120±0.227[b] | 18.40±4.13 | 0.220±0.078 | 0.310±0.089 | 14.30±4.74 |
| Yohimbine | 0.699±0.192[a] | 12.50±3.61 | 0.140±0.077 | 0.410±0.197 | 2.73±1.64 |
| High-dose | | | | | |
| Baseline | 0.569±0.060 | 7.95±1.22 | 0.130±0.044 | 0.330±0.116 | 1.39±0.68 |
| Brimonidine | 1.020±0.259 | 16.60±3.63 | 0.110±0.060 | 0.370±0.133 | 7.26±4.26 |
| Yohimbine | 0.651±0.133 | 10.10±1.97 | 0.030±0.018 | 0.360±0.127 | 2.91±2.17 |

The data were shown as mean ± SE.

[a,b] means with different superscripts differ significantly ($p<0.05$).

Fractional excretion (FE) of sodium after low dose of brimonidine administration increased significantly and return to baseline levels after injection of yohimbine. FE of potassium and phosphorus tended to be increased in response to brimonidine administration and also returned to baseline level following the

yohimbine intravenous injection. There were no any apparent alterations after brimonidine administration of FE chloride and calcium when comparing to baseline level.

### 3. Effects of brimonidine on osmolar, free water clearance and urine production

**Table 4.8** - Osmolar clearance ($C_{OSM}$), free water clearance($C_{H2O}$) and urine output of low and high dose of brimonidine in 5 dogs of each group.

| | $C_{OSM}$ (ml/kg/min) | $C_{H2O}$ (ml/kg/min) | Urine Output (ml/kg/min) |
|---|---|---|---|
| Low-dose | | | |
| Baseline | 0.048±0.004 | -0.035±0.003 | 0.012±0.002 |
| Brimonidine | 0.046±0.005 | -0.029±0.006 | 0.015±0.002 |
| Yohimbine | 0.042±0.008 | -0.032±0.008 | 0.012±0.002 |
| High-dose | | | |
| Baseline | 0.052±0.005 | -0.038±0.003 | 0.016±0.003 |
| Brimonidine | 0.052±0.004 | -0.037±0.003 | 0.016±0.0003 |
| Yohimbine | 0.058±0.004 | -0.041±0.004 | 0.017±0.001 |

The data were shown as mean ± SE.

Neither low nor high dose of brimonidine caused changes of osmolar clearances ($C_{OSM}$) as well as free water clearance ($C_{H2O}$) from baseline values. Urine outputs in both groups were unchanged in any conditions.

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## Effects of brimonidine on other parameters

### 1. Effects of brimonidine on respiratory rate and rectal temperature

**Table 4.9-** The respiratory rate (RR) and rectal temperature (RT) of low and high doses of brimonidine administration in 5 dogs of each group.

| | *RR* *(breaths/min)* | *RT* *(°F)* |
|---|---|---|
| Low-dose | | |
| Baseline | 42.2±4.54 | 102.38±0.23 |
| B1 | 20.4±4.97 $^{\pi}$ | 102.20±0.30 |
| B2 | 22.2±4.50 $^{\pi}$ | 102.08±0.11 |
| B3 | 23.4±7.17 $^{\pi}$ | 102.06±0.26 |
| Yohimbine | 35.0±3.41 $^{\pi}$ | 103.06±0.64 |
| High-dose | | |
| Baseline | 41.2±8.09 | 101.58±0.26 |
| B1 | 18.4±1.72 $^{\pi}$ | 102.30±0.59 |
| B2 | 13.0±2.76 $^{\pi}$ | 101.98±0.54 |
| B3 | 15.0±2.49 $^{\pi}$ | 101.80±0.56 |
| Yohimbine | 31.2±2.24 | 103.54±0.47 * |

The data were shown as mean ± SE.

*, $P < 0.05$, significant difference from corresponding baseline value.

$^{\pi}$ significant difference in non-parametric method ($P < 0.05$).

B1-B3 = first to third hour after brimonidine administration.

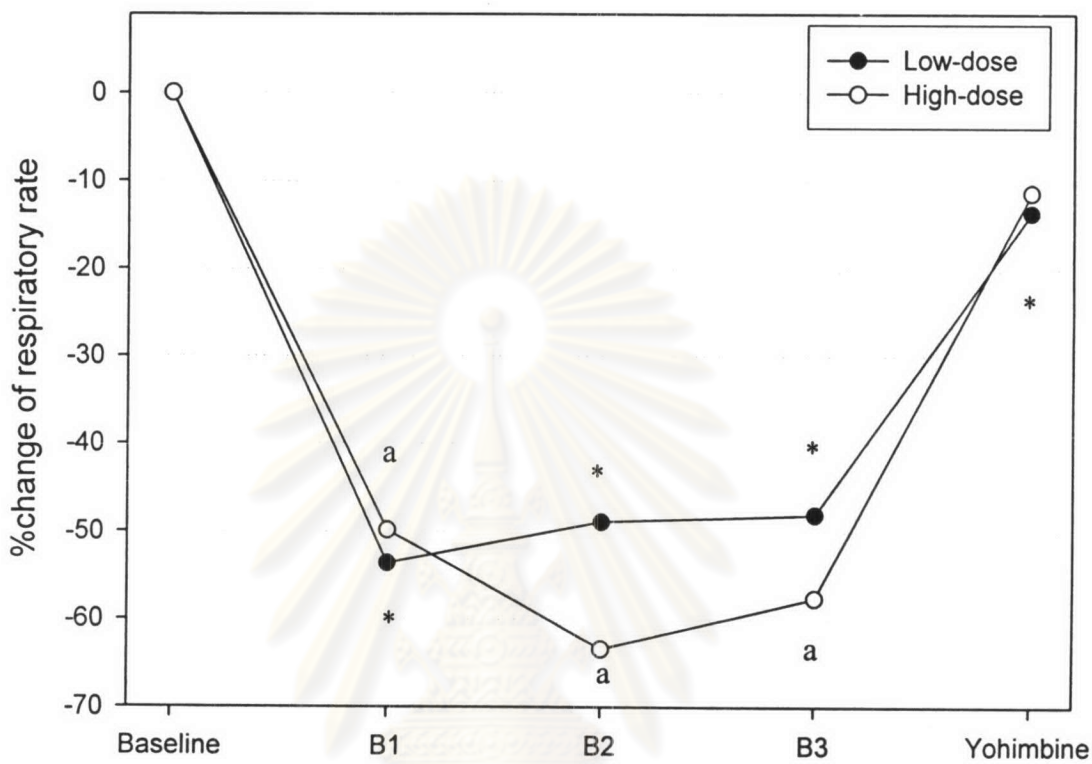


**Figure 4.7** - Percent changes of respiratory rate (RR) after low and high-dose of brimonidine administrations and yohimbine injection in 5 dogs of each group.
Data were present as percent change of mean.
* and [a], $P < 0.05$, significant difference from corresponding baseline value in low- and high-dose groups respectively.
B1-B3 = first to third hour after brimonidine administration.

Respiratory rate (RR) declined in all recording period after low and high doses of brimonidine administration significantly. In high-dose group, the values could be reversed but still lower than baseline levels after administration of yohimbine. (Table 4.9 and fig. 4.7)

The rectal temperature (RT) was not altered after either low or high dose of brimonidine administration. Following the yohimbine intravenous injection, RTs were elevated in both dose-groups as shown in table 4.9

## 2. Effects of brimonidine on hematocrit and total solid

**Table 4.10** - Hematocrit (HCT) and total solid (TS) of low and high-dose group of brimonidine administration in 5 dogs of each group.

| | *HCT* (%) | *TS* (g%) |
|---|---|---|
| Low-dose | | |
| Baseline | 35.4±2.02 | 8.84±0.30 |
| Brimonidine | 29.8±2.65 | 7.63±0.76 |
| Yohimbine | 38.0±2.70 | 9.06±0.88 |
| High-dose | | |
| Baseline | 39.0±2.83 [a] | 9.34±0.26 |
| Brimonidine | 33.2±1.53 [b] | 9.17±0.52 |
| Yohimbine | 44.2±2.63 [a] | 9.65±0.58 |

The data were shown as mean ± SE.

[a,b] means with different superscripts differ significantly ($p<0.05$).

Hematocrit (HCT) and total solid (TS) reduced after brimonidine ingestion. Following yohimbine intravenous injection, they returned into baseline levels. The significant differences of hematocrit were found only in high-dose group.

### 3. Effects of brimonidine on blood glucose level

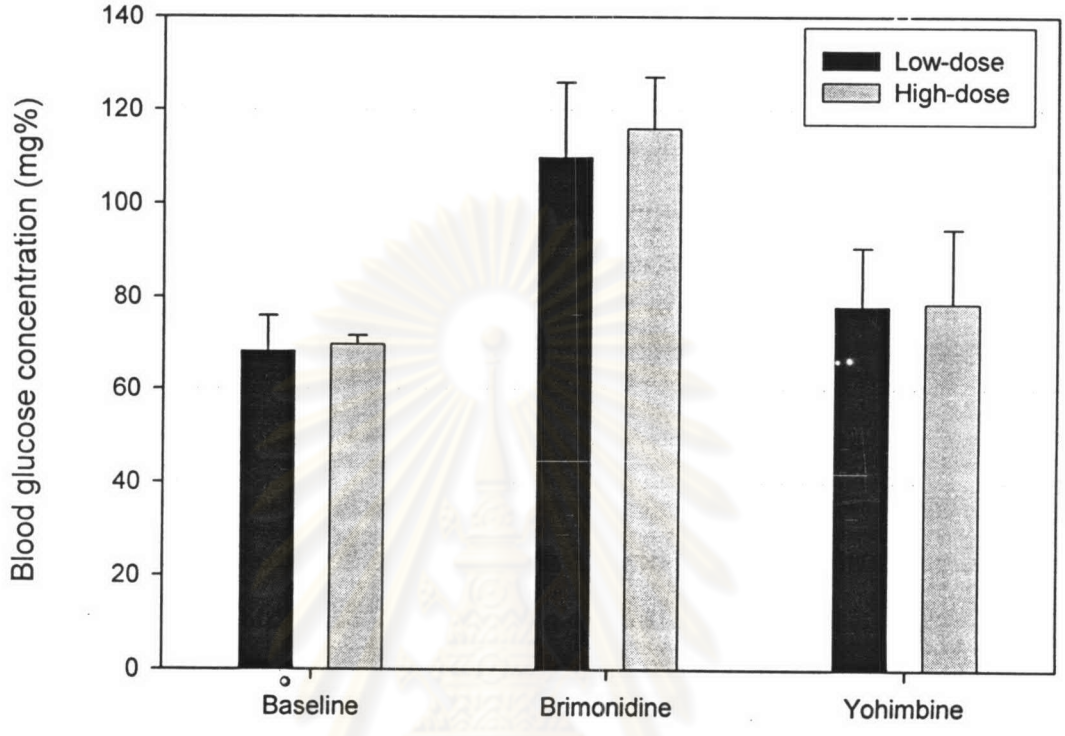


**Figure 4.8**- Blood glucose level after low and high dose of brimonidine and also reversed effect after administration of yohimbine in 5 dogs of each group.
Data were present as mean ± SE.

As shown in figure 4.8, baseline blood glucose levels appeared to be elevated after low and high doses of brimonidine administrations (68.20±7.72 and 69.60±1.96 mg% to 109.80±16.05 and 116.00±11.01 mg% in low and high-dose groups respectively) and returned to baseline values following the administration of yohimbine (78.00±12.70 and 78.60±16.04 mg% in low and high-dose respectively). However, there were no statistically significant differences detected in these observations

## 4. Effects of brimonidine on plasma osmolarity and concentration of electrolytes

**Table 4.11** - Arterial plasma osmolarity and concentration of electrolytes of low- and high-dose of brimonidine administration and yohimbine administration in 5 dogs of each group.

| | $P_{Osm}$ (mOsm) | $P_{Na}$ (mEq/L) | $P_K$ (mEq/L) | $P_{Cl}$ (mEq/L) | $P_{Ca}$ (mg%) | $P_P$ (mg%) |
|---|---|---|---|---|---|---|
| Low-dose | | | | | | |
| Baseline | 217.84±6.87 | 134.68±3.12 | 3.71±0.25[a] | 110.56±1.31 | 9.13±0.34 | 2.76±0.3 |
| Brimonidine | 273.12±11.58 | 131.68±4.23 | 3.86±0.35[a] | 108.24±2.04 | 9.19±0.25 | 3.90±0.3 |
| Yohimbine | 281.15±4.02 | 132.15±3.57 | 3.18±0.37[b] | 112.95±2.95 | 8.63±0.32 | 2.81±0.2 |
| High-dose | | | | | | |
| Baseline | 271.60±8.16[a] | 123.48±1.17 | 3.46±0.15[a] | 107.88±3.14 | 9.39±0.23 | 3.27±0.3 |
| Brimonidine | 287.12±4.77[ab] | 125.92±0.83 | 3.86±0.16[b] | 107.20±0.81 | 9.78±0.25 | 4.30±0.1 |
| Yohimbine | 294.00±2.71[b] | 125.90±1.68 | 3.42±0.12[a] | 108.65±0.55 | 9.27±0.42 | 2.94±0.3 |

The data were shown as mean±SE.

[a,b] means with different superscripts differ significantly ($p<0.05$).

Following high dose of brimonidine administration, plasma concentration of potassium and phosphorus were elevated significantly and had tendency to increase after low-dose administration of brimonidine.

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## 5. Effects of brimonidine on blood gas analysis

**Table 4.12-** Arterial blood gas analysis of low and high-dose of brimonidine administrations and after yohimbine administration in 5 dogs of each group.

| | *pH* | *$P_{CO2}$ (mmHg)* | *$P_{O2}$ (mmHg)* | *$HCO_3$ (mmol/L)* | *$O_2$sat (%)* |
|---|---|---|---|---|---|
| Low-dose | | | | | |
| Baseline | 7.37±0.01 | 32.06±1.62 | 108.62±3.97 | 20.660±0.546 | 97.640±0.163 |
| Brimonidine | 7.38±0.02 | 32.64±2.37 | 116.10±6.59 | 19.720±1.002 | 97.740±0.375 |
| Yohimbine | 7.37±0.03 | 29.36±2.09 | 113.82±7.07 | 18.540±0.585 | 97.300±0.652 |
| High-dose | | | | | |
| Baseline | 7.37±0.01 | 33.90±2.33 | 101.30±3.15 | 21.140±0.794 | 97.000±0.335 |
| Brimonidine | 7.41±0.02 | 33.68±3.08 | 113.98±4.36 | 22.780±0.364 | 97.960±0.287 |
| Yohimbine | 7.39±0.02 | 31.66±1.12 | 105.00±2.64 | 21.360±0.813 | 97.260±0.268 |

The data were shown as mean±SE.

pH was arterial blood pH, $P_{CO2}$ and $P_{O2}$ were partial pressure of carbondioxide and oxygen in arterial blood respectively, $HCO_3$ was arterial bicarbonate levels, and $O_2$sat was oxygen saturation.

Regarding to arterial blood gas analyses, there were no significant differences among each condition in each dose-group of brimonidine. Arterial blood pH, $P_{CO2}$, $P_{O2}$, $HCO_3^-$ levels, and $O_2$ saturation were unaltered after both doses of brimonidine.

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