Acute and Chronic Effects of Ethanol on the Cardiovascular and Hormonal Responses to Hemorrhage in Conscious Normotensive and Spontaneously Hypertensive Rats

Yoon-Yub Park, Joong-Hee Lee, Jae-Sik Park, Eun-Kyoung Yang
Dong-Kuk Ahn, Hyeong-Jin Kim and Won-Jung Lee

Department of Physiology, School of Medicine, Kyungpook National University
Taegu 700-422, Korea

= ABSTRACT=

Acute and chronic effects of ethanol (EOH) administration on the cardiovascular and hormonal responses to repeated hemorrhage were investigated in conscious normotensive Wistar rats and spontaneously hypertensive rats (SHR). The chronic EOH-treated group received 5% EOH (vol/vol) ad libitum in the drinking water for the first week, 10% for the next 2 weeks, and 20% for the last 5 weeks from the age of 6 weeks. The EOH-free group received tap water. Chronic EOH and EOH-free groups were randomly subdivided into acute EOH infusion and control groups. Under ether anesthesia, catheters were inserted into the femoral vein and both femoral arteries. After rats regained consciousness and their blood pressure was stabilized, responses to quick hemorrhage (5 ml/kg BW) were tested. In the acute EOH infusion group, hemorrhage was induced 20 min after EOH infusion (1.0 g/kg BW). Baroreceptor reflex sensitivity was assessed by the ratio of changes in heart rate and mean arterial pressure ($\triangle$HR/$\triangle$MAP) immediately after the hemorrhage.

Chronic EOH administration elevated MAP in Wistar rats. During acute EOH infusion, MAP decreased and HR increased in all groups. In comparison to EOH-free control rats, acute or chronic EOH-treated rats showed a greater reduction in MAP and a smaller elevation in heart rate in response to a hemorrhage. The degree of MAP reduction was significantly greater in SHR than in Wistar rats. Both the acute and chronic EOH administration attenuated the baroreceptor reflex and retarded MAP recovery, again the trend being much more prominent in SHR. The increase in plasma vasopressin and renin concentrations after hemorrhage were intensified by the chronic EOH administration. SHR showed a greater vasopressin response but a smaller renin response than Wistar rats.

These results indicate that the EOH-treated rats, particularly SHR, are prone to shock by a hemorrhage, which may be partly attributed to an impaired baroreceptor reflex function.

Key Words: Ethanol, Hemorrhage, Baroreceptor reflex sensitivity, SHR, Vasopressin, Renin

INTRODUCTION

Hemorrhage is the most common cause of

hypovolemic shock. Hemorrhagic hypotension elicits several neurohumoral homeostatic mechanisms such as reflex sympathoexcitation and peripheral vasoconstriction. In this situation, the baroreceptor reflex is one of the most important compensating mechanisms for the recovery from a hypovolemic hypotension (Cornish et al, 1990; Courneya & Korner, 1991). In addition, pressor hormones, such as vaso-

pressin and angiotensin II, also act to prevent progression of the shock (Yamazaki & Sagawa 1985; Katoh et al, 1989).

Since the baroreceptor reflex is the most powerful and rapidly acting homeostatic mechanism in maintaining blood pressure, the baroreceptor reflex sensitivity is widely used as an index of the pressure buffering capability of the baroreceptors. This reflex has been shown to be depressed in hypertensive humans (Takeshita et al, 1975; Goldstein, 1983) and experimental animals (Luft et al, 1986; Michelini et al, 1992). Our previous study (Park et al, 1990) also indicated that the baroreceptor reflex is attenuated in spontaneously hypertensive rats (SHR), and thus SHR are prone to shock by hemorrhage compared with the normotensive Wistar rats.

It has been documented that acute or chronic administration of ethanol (EOH) attenuate baroreceptor reflex function (Abdel-Rahman et al, 1985; Abdel-Rahman & Wooles 1987; Russ et al, 1991). Few studies, however, have been conducted on the effect of EOH on the cardiovascular and hormonal responses to hemorrhage in the hypertensives. Furthermore, the effect of EOH administration on the recovery from the hemorrhagic hypotension is controversial (Ward et al, 1982; Hórton, 1986; Newsome, 1988). Moreover, most studies on the cardiovascular and hormonal responses have dealt with a single hemorrhage. However, experimentally repeated hemorrhage may correspond to a common clinical situation with intermittent hemorrhage. Hemorrhagic shock frequently occurs in trauma patients with alcoholism (Huth et al, 1983).

Accordingly, in the present study, we systematically evaluated 1) the effects of acute and chronic (8 weeks) EOH administration on the arterial pressure and heart rate in normotensive Wistar and spontaneously hypertensive rats, and 2) the effects of EOH on the cardiovascular system and vasopressin and renin release following repeated hemorrhage.

METHODS

Animals and chronic ethanol administration

Six-week-old male normotensive Wistar and spontaneously hypertensive rats (SHR) were used in this study. Each strain of rats was randomly divided into two groups: chronic EOH-treated and EOH-free groups. According to the method of Chan and Sutter (1982), the rats of the chronic EOH-treated group received EOH solution as the only source of drinking water ad libitum in the following sequence: 5% (vol/vol) EOH solution ad libitum for the first week, 10 % solution for the next 2 weeks, and 20% solution for the last 5 weeks. Rats of the EOH-free group received tap water.

Animals in each group were tested for cardiovascular and hormonal responses to repeated hemorrhage either with or without an acute EOH infusion. Thus, the data were analyzed for the four subgroups in each strain, as depicted in Figure. 1.

Experimental protocol

Under ether anesthesia, cannulae (PE50) filled with heparinized saline (50 units/ml) were inserted into a femoral vein for EOH infusion and into both femoral arteries for the direct measurement of arterial pressure and blood drawing for hemorrhage. After the surgery, the rat was allowed approximately 2 hours to regain consciousness and to stabilize blood pressure, recovering from the anesthesia-induced attenuation of the baroreceptor reflex (Stornetta et al, 1987).

Arterial pressure was measured using a Statham P50 pressure transducer and the electronically damped mean arterial pressure (MAP) was continuously recorded on a physiograph (Narco, MK-IV-P). Heart rate (HR) was obtained from the arterial pressure pulse using a biotachometer coupler.

A quantity of blood equivalent to 5 ml/kg BW was withdrawn through an arterial catheter

into a plastic syringe as rapidly as possible and the changes in MAP and HR were recorded for 20 min. The second hemorrhage was performed by the same procedure.

In the acute EOH infusion group, 1.0 g/kg BW of 30% EOH (vol/vol) was infused into a femoral vein using an infusion pump (Harvard, Model 22) at a rate of 0.05 ml/min. Twenty minutes after the EOH infusion, hemorrhage was induced.

Assessment of baroreceptor reflex sensitivity (BRS)

BRS was assessed as the gain in the baroreceptor reflex function using the widely used method (Luft et al, 1986; Abdel-Rahman & Wooles, 1987; Michelini et al, 1992). The peak change in MAP and the reflex change in

HR after hemorrhage were used to calculate the $\triangle HR/\triangle MAP$ ratio (expressed as beats/min/mmHg) as a measure of BRS.

Assays

Upon completion of the experiment, blood samples were centrifuged at 2,000 rpm for 20 min at 4°C. For arginine vasopressin (AVP) assay, the plasma was acidified with 1 N HCl and stored at −20°C. For the determination of plasma renin concentration (PRC), 50 μl of plasma was stored in a tube containing 50 μg of EDTA. Plasma AVP concentration and PRC were determined using the radioimmunoassay methods described by Lee et al. (1987) and Cho et al. (1989), respectively.

Statistical analysis

All data are presented as mean±SE. The Mann-Whitney U test was used to make comparisons between groups: the Wilcoxon signed rank test was used for paired observation. Probability levels of less than 0.05 were considered statistically significant.

RESULTS

Cardiovascular responses to ethanol administration

The effects of chronic (8 weeks) EOH

```
                    Wistar (or SHR)
                           |
            ┌──────────────┴──────────────┐
        EOH-free                     Chronic EOH
       ┌────┴────┐                  ┌────┴────┐
   Control   Acute EOH          Control   Acute EOH
      ‖          ‖                 ‖          ‖
   WC (SC)    WE (SE)          EWC (ESC)   EWE (ESE)
```
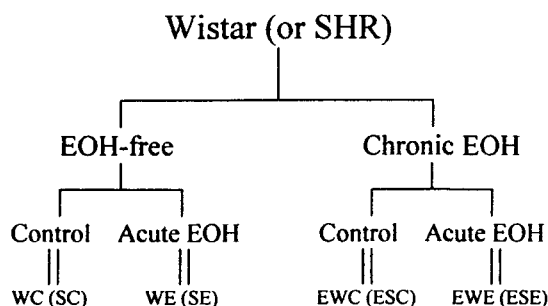
Fig. 1. The animal groups and their symbols.

Table 1. Effects of chronic (8 weeks) ethanol (EOH) administration on mean arterial pressure (MAP), heart rate (HR) and body weight in normotensive Wistar and spontaneously hypertensive rats (SHR)

Group	N	MAP (mmHg)	HR (beats/min)	Body Weight (g)
Wistar EOH-free	19	126±1	488±8	290±8
Wistar Chronic EOH	21	137±1**	487±9	293±9
SHR EOH-free	18	166±2	427±6	278±3
SHR Chronic EOH	14	171±3	471±4**	272±5

N indicates number of rats.
All values are mean±SE.
**p<0.01 significantly different from the corresponding EOH-free group.
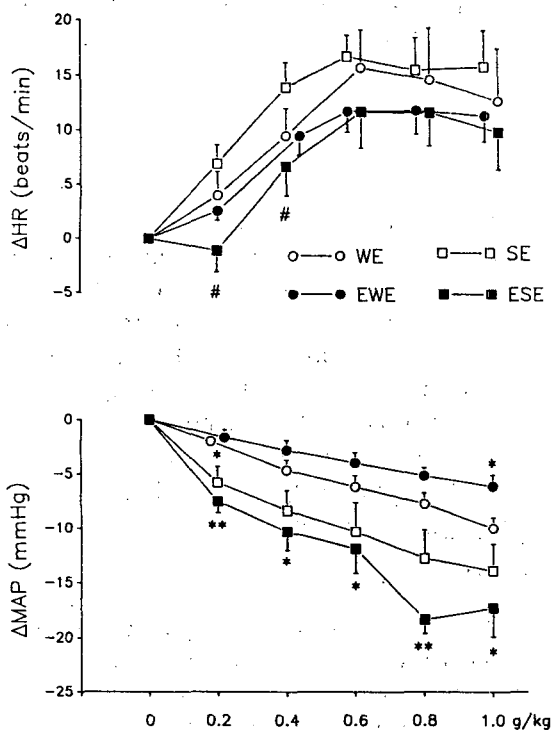Abbreviation for each group is shown in Fig. 1.

Fig. 2. *Changes in mean arterial pressure (△MAP)
and heart rate (△HR) during actue ethanol infusion
(1 g/kg BW) in Wistar and spontaneously hyperten-
sive rats (SHR). Values are mean±SE.*

**p<0.05, **p<0.01, significantly different from
the WE group.*

*#p<0.05, significantly different from the corre-
sponding EOH-free-group.*

Abbreviation for each group is shown in Fig. 1.

Numbers of cases are shown in Table 2.

administration on the resting MAP and HR in
Wistar and SHR are shown in Table 1. Chronic
EOH administration elevated MAP significant-
ly in Wistar rats but not in SHR. On the other
hand, it increased HR markedly in SHR, but
not in Wistar rats. Body weight was not differ-
ent between the chronic EOH-treated and
EOH-free groups.

Figure 2 shows the effects of acute EOH infu-
sion (1.0 g/kg BW) on MAP and HR both in
the chronic EOH-treated and EOH-free groups.
During EOH infusion there was a progressive

decrease in MAP and an increase in HR in all
groups. However, the reduction of MAP was
greater in SHR than in Wistar rats.

**Cardiovascular responses to repeated
hemorrhage**

Effects of the first hemorrhage (5 ml/kg BW)
on MAP and HR are illustrated in Figure 3.
Following hemorrhage, the acute (WE) and
chronic EOH-treated Wistar rats (EWC and
EWE) showed a greater reduction of MAP but
a smaller elevation of HR as compared with
EOH-free control (WC) rats. Five min after the
hemorrhage, WC rats recovered MAP almost
completely to the prehemorrhagic level, but
their HR remained elevated. However, the
acute or chronic EOH-treated rats showed a
partial recovery of MAP, and failed to main-
tain the tachycardia during the recovery period.

Among SHR, the MAP reduction after hem-
orrhage was significantly greater in the chronic
EOH-treated (ESC & ESE) than in the EOH-
free (SC & SE) rats. ESE rats showed a conspic-
uously greater reduction and a slower recovery
of MAP than the other groups. On the other
hand, SC rats maintained the tachycardia dur-
ing the recovery period, whereas the HR in the
other groups decreased rapidly and failed to
maintain tachycardia. Furthermore, in the ESE
group, the HR decreased more rapidly to a
value much below the prehemorrhagic level and
remained low thereafter.

After the second hemorrhage (Fig. 4 & Table
2), all groups showed a greater reduction and a
slower recovery of MAP than after the first
hemorrhage. The retardation of MAP recovery
was particularly evident in SHR. The
tachycardic response shown immediately after
the hemorrhage was attenuated compared with
the first hemorrhage in all groups. In fact, ESE
rats hardly showed any tachycardic response,
and 2 of them showed bradycardia rather than
tachycardia immediately after hemorrhage. The
HR change during the recovery period was also
different from that with the first hemorrhage.
In all groups except WC, the HR markedly de-
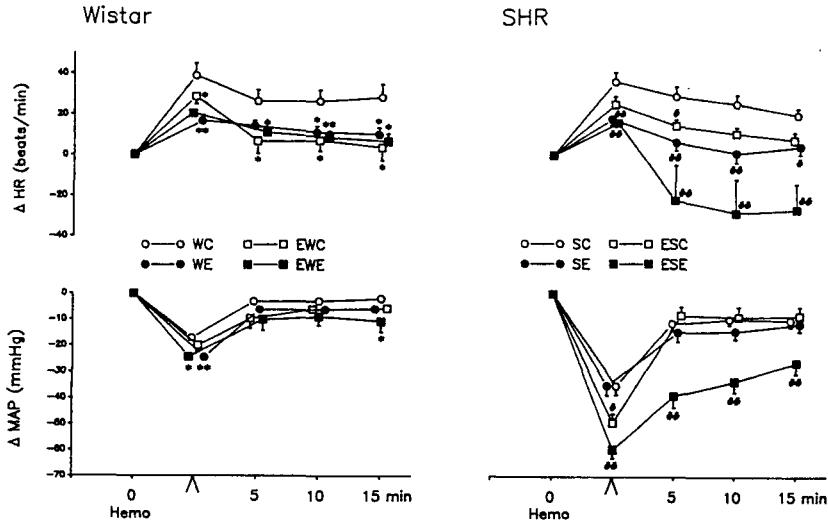clined to a value far below the prehemorrhagic

Fig. 3. Changes in mean arterial pressure (△MAP) and heart rate (△HR) after the first hemorrhage (5 ml/kg BW) in Wistar and spontaneously hypertensive rats (SHR). Values are mean±SE. Hemo, hemorrhage; ^, maximal changes in MAP and HR, which appeared before 5 minutes after hemorrhage.

*p<0.05, **p<0.01, significantly different from the WC group.

#p<0.05, ##p<0.01, significantly different from the SC group.

Abbreviation for each group is shown in Fig. 1.

Numbers of cases are shown in Table 2.

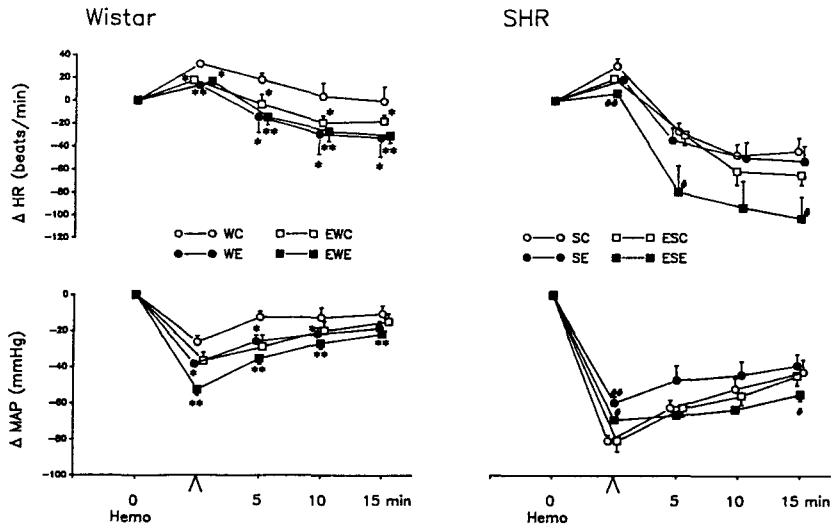Fig. 4. Changes in mean arterial pressure (△MAP) and heart rate (△HR) after the second hemorrhage (5 ml/kg BW) in Wistar and spontaneously hypertensive rats (SHR). Values are mean±SE. Hemo, hemorrhage; ^, maximal changes in MAP and HR, which appeared before 5 minutes after hemorrhage.

*p<0.05, **p<0.01, significantly different from the WC group.

#p<0.05, ##p<0.01, significantly different from the SC group.

Abbreviation for each group is shown in Fig. 1.

Numbers of cases are shown in Table 2.

Table 2. Maximal changes in mean arterial pressure ($\triangle$MAP), heart rate ($\triangle$HR) after the first and second hemorrhages (5 ml/kg BW) and baroreceptor reflex sensitivity (BRS) in Wistar and spontaneously hypertensive rats

Animal Group	N	$\triangle$MAP (mmHg)	$\triangle$HR (beats/min)	BRS (beats/min/mmHg)
First Hemorrhage				
WC	9	-17 ± 2	39 ± 6	-2.61 ± 0.58
WE	10	-24 ± 2**	16 ± 3**	-0.77 ± 0.23**
EWC	10	-20 ± 2	28 ± 4	-1.57 ± 0.26
EWE	11	-24 ± 2*	20 ± 2*	-0.87 ± 0.09**
SC	9	-35 ± 3	36 ± 5	-1.09 ± 0.15
SE	9	-35 ± 4	18 ± 3**	-0.57 ± 0.12*
ESC	7	-49 ± 3*	25 ± 4	-0.50 ± 0.07**
ESE	7	-60 ± 3**	16 ± 1**	-0.28 ± 0.03**
Second Hemorrhage				
WC	9	-26 ± 4	32 ± 4	-1.57 ± 0.43
WE	10	-38 ± 2*	13 ± 2**	-0.35 ± 0.05**
EWC	10	-37 ± 5	17 ± 3*	-0.59 ± 0.17*
EWE	11	-53 ± 3**	16 ± 2*	-0.33 ± 0.05**
SC	9	-81 ± 3	30 ± 7	-0.37 ± 0.08
SE	9	-60 ± 3**	18 ± 2	-0.32 ± 0.05
ESC	7	-81 ± 6	19 ± 3	-0.23 ± 0.02
ESE	7	-69 ± 1*	6 ± 2**	-0.09 ± 0.03**

BRS is expressed as the $\triangle$HR/$\triangle$MAP ratio.
N indicates the number of rats.
All values are mean$\pm$SE.
*$p<0.05$, **$p<0.01$ significantly different from the corresponding EOH-free control group.
Abbreviation for each group is shown in Fig. 1.

level, the trend being much more prominent in SHR than in Wistar rats.

Table 2 presents the maximal changes in MAP and HR after hemorrhage, and the baroreceptor reflex sensitivity (BRS) expressed as the $\triangle$HR/$\triangle$MAP ratio following hemorrhagic hypotension. Acute or chronic adminstration of EOH resulted in attenuation of the BRS both in Wistar and SHR. In all conditions, the MAP response was much greater in the SHR than in Wistar rats, but the HR response was similar. Consequently, SHR showed markedly lower BRS than Wistar rats. The second hemorrhage reduced BRS to about half of that after the first hemorrhage in most groups and to one

third in the ESE group.

Hormonal responses to repeated hemorrhage

Plasma concentrations of arginine vasopressin (pAVP) and renin (PRC) following the first and second hemorrhages are shown in Table 3. On the whole, SHR showed a higher pAVP but lower PRC than Wistar rats. The chronic EOH administration significantly enhanced the pAVP response to hemorrhage, whereas the acute EOH administration did not alter it. In all groups, the pAVP response was potentiated after the second hemorrhage.

As in the pAVP response, the PRC response was also increased in chronic EOH-treated rats,

Table 3. Plasma concentrations of vasopressin (pAVP) and renin (PRC) after the first and second hemorrhage (5 ml/kg BW) in Wistar and spontaneously hypertensive rats

Group	N	pAVP (pg/ml)	PRC (ng AI/ml/hr)
First Hemorrhage			
WC	9	4.1 ± 1.1	26.7 ± 3.1
WE	10	6.1 ± 1.9	38.0 ± 5.4
EWC	10	9.7 ± 1.7**	43.1 ± 4.8*
EWE	11	8.9 ± 0.9*	47.6 ± 4.9**
SC	9	6.2 ± 1.5	16.8 ± 3.3
SE	9	3.7 ± 0.4	16.9 ± 1.8
ESC	7	16.3 ± 2.1**	16.4 ± 1.8
ESE	7	14.0 ± 2.3*	29.7 ± 4.0*
Second Hemorrhage			
WC	9	7.5 ± 1.7	45.6 ± 4.9
WE	10	9.6 ± 1.8	53.8 ± 5.5
EWC	10	18.6 ± 2.9**	67.0 ± 6.4*
EWE	11	21.8 ± 3.9**	71.5 ± 7.7*
SC	9	15.6 ± 2.8	24.9 ± 4.4
SE	9	10.2 ± 2.2	26.5 ± 2.3
ESC	7	36.8 ± 5.4**	29.2 ± 4.2
ESE	7	32.2 ± 7.6	38.3 ± 2.7*

N indicates the number of rats.
All values are mean ± SE.
*$p < 0.05$, **$p < 0.01$ significantly different from the corresponding EOH-free control group.
Abbreviation for each group is shown in Fig. 1.

particularly in EWE and ESE. However, unlike the pAVP response, the degree of increased PRC response to the repeated hemorrhage was greater in Wistar rats than in SHR.

DISCUSSION

The present study was conducted to investigate the acute and chronic effects of EOH administration on the cardiovascular and hormonal responses to hemorrhagic hypotension. For chronic administration of EOH, we adopted the method of Chan and Sutter (1982), which has a great advantage in feeding large groups of animals. In addition, Russ et al. (1991) reported that feeding EOH by this meth-

od did not alter the fluid intake and body weight of the animal. In agreement with this report, we observed in the present study no difference in the body weight between the chronic EOH-treated and EOH-free groups (Table 1).

Cardiovascular responses to chronic ethanol administration

In the present study, the chronic EOH administration significantly elevated MAP in Wistar rats and caused similar tendency in SHR (Table 1), in accordance with other reports (Abdel-Rahman & Wooles, 1987; Russ et al, 1991). Many epidemiological studies (Jackson et al, 1985; Trell et al, 1985) have demonstrated a positive correlation between the duration and extent of EOH intake and the develop-

ment of hypertension. Such results suggest that chronic EOH intake may be an aggravating factor in the development of hypertension in SHR as well as in Wistar rats. The underlying mechanism(s) is not clear at present, although it has been suggested that an increase in sympathetic nerve activity may be involved (Abdel-Rahman & Wooles, 1987; Russ et al, 1991). In contrast, Hatton et al. (1992) reported that chronic EOH administration lowered blood pressure in Wistar rats using the same method as ours. In addition, Howe et al. (1989) have observed a retarded development of hypertension in SHR and stroke-prone SHR fed EOH from weaning. Certainly, many more studies are required to elucidate the chronic effects of EOH on the blood pressure, particularly in hypertensives.

Cardiovascular responses to acute ethanol administration

The effect of acute administration of EOH on the arterial pressure is still controversial. While some investigators reported an increase in blood pressure (Ireland et al, 1984), others reported a decrease (Hellström & Tottmar, 1982; Malinowska et al, 1989) or no change (Zsoter & Sellers, 1977; Zhang et al, 1988). In the present study, acute EOH administration produced a progressive decrease in MAP, in contrast to the chronic administration. Although we presume that this discrepancy is in part attributed to the difference in the experimental protocol and the dose of EOH administered, it may also be associated with the complex nature of the central and peripheral actions of EOH (Zhang et al, 1988). SHR showed a greater reduction of MAP during EOH infusion than Wistar rats (Fig. 2). Chronic EOH-treated SHR, but not Wistar rats, showed a greater fall in MAP during acute EOH infusion than the control SHR (SC). It is not clear why the MAP response of SHR was different from Wistar rats.

In contrast to the MAP response, many investigators agree that acute EOH administration increases HR (Zsoter & Sellers, 1977; Ireland et al, 1984). The present study also showed that the HR increased progressively during acute EOH infusion in all groups. This increase in HR probably resulted from a reflex control to preserve blood pressure after arteriolar and venous dilation, or volume depletion as a consequence of EOH-induced diuresis (Howes & Reid, 1986).

Cardiovascular responses to repeated hemorrhage

Following hemorrhage, the EOH-treated rats showed a greater reduction and an attenuated recovery of MAP than the EOH-free control rats. Reves and Newman (1972) reported that an acute EOH administration aggravated hypotension in response to hemorrhage. The mechanism for the detrimental effect of EOH on the recovery from hemorrhagic hypotension is not certain, although some investigators have suggested that EOH produces cardiac contractile dysfunction (Horton, 1986; Cappasso et al, 1991) and suppresses the vasoconstrictive effect of norepinephrine (Newsome, 1988).

The second hemorrhage produced a greater reduction and slower recovery of MAP than the first hemorrhage. Similar observations have been made by Hjelmqvist et al. (1991). They found a delayed and impaired increase of the systemic vascular resistance after the second hemorrhage, which they suggested as the major cause of the impaired recovery from hemorrhagic hypotension. We observed that the tachycardic response to hemorrhage was greatly attenuated or abolished after the second hemorrhage. This might be due to sympathetic inhibition induced by a severe hemorrhage, as suggested by Brizzee et al. (1991). They observed that a mild hemorrhage increased HR and total peripheral resistance without hypotension, whereas a severe hemorrhage decreased them with hypotension. Therefore, they proposed that a severe hemorrhage produces a sympathetic inhibition rather than activation.

Our previous study (Park et al, 1990) showed that SHR produced a greater reduction of MAP but a smaller increase in HR after hemorrhage than Wistar rats. The present study also

showed a retarded recovery of MAP from hemorrhagic hypotension in SHR, particularly in EOH-treated rats. Accordingly, we presume that the EOH administration plays a more detrimental role in cardiovascular regulation after hemorrhage in the hypertensives than in the normotensives.

Baroreceptor reflex sensitivity (BRS)

BRS expressed as the $\triangle HR/\triangle MAP$ ratio is a useful index of the baroreceptor reflex function. It is well known that BRS is depressed in hypertensive humans (Takeshita et al, 1975; Goldstein, 1983) and animals (Luft et al, 1986; Park et al, 1990; Michelini et al, 1992).

Many investigators (Abdel-Rahman et al, 1985; Abdel-Rahman & Wooles, 1987; Russ et al, 1991) have reported that EOH administration attenuates the baroreceptor reflex. The present study confirmed this, and established that the trend is much more prominent in SHR. Chronic EOH-treated rats without acute EOH administration (EWC & ESC) also showed a significantly reduced BRS. This attenuation of BRS can account for a greater decrease and a slower recovery of MAP following hemorrhage observed in EOH-treated rats. After the second hemorrhage, the BRS was more severely attenuated compared with the first hemorrhage, as evidenced by a greatly diminished or completely abolished tachycardic response in the face of an augmented MAP drop.

Hormonal responses to repeated hemorrhage

Release of vasopressin and renin (i.e., angiotensin II production), the two major compensatory adjustments to hemorrhage, is stimulated by hypovolemia and hypotension. These hormones help to defend arterial pressure against the hemorrhage (Korner et al, 1990; Schadt & Gaddis, 1990). The plasma concentration of AVP was significantly elevated after the second hemorrhage. This might be due to a greater reduction of MAP after the second hemorrhage.

Chronic, but not acute, EOH administration significantly enhanced AVP release after hemorrhage both in Wistar rats and SHR. The mechanism for this effect of chronic EOH administration is not entirely clear. However, it does not seem to be associated with a greater reduction of MAP after hemorrhage, since an acute EOH administration also potentiated the MAP response to hemorrhage without changing the AVP response. Hoffman and Dave (1991) reported that chronic EOH administration decreased the hypothalamic level of AVP mRNA but increased plasma AVP level in rats. They suggested that chronic EOH administration produces a disruption of AVP synthesis-secretion coupling.

SHR showed a higher plasma concentration of AVP after hemorrhage than Wistar rats. Again, the mechanisms are not clear, but the following possibilities can be considered. First of all, the basal plasma concentration of AVP is already elevated in SHR (Crofton et al, 1987). Secondly, a greater reduction of MAP may cause an increased release of AVP in SHR.

Chronic EOH administration also enhanced renin release after hemorrhage. Similarly, Potter et al. (1983) reported that the plasma levels of renin and aldosterone increased with chronic EOH consumption in man. Such an effect of chronic EOH administration may be associated with a greater reduction of MAP after hemorrhage and/or a sympathetic overactivity (Kaysen & Noth, 1984; Howes & Reid, 1986). After the second hemorrhage, renin release was also greatly enhanced. In contrast to the AVP response, the PRC response to hemorrhage was weaker in SHR than in Wistar rats, probably due to a depressed renin-angiotensin system and a lower basal PRC level in SHR (Freeman et al, 1975; Shiono & Sokabe, 1976).

In summary, chronic EOH administration increased arterial pressure in Wistar rats, whereas acute EOH administration decreased it both in Wistar and SHR. Acute and chronic administrations of EOH produced a greater reduction of MAP after repeated hemorrhage, attenuated the BRS, and retarded the recovery from hemorrhagic hypotension. In SHR, EOH elicit

ed remarkably greater alterations in the cardio-vascular responses to hemorrhage than in Wistar rats. Chronic, but not acute, admini-stration of EOH enhanced the release of AVP and renin following hemorrhage.

We conclude, therefore, that 1) EOH admini-stration impairs arterial pressure recovery from hemorrhagic hypotension, and 2) SHRs are prone to shock by hemorrhage.

REFERENCES

Abdel-Rahman ARA, Dar MS & Wooles WR (1985) Effect of chronic ethanol administration on arterial baroreceptor function and pressor and depressor responsiveness · in rats. *J Pharmacol Exp Ther* **232**, 194-201

Abdel-Rahman ARA & Wooles WR (1987) Etha-nol-induced hypertension involves impairment of baroreceptors. *Hypertension* **10**, 67-73

Brizzee BL, Russ RD & Walker BR (1991) Role of vasopressin in acutely altered baroreflex sensi-tivity during hemorrhage in rats. *Am J Physiol* **261**, R677-R685

Cappasso JM, Li P & Anversa P (1991) Myocardial mechanics predict hemodynamic performance during normal function and alcohol-induced dysfunction in rats. *Am J Physiol* **261**, H1880-H1883

Chan TCK & Sutter MC (1982) The effects of chronic ethanol consumption on cardiac func-tion in rats. *Can J Physiol Pharmacol* **60**, 777-782

Cho KW, Kim SH, So JN, Ryu H & Seul KH (1989) Effect of atrial natriuretic peptide on the renal function in two-kidney one-clip hyperten-sive rats. *Kor J Physiol* **23**, 67-78 (in Korean)

Cornish KG, Barazanji MW & Iaffaldano R (1990) Neural and hormonal control of blood pressure in conscious monkeys. *Am J Physiol* **258**, H107-H112

Courneya CA & Korner PI (1991) Neurohumoral mechanisms and the role of arterial barorecep-tors in the reno-vascular response to haemor-rhage in rabbits. *J Physiol (London)* **437**, 393-407

Crofton JT, Share L, Shade RE & Allen C (1978)

Vasopressin in the rat with spontaneous hypertension. *Am J Physiol* **235**, H361-H366

Freeman RH, Davis JO, Varsono-Aharon N, Ulick S & Weinberger MH (1975) Control of aldoste-rone secretion in the spontaneously hyperten-sive rat. *Circ Res* **37**, 66-71

Goldstein DS (1983) Arterial baroreflex sensitivity, plasma catechol-amine, and pressor respon-siveness in essential hypertension. *Circulation* **68**, 234-240

Hatton DC, Bukoski RD, Edgar S & McCarron DA (1992) Chronic alcohol consumption lowers blood pressure but enhances vascular contractil-ity in Wistar rats. *J Hypertens* **10**, 529-537

Hellström E & Tottmar O (1982) Acute effects of ethanol and acetaldehyde on blood pressure and heart rate in disulfiram-treated and control rats. *Pharmac Biochem Behav* **17**, 1103-1109

Hjelmqvist H, Ullman J, Gunnarsson U, Lundberg JM & Rundgren M (1991) Haemodynamic and humoral responses to repeated hypotensive haemorrhage in conscious sheep. *Acta Physiol Scand* **143**, 55-64

Hoffman PL & Dave JR (1991) Chronic ethanol exposure uncouples vasopressin synthesis and secretion in rats. *Neuropharmacology* **30**, 1245-1249

Horton JW (1986) Ethanol impairs cardiocircula-tory function in treated canine hemorrhagic shock. *Surgery* **100**, 520-530

Howe PRC, Rogers PF & Smith RM (1989) Antihypertensive effect of alcohol in spontane-ously hypertensive rats. *Hypertension* **13**, 607-611

Howes LG & Reid JL (1986) The effects of alcohol on local, neural and humoral cardiovascular regulation. *Clin Sci* **71**, 9-15

Huth JF, Maier RV, Simonowitz DA & Herman CM (1983) Effect of acute ethanolism on the hospital course and outcome of injured automo-bile drivers. *J Trauma* **23**, 494-498

Ireland MA, Vandongen R, Davidson R, Beilin LJ & Rouse IL (1984) Acute effects of moderate alcohol consumption on blood pressure and plasma catecholamines. *Clin Sci* **66**, 643-648

Jackson R, Stewart A, Beaglehole R & Scragg R (1985) Alcohol consumption and blood pres-sure. *Am J Epidemiol* **122**, 1037-1044

Katoh N, Sheriff DD, Siu CO & Sagawa K (1989)

Relative importance of four pressoregulatory mechanisms after 10% bleeding in rabbits. *Am J Physiol* **256**, H291-H296

Kaysen G & Noth RH (1984) The effects of alcohol on blood pressure and electrolytes. *Med Clin North Am* **68**, 221-246

Korner PI, Oliver JR, Zhu JL Gipps J & Hanneman F (1990) Autonomic, hormonal, and local circulatory effects of hemorrhage in conscious rabbits. *Am J Physiol* **258**, H229-H239

Lee WJ, Choo YE & Koo JH (1987) Role of plasma osmolality in AVP and aldosterone release in Korean young men. *Kor J Physiol* **21**, 297-304 (in Korean)

Luft FC, Demmert G, Rohmeiss P & Unger T (1986) Baroreceptor reflex effect on sympathetic nerve activity in stroke-prone spontaneously hypertensive rats. *J Auton Nerv Syst* **17**, 199-209

Malinowska B, Pawlak D, Chabielska E & Buczko W (1989) Cardiovascular effects of ethanol in ansthetized, conscious and pithed rats. *Drug Alcohol Depend* **24**, 51-56

Michelini LC, Oliviera M & Santos M (1992) Baroreceptor reflex control of heart rate during development of coarctation of hypertension. *Hypertension* **19** [suppl II], 159-163

Newsome HH (1988) Ethanol modulation of plasma norepinephrine response to trauma and hemorrhage. *J Trauma* **28**, 1-9

Park YY, Kim HJ, Park JS, Lee WJ & Choo YE (1990) Comparison of recovery from cardiovascular changes after norepinephrine injection and hemorrhage between SHR and age-matched Wistar rats. *Kyungpook Univ Med J* **31**, 121-127 (in Korean)

Potter JF, Bannan LT, Saunders JB, Ingram MC & Beevers DG (1983) Blood pressure and pressor mechanisms during alcohol withdrawal. *J Hypertens* **1** (Suppl 2), 97-99

Reves JG & Newman WH (1972) Cardiovascular response to hemorrhage after alcohol in dogs. *Quart J Stud Alc* **33**, 464-475

Russ R, Abdel-Rahman ARA & Wooles WR (1991) Role of the sympathetic nervous system in ethanol-induced hypertension in rats. *Alcohol* **8**, 301-307

Schadt JC & Gaddis RR (1990) Renin-angiotensin system and opioids during acute hemorrhage in conscious rabbits. *Am J Physiol* **258**, R543-R551

Shiono K & Sokabe H (1976) Renin-angiotensin system in spontaneously hypertensive rats. *Am J Physiol* **231**, 1295-1299

Stornetta RL, Guyenet PG & McCarty RC (1987) Autonomic nervous system control of heart rate during baroreceptor activation in conscious and anesthetized rats. *J Auton Nerv Syst* **20**, 121-127

Takeshita A, Tanaka S, Kuroiwa A & Nakamura M (1975) Reduced baroreceptor sensitivity in borderline hypertension. *Circulation* **51**, 738-742

Trell E, Henningsen NC, Petersson B, Westin L & Hood B (1985) Alcohol and the vascular system. *Acta Med Scand Suppl* **703**, 281-290

Ward RE, Flynn TC, Miller PW & Blaisdell WF (1982) Effects of ethanol ingestion on the severity and outcome of trauma. *Am J Surg* **144**, 153-157

Yamazaki T & Sagawa K (1985) Hypotension 1.5 min after 10% hemorrhage permits evaluation of rabbit's baroreflex. *Am J Physiol* **249**, H450-H456

Zhang X, Abdel-Rahman ARA & Wooles WR (1988) A differential action for ethanol on baroreceptor reflex control of heart rate and sympathetic efferent discharge in rats. *Proc Soc Exp Biol Med* **187**, 14-21

Zsoter TT & Sellers EM (1977) Effects of alcohol on cardiovascular reflexes. *J Stud Alcohol* **38**, 1-10