Korean J Physiol Pharmacol
Vol 3: 605-613, December, 1999

Spectral Analysis of Heart Rate Variability during Passive Standing after Ethanol Ingestion

Hyeong Jin Kim, Chun Duk Han, Eun Kyoung Yang, and Won Jung Lee

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

The purpose of the present study was to evaluate cardiovascular regulation during passive standing (PS) after ethanol ingestion by spectral analysis of heart rate variability (HRV) in flushed and nonflushed subjects. Of 24 young male subjects, 8 belonged to flushed group (F) and 16 to nonflushed group (NF). Two sessions of 10-min PS were performed before and after ethanol (0.5 g/kg) ingestion. Powers of R-R interval variability in very low frequency (VLF, 0~0.05 Hz), low frequency (LF, 0.05~0.15 Hz) and high frequency (HF, 0.15~0.50 Hz) bands, normalized powers (LFn and HFn) and LF/HF ratio were obtained. After ethanol ingestion, F showed higher heart rate than NF. PS increased LFn (+22.9±3.6 in NF, +12.8±4.7 in F, in normalized units) and LF/HF (+3.10±0.57 in NF, +3.00±1.08 in F) and decreased HFn powers. Ethanol ingestion increased LFn and LF/HF and decreased HFn. PS after ethanol resulted in higher LFn and LF/HF and lower HFn than the prior PS. F showed a greater and more sustained HRV change than NF after ethanol. In conclusion, PS or ethanol ingestion increased LFn and LF/HF and decreased HFn. Flushed subjects showed an accentuated HRV response to ethanol.

Key Words: Alcohol, Arterial pressure, FFT, Flushing, Orthostasis

INTRODUCTION

The regulation of the cardiovascular system during orthostatic stress has been an important issue in physiology. A change in position from supine to upright results in an abrupt translocation of thoracic blood volume to the lower body. The consequent reductions in venous return, stroke volume, and cardiac output evoke a number of reflex autonomic circulatory adjustments to maintain arterial blood pressure (Norsk, 1992; Sagawa et al, 1992). In humans these adjustments include increases in heart rate, total peripheral resistance and plasma vasopressin, renin activity, aldosterone and norepinephrine and decreases in forearm and skin blood flow and plasma atrial natriuretic peptide (Victor et al, 1987; Seals, 1988; Joyner et al, 1990). Although systolic arterial pressure may decrease during head-up tilt because of the reduced stroke volume and cardiac output, the reflex vasoconstriction typically produces an increase in diastolic arterial pressure, thus maintaining mean arterial pressure at supine levels (Norsk, 1992; Taylor et al, 1992; Sagawa et al, 1993).

Acute administration of ethanol is known to have a variety of cardiovascular effects including peripheral vasodilation, myocardial depression, and reduced circulating blood volume that lead to a fall in arterial pressure (Horowitz & Atkins, 1974; Timmis et al, 1975; Kim et al, 1985; Howes & Reid, 1986). Ethanol ingestion resulted in greater increases of heart rate and plasma vasopressin during passive standing in normal subjects (Kim et al, 1987) and a greater fall of arterial pressure during head-up tilt in patients with primary autonomic failure (Chaudhuri et al, 1994).

Ethanol-induced facial flushing is often observed in Asians. Over half of Chinese, Japanese, and Koreans manifest facial flushing after ingestion of alcoholic beverages due to vasodilation of the facial skin (Wolff, 1972, 1973) that may later include the neck, arms and torso (Wall et al, 1996). Facial flush reaction has been reported to be accompanied by

Corresponding to: Won Jung Lee, Department of Physiology, School of Medicine, Kyungpook National University, 2-101 Tongin-dong, Chung-gu, Taegu 700-422, Korea. (Tel) 82-53-420-6926, (Fax) 82-53-424-3349, (E-mail) wjleek@knu.ac.kr

tachycardia, dizziness, headache, nausea, occasional vomiting, and sometimes hypotension and bronchoconstriction (Crabb et al, 1993). Elevated acetaldehyde levels found in individuals with the flush reaction after drinking (Zeiner et al, 1979) may cause vasodilation via the release of vasoactive substances by mast, endothelial, or other cells (Crabb et al, 1993). Kim et al (1987) reported a similar magnitude of cardiovascular responses to passive standing after ethanol ingestion between flushed and nonflushed subjects.

Spectral analysis of beat-to-beat variability of cardiovascular parameters has been used to investigate the cardiovascular control system. Periodic components of heart rate variability (HRV) tend to aggregate within several frequency bands. The high frequency (HF) fluctuation, centered at respiratory frequency, is mediated primarily by cardiac vagal efferent activity. (Akselrod et al, 1981; Pomeranz et al, 1985; Malliani et al, 1991; Parati et al, 1995). The low frequency (LF) fluctuation, centered around 0.1 Hz, reflects both sympathetic and vagal influences related to baroreflex mechanisms. (Akselrod et al, 1981; Pomeranz et al, 1985; Berntson et al, 1997). Although the very low frequency (VLF), 0.04 Hz and lower, fluctuation may reflect thermoregulatory cycles (Sayers, 1973) or fluctuations related to plasma renin activity (Akselrod et al, 1981; Bonaduce et al, 1994), its physiological explanation is yet far from settled (Task Force, 1996; Berntson et al, 1997).

Both orthostatic challenge and ethanol have been reported to alter HRV. Orthostatic challenge was shown to increase LF power and LF/HF ratio (Mukai & Hayano, 1995; Schmedtje et al, 1995; Sanderson et al, 1996) and to decrease HF (Mukai & Hayano, 1995; Kochiadakis et al, 1997). Montano et al (1994) demonstrated that the tilt angle was highly correlated to both LF and HF powers when expressed in normalized units. Ingestion of moderate doses of ethanol was shown to decrease HRV, primarily the HF component, while increasing the heart rate (Koskinen et al, 1994; Murata et al, 1994). However, the response of HRV to orthostatic stress plus ethanol ingestion and the characteristics of HRV in subjects with ethanol-induced facial flushing have not been studied. Since flushed subjects generally show an accentuated cardiovascular response to ethanol, it would be valuable to compare the HRV response of flushed subjects to that of the nonflushed.

Therefore the purpose of the present study was to investigate the cardiovascular regulation by use of spectral HRV analysis during passive standing after ethanol ingestion in flushed and nonflushed subjects.

METHODS

Subjects

Twenty-four Korean male volunteers aged 20~26 yr participated in this study (Table 1). Eight subjects who showed prominent facial flushing after ethanol ingestion were assigned to flushed group, and the remaining 16 who did not to nonflushed group. None of the subjects had a history of cardiovascular diseases, were alcoholic or on medication. All subjects were briefed about the experimental procedures and were familiarized with the protocol, prior to the experiments.

Protocol

Each subject reported to the laboratory at 1300 h after fasting for >6 h. The room temperature was kept within 20~23°C. Each subject participated in both control and ethanol experiments which were separated by a 2-min period of ethanol ingestion. The control experiment consisted of supine rest (20 min),

Table 1. Physical characteristics of flushed and nonflushed subjects

	Age (yr)	Height (cm)	Body weight (kg)
Flushed (n=8)	22.5±0.7	173.8±1.0#	62.3±2.1
Nonflushed (n=16)	22.0±0.4	174.4±1.4	65.0±1.7

Values are means±standard errors.
#P<0.05 vs Nonflushed.

passive standing (10 min), and supine rest (30 min). Ethanol experiment consisted of supine rest (45 min), passive standing (10 min), and supine rest (30 min).

Passive standing (PS) meant standing with one's back leaned on the wall and with minimal tension applied on two feet which were separated by 15 cm from each other and positioned 23 cm apart from the wall (Bungo & Jonsen, 1983). Subjects ingested ethanol in a sitting position. The dose used was 2.5 ml of soju (Korean alcoholic beverage with 25% ethanol) per kg of body wt (0.5 g ethanol/kg).

During the control experiment, time was expressed with the prefix 'C' followed by the number of minutes that elapsed after the first measurement. Parameters were measured at the end of initial supine rest (C0), during PS (at C5 and C10), and during supine rest after PS (C25 and C40). During ethanol experiment, time was expressed with the prefix 'E' and the number of minutes that passed after ethanol ingestion. Parameters were measured during supine rest before PS (E15, E30 and E45), during PS (at E50 and E55), and during supine rest after PS (E70 and E85).

Facial flush index

The degree of ethanol-induced facial flushing was determined using the following 7-point scale (Schuckit & Duby, 1982). The index at C40 (immediately before ethanol ingestion) was assumed to be 3.

Facial flush index	Degree of facial flushing
0	Severely blanched
1	Blanched
2	Somewhat blanched
3	Normal
4	Somewhat flushed
5	Flushed
6	Severely flushed

Skin temperature

In order to evaluate facial and chest flushing, skin temperature was measured using temperature probes (model 408, Yellow Springs Instrument) attached on left temporal and pectoral areas and connected to a telethermometer (44TA, Yellow Springs Instrument).

ECG and blood pressure

Lead II electrocardiogram (ECG) obtained with a physiologic recorder (MK-IV-P, Narco BioSystems) was fed into a data acquisition system (1401 Plus, Cambridge Electronic Design Limited, CED), digitized at 250 Hz and transmitted into a personal computer which displayed the signal while storing them on the disk. ECG was stored for the 5-min period preceding every designated time of measurement. Brachial arterial blood pressure was measured with a sphygmomanometer.

Spectral analysis of heart rate variability

A script language program written with a software command set (Spike 2 version 4, CED) was used for the power spectral analysis of R-R interval variability. R-R interval was measured from peaks of QRS complex in the ECG. Equidistant time series of R-R was constructed at 4 Hz by interpolating with a cubic spline function. DC trends were eliminated by subtracting a linear regression equation from the time series. Power spectra of R-R variability were obtained by use of a fast Fourier transform (FFT) algorithm. The 5-min-long ECG recordings usually provided a 256-sec block available for the analysis, from which 3 128-sec segments overlapping by 50% were extracted, smoothed with a raised cosine window, and submitted to FFT to yield a frequency resolution of 0.0078 (=1/128) Hz. Power spectral density functions derived from all the segments were averaged to produce the final spectrum, from which VLF (0~0.05 Hz), LF (0.05~0.15 Hz) and HF (0.15~0.50 Hz) powers were obtained. Total power (σ^2) was calculated as sum of VLF, LF and HF. Normalized LF and HF powers were calculated as follows.

$$LFn = LF/(\sigma^2 - VLF) \times 100$$
$$HFn = HF/(\sigma^2 - VLF) \times 100$$

Statistics

The results were presented as means±standard errors. The differences between groups were examined by Kruskal-Wallis test and Mann-Whitney two sample test. Differences over time of measurement were evaluated by Wilcoxon test for paired samples. A $P<0.05$ level of significance was used.

RESULTS

Ethanol-induced flushing

While facial flush index after ethanol ingestion was increased to 3.4±0.1 ($P<0.05$) at E55 and returned to pre-ethanol level at E85 in nonflushed (NF) group, it remained above 4 (somewhat flushed) ($P<0.05$ vs pre-ethanol and vs NF) from E15 to E70 in flushed (F) group (Fig. 1).

Temporal skin temperature was 34.62±0.30 and 34.43±0.34°C at C0 in NF and F groups, respectively, and showed a significant increase during 40 min of control experiment in both groups (Fig. 1). After ethanol ingestion, it was further increased by 0.18±0.08°C ($P<0.05$ vs C40) at E15 and returned to pre-ethanol level thereafter in NF group, whereas it was increased by 0.90±0.26°C ($P<0.05$ vs C40) at E15 and was still significantly higher than pre-ethanol level at E70 in F group.

Pectoral skin temperature was 34.29±0.24 and 34.78±0.25°C at C0 in NF and F groups, respectively, and was not changed significantly during the period of entire experiment in both groups (Fig. 1).

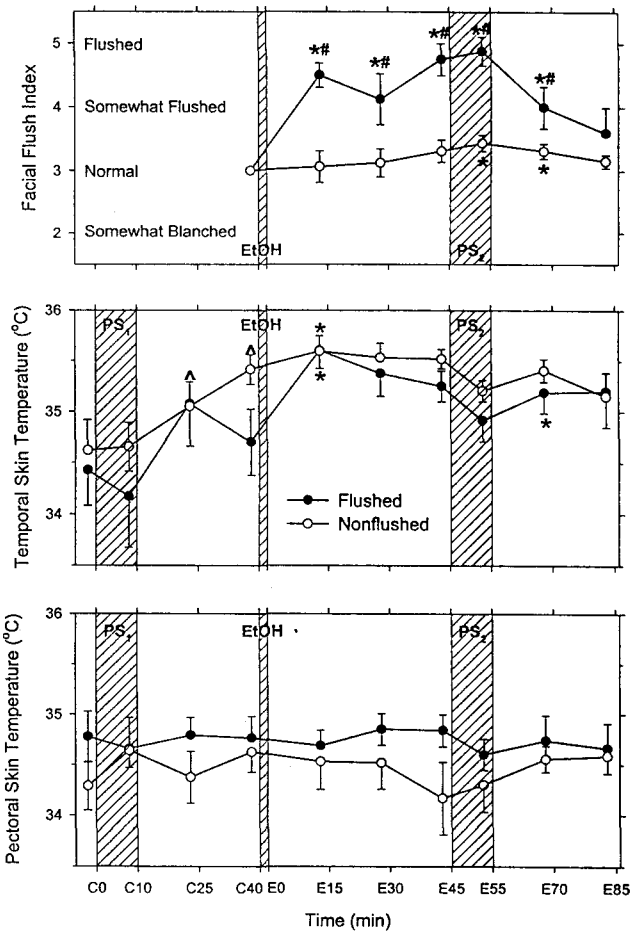

Fig. 1. Facial flush index, and temporal and pectoral skin temperature during passive standing (PS) before and after ethanol ingestion (EtOH, 0.5 g/kg, sitting) in flushed (n=8) and nonflushed (n=16) subjects. Subjects remained in a supine position except for PS and EtOH. Time during the control experiment is prefixed with 'C', and that during ethanol experiment with 'E'. Vertical bars represent standard errors. ^$P<0.05$ vs C0 (before PS_1), *$P<0.05$ vs C40 (before EtOH), #$P<0.05$ vs Nonflushed.

Heart rate and blood pressure

Initial supine heart rate at C0 was 74.5±3.0 and 77.3±3.1 beats/min in NF and F groups, respectively (Fig. 2). During PS, heart rate increased significantly by 12.1±2.0 and 15.3±4.9 beats/min in NF and F groups, respectively. In NF group, ethanol ingestion per se did not alter heart rate, whereas in F group it produced a significant increase in heart rate by 10.5±4.2 beats/min at E15 and a higher heart rate than in NF at E30 and E45. PS after ethanol caused significant increases in heart rate by 25.0±1.7 and 25.0±3.4 beats/min ($P<0.05$ vs E45) in NF and F

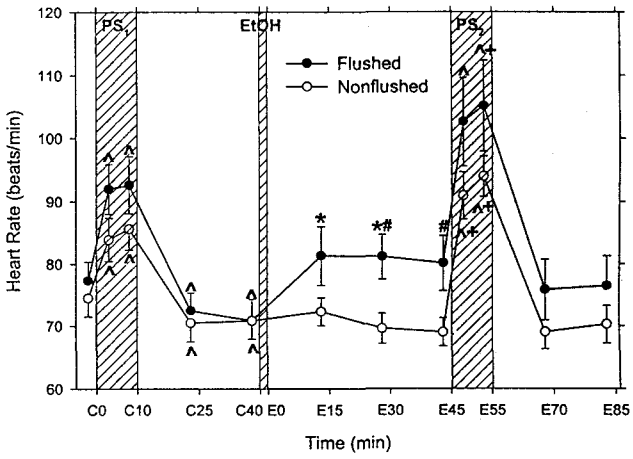

Fig. 2. Heart rate during passive standing (PS) before and after ethanol ingestion (EtOH, 0.5 g/kg, sitting) in flushed (n=7) and nonflushed (n=15) subjects. Subjects remained in a supine position except for PS and EtOH. Time during the control experiment is prefixed with 'C', and that during ethanol experiment with 'E'. Vertical bars represent standard errors. ^$P<0.05$ vs C0 (before PS_1) or E45 (before PS_2), +$P<0.05$ vs C5 or C10 (PS_1), *$P<0.05$ vs C40 (before EtOH), #$P<0.05$ vs Nonflushed.

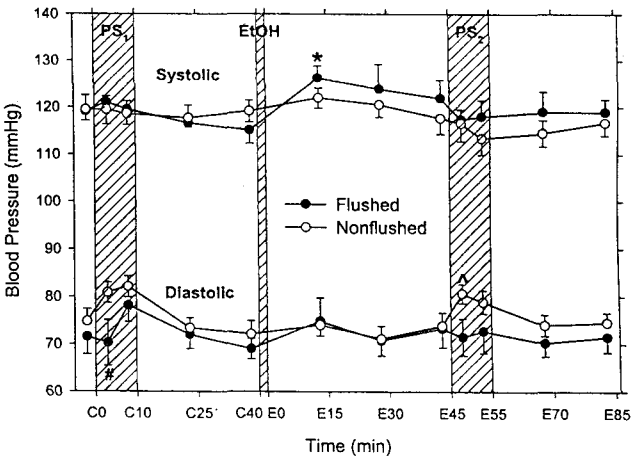

Fig. 3. Systolic and diastolic arterial pressure during passive standing (PS) before and after ethanol ingestion (EtOH, 0.5 g/kg, sitting) in flushed (n=8) and nonflushed (n=16) subjects. Subjects remained in a supine position except for PS and EtOH. Time during the control experiment is prefixed with 'C', and that during ethanol experiment with 'E'. Vertical bars represent standard errors. $^{\wedge}P<0.05$ vs E45 (before PS_2), $^{*}P<0.05$ vs C40 (before EtOH), $^{\#}P<0.05$ vs Nonflushed.

groups, respectively. Heart rate during the second PS was significantly higher than the first in both groups.

Systolic pressure was 119.4±2.3 and 119.1±3.4 mmHg at C0 in NF and F groups, respectively, and was not changed significantly during the entire experiment except for an increase after ethanol ingestion in F group (Fig. 3). Diastolic pressure was 74.8±2.6 and 71.5±3.6 mmHg at C0 in NF and F groups, respectively, and tended to increase during the first PS in both groups, while in F group it was significantly lower than in NF at C5 (Fig. 3). During PS after ethanol ingestion, diastolic pressure was increased by 6.7±2.4 mmHg ($P<0.05$ vs E45) in NF group, whereas it was not changed throughout the ethanol experiment in F group.

Spectral analysis of R-R interval variability

Total power of R-R variability was 3896±936 and 2612±673 $msec^2$ at C0 in NF and F groups, respectively, and tended to decrease during the first PS ($P<0.05$ in NF) (Table 2). Ethanol ingestion caused a significant decrease in total power in F group. During PS after ethanol ingestion, it was significantly decreased in both groups.

LFn power of R-R variability in normalized units

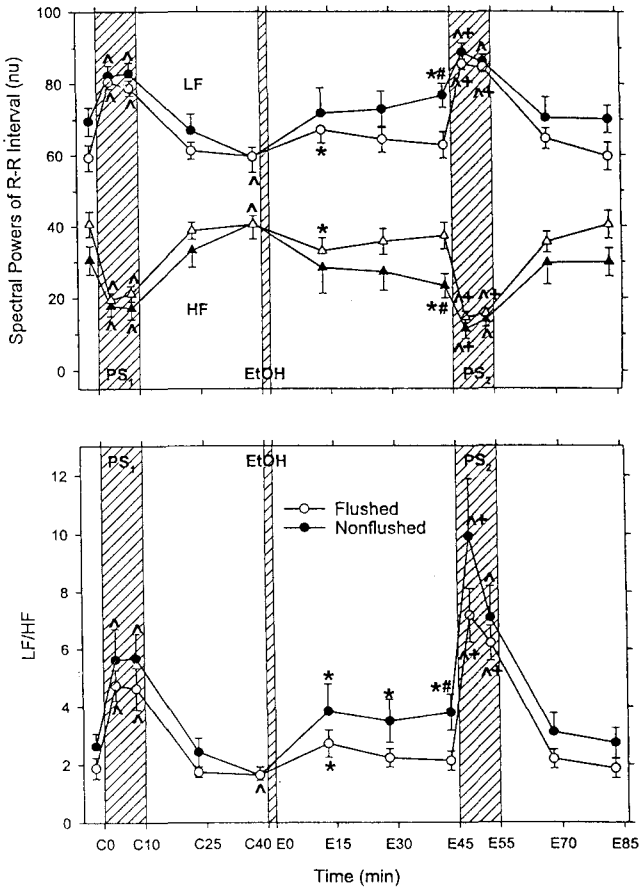

Fig. 4. Low frequency (LFn) and high frequency (HFn) powers in normalized units (nu) and ratio of low frequency to high frequency power (LF/HF) of R-R interval variability during passive standing (PS) before and after ethanol ingestion (EtOH, 0.5 g/kg, sitting) in flushed (n=7) and nonflushed (n=15) subjects. Subjects remained in a supine position except for PS and EtOH. Time during the control experiment is prefixed with 'C', and that during ethanol experiment with 'E'. Vertical bars represent standard errors. $^{\wedge}P<0.05$ vs C0 (before PS_1) or E45 (before PS_2), $^{+}P<0.05$ vs C5 or C10 (PS_1), $^{*}P<0.05$ vs C40 (before EtOH), $^{\#}P<0.05$ vs Nonflushed.

(nu) was 59.4±3.6 and 69.5±4.0 nu at C0 in NF and F groups, respectively, was significantly increased during PS by 22.9±3.6 and 12.8±4.7 nu at C5 in NF and F groups, respectively, and was restored to supine values after PS (Fig. 4). After ethanol ingestion, LFn was increased by 7.5±3.4 nu at E15 ($P<0.05$ vs C40) and returned to pre-ethanol level thereafter in NF group. In F group, LFn after ethanol ingestion was significantly increased by 17.4±4.4 nu at E45 ($P<0.05$ vs C40 and vs NF). PS after ethanol ingestion also caused a significant increase in LFn by

Table 2. Spectral analysis of R-R interval variability during passive standing with or without ethanol ingestion

		Control					After ethanol ingestion						
		C0	C5 (PS_1)	C10 (PS_1)	C25	C40	E15	E30	E45	E50 (PS_2)	E55 (PS_2)	E70	E85 min
R-R (msec)	F	785	659^	657^	837^	860^	752*	748*#	763#	601^	588^+	811	804
		35	26	31	37	47	42	31	41	49	41	51	50
	NF	823	731^	714^	871^	865^	840	875	881	673^+	647^+	884	871
		31	28	26	34	32	25	27	25	24	19	27	31
Total power ($msec^2$)	F	2612	1568	1520	3360	2479	1468*#	2344	2420	2568	1547^	2131	2574
		673	423	438	709	313	349	547	667	1785	640	975	752
	NF	3896	2006^	1892^	4359	4435	3739	4459	3592	2041^	1673^	3514	4285
		936	352	381	724	796	549	652	611	363	300	570	922
VLF ($msec^2$)	F	1191	840	713	1853	1238	764#	1738	1557	1664	1030	1397	1677
		174	225	208	376	156	169	398	458	1142	418	716	400
	NF	2281	1104^	1044^	2243	2242	1992	2630	1929	1216^	1035^	2191	2532
		664	227	258	361	379	313	459	391	305	188	526	852
LF ($msec^2$)	F	909	586	682	991	691	484#	408#	607	724	441	488	585
		337	165	291	285	133	192	93	208	486	206	224	229
	NF	931	726	684	1296^	1308^	1178	1198	1095	719+	549^	843	1034
		230	115	121	256	274	205	185	209	140	126	120	199
HF ($msec^2$)	F	512	142	125^	516	549	220*#	198*#	256*#	180^#	76^+	246	313#
		294	59	52	171	185	105	75	138	158	43	118	161
	NF	684	175^	164^	820	885^	568*	631	568	106^+	89^+	480	719
		239	34	27	184	250	93	109	98	18	17	90	153

Values are means and standard errors.
Each column represents a 5-min period of data collection that ended at designated time.
(PS) denotes data collected during passive standing which lasted for 10 min.
Ethanol (0.5 g/kg) was ingested for 2 min in a sitting position.
Otherwise subjects remained in a supine position.
VLF: very low frequency, LF: low frequency, HF: high frequency power of R-R variability.
F: flushed group (n=7), NF: nonflushed group (n=15).
^$P<0.05$ vs C0 or E45 (before PS), $^{+}P<0.05$ vs C5 or C10 (PS_1), *$P<0.05$ vs C40 (before ethanol), $^{\#}P<0.05$ vs NF.

22.6±3.5 and 12.6±2.7 nu in NF and F groups, respectively. LFn during the second PS was significantly higher than the first in both groups.

HFn power was 40.6±3.6 and 30.5±4.0 nu at C0 in NF and F groups, respectively, and changed reciprocally to LFn throughout the whole experiment (Fig. 4). Briefly, it was significantly decreased during each PS in both groups. After ethanol ingestion, HFn showed a significant decrease in both groups, to a lower value in F than in NF group.

LF/HF ratio was 1.88±0.37 and 2.62±0.45 at C0 in NF and F groups, respectively, was significantly increased during PS by 3.10±0.57 and 3.00±1.08 at C5 in NF and F groups, respectively, and was restored to supine values after PS (Fig. 4). After ethanol ingestion, the ratio was significantly increased by 1.08 ±0.46 and 2.20±0.76 at E15 in NF and F groups, respectively. While LF/HF was restored to pre-ethanol level at E30 in NF group, it remained significantly higher than pre-ethanol level until E45 in F group. LF/HF was significantly greater at E45 in F than in NF group. PS after ethanol ingestion also caused a significant increase in LF/HF by 5.05±0.89 and 6.19±1.92 in NF and F groups, respectively. LF/HF during the second PS was significantly higher than the first in both groups.

DISCUSSION

Orthostatic challenge is known to evoke a number of reflex autonomic circulatory adjustments to maintain arterial blood pressure (Norsk, 1992; Sagawa et al, 1992). The primary mechanisms involved in mean arterial pressure regulation during head-up tilt include increased sympathetic efferent activity and decreased vagal outflow, which can be manifested as increased LF and decreased HF HRV (Mukai & Hayano, 1995; Kochiadakis et al, 1997). The correlation between the tilt angle and parameters of HRV was shown to be enhanced by expressing HRV powers in normalized units and by using the LF/HF ratio (Montano et al, 1994; Task Force, 1996). Since the tachycardia resulting from sympathetic activation is usually accompanied by a marked reduction in total power of HRV, the normalization procedure has proven crucial to the interpretation of spectral parameters of HRV (Lombardi et al, 1996; Task Force, 1996). An alternative procedure to eliminate the influence of total power is to use the LF/HF ratio which seems to accurately reflect the sympathovagal balance (Montano et al, 1994; Parati et al, 1995; Lombardi et al, 1996).

In the present study, both sessions of PS caused increased heart rate, LFn and LF/HF of HRV and decreased total and HFn powers of HRV in both groups. This result of spectral HRV analysis in response to PS may be attributable to the increased sympathetic activity and decreased cardiac vagal activity. These autonomic adjustments constitute the primary mechanism to maintain the arterial pressure against the orthostatic stress (Norsk, 1992; Sagawa et al, 1992).

Koskinen et al (1994) observed a decreased HF power of HRV following ingestion of moderate doses of ethanol and attributed it to the reduced vagal modulation of heart rate. Orthostatic challenge after ethanol ingestion was reported to cause greater increases of heart rate and plasma vasopressin than without ethanol in normal subjects (Kim et al, 1987) and a greater fall of arterial pressure in patients with primary autonomic failure (Chaudhuri et al, 1994). In the present study, ethanol ingestion per se resulted in increases of LFn and LF/HF and a decrease in HFn in both groups. This result suggests that ethanol caused a shift in the sympathovagal balance to a sympathetic dominance in both groups (Montano et al, 1994; Parati et al, 1995).

With an ethanol dose of 0.5 g/kg as used in the present study, the peak blood ethanol level is well expected to occur during 30~60 min after ethanol, based on reports by Huh et al (1986) who administered 0.49 g/kg of ethanol to young males to obtain the peak blood ethanol level of ~40 mg/dl at 30 and 60 min and by Crabb et al (1993) who used a dose of 0.56 g/kg to young males to observe the peak plasma ethanol level during 30~60 min following ethanol administration. Thus PS was performed at 45 min after ethanol in the present study. Compared with the first PS before ethanol, the second PS caused greater increases in heart rate, LFn and LF/HF, and a greater decrease in HFn of HRV. Diastolic pressure was significantly increased during the second PS in NF group. Since the increased diastolic pressure reflects the reflex vasoconstrition (Taylor et al, 1992; Sagawa et al, 1993), it is apparent that ethanol augmented the autonomic response to PS by enhancing the basal level of sympathetic activity. It is notable that F group lacked an increase in diastolic pressure.

Ethanol is oxidized by alcohol dehydrogenase to acetaldehyde, which in turn is oxidized by aldehyde dehydrogenase (ALDH). Of the two isoenzymes of ALDH, ALDH2 is crucial for oxidizing acetaldehyde while ALDH1 also contributes to the reaction (Crabb et al, 1993). Harada et al (1981) first reported that individuals with the flush response to ethanol ingestion lacked ALDH2 activity. Elevated acetaldehyde levels after drinking were found in ALDH2-deficient individuals (Enomoto et al, 1991) and in individuals with the flush reaction (Zeiner et al, 1979; Mizoi et al, 1983).

Wall et al (1996) demonstrated that investigator-observed flushing was both a sensitive and specific predictor of ALDH2 deficiency. They categorized those subjects who rated 4, 5 or 6 with the 7-point scale (Schukit & Duby, 1982) following alcohol as flushers. In the present study, 8 subjects who reached 5 or 6 after ethanol were grouped as flushed, and 10 who rated 4 or less and 6 who rated 3 or less after ethanol were grouped together as nonflushed. Kim et al (1985) and Kim et al (1987) reported a significant increase in facial skin temperature after ethanol in flushed subjects. In the present study, temporal skin temperature was increased after ethanol in both groups but the amplitude of increase tended to be higher in F than in NF group.

After ethanol ingestion, F group showed a higher heart rate, significant increase in systolic pressure,

and a greater and more sustained change in HRV compared with NF group. These results indicate that the autonomic responses to ethanol are much accentuated in F group. During PS after ethanol ingestion, in contrast, F group lacked the increase in diastolic pressure that was evident in NF group. Even during the first PS performed before ethanol, F group showed a slower increase in diastolic pressure than NF. While flushers seem to have an accentuated autonomic response to ethanol resulting in higher heart rate and LF/HF, it is suggested that they have a weaker vasocontrictive response to PS. This might be attributable to the release of vasoactive substances by mast, endothelial, or other cells after ethanol ingestion in flushed subjects (Crabb et al, 1993).

In summary, PS increased LFn and LF/HF and decreased HFn powers of HRV in both groups. Ethanol ingestion per se resulted in increases of LFn and LF/HF and a decrease in HFn in both groups. The flushed subjects showed a greater and more sustained change in HRV and a higher heart rate than NF after ethanol, and lacked the increase in diastolic pressure during PS after ethanol.

ACKNOWLEDGEMENT

This paper was supported by Kyungpook National University Research Fund, 1997.

REFERENCES

Akselrod S, Gordon D, Ubel FA, Shannon DC, Barger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. *Science* 213: 220−222, 1981

Berntson GG, Bigger JT Jr, Eckberg DL, Paul Grossman, Kaufmann PG, Malik M, Nagaraja HN, Porges SW, Saul JP, Stone PH, van der Molen MW: Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology* 34: 623−648, 1997

Bonaduce D, Marciano F, Petretta M, Migaux ML, Morgano G, Bianchi V, Salemme L, Valva G, Conderelli M. Effects of converting enzyme inhibition on heart period variability in patients with acute myocardial infarction. *Circulation* 90: 108−113, 1994

Bungo MW, Jonsen PC. Cardiovascular examinations and observations of deconditioning during the space shuttle orbital flight test programs. *Aviat Space Environ Med* 54: 1001−1004. 1983

Chaudhuri KR, Maule S, Thomaides T, Pavitt D, Mathias CJ. Alcohol ingestion lowers supine blood pressure, causes splanchinc vasodilatation and worsens postural hypotension in primary autonomic failure. *J Neurol* 241: 145−152, 1994

Crabb DW, Dipple KM, Thomasson HR. Alcohol sensitivity, alcohol metabolism, risk of alcoholism, and the role of alcohol and aldehyde dehydrogenase genotypes. *J Lab Clin Med* 122: 234−240, 1993

Enomoto N, Takase S, Yasuhara M, Takada A. Acetaldehyde metabolism in different aldehyde dehydrogenase 2 genotypes. Alcoholism: *Clin Exp Res* 15: 141−144, 1991

Harada S, Agarwal DP, Goedde HW. Aldehyde dehydrogenase deficiency as cause of facial flushing reaction to alcohol in Japanese. *Lancet* 2: 982, 1981

Horowitz LD, Atkins JM. Acute effects of ethanol of left ventricular performance. *Circulation* 48: 124−128, 1974

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

Huh B, Hwang SK, Choo YE. Effect of ethanol on the pulmonary function in athletes. *Kyungpook Educ Forum* 28: 143−153, 1986.

Joyner MJ, Shepherd JT, Seals DR. Sustained increases in sympathetic outflow during prolonged lower body negative pressure in humans. *J Appl Physiol* 68: 1004−1009, 1990

Kim HJ, Park JS, Lee WJ, Choo YE. Blood ethanol curve analysis and characteristics of circulatory function in men who show facial flushing after drinking. *J Korean Med Assoc* 28(10): 1009−1024, 1985

Kim YN, Lee WJ, Choo YE. ADH and cardiovascular responses to passive standing in flushed and non-flushed man following acute administration of ethanol. *Keimyung Univ Med J* 6: 1−13, 1987

Kochiadakis GE, Orfanakis A, Chryssostomakis SI, Manios EG, Kounali DK. Autonomic nervous system activity during tilt testing in syncopal patients, estimated by power spectral analysis of heart rate variablilty. *Pacing Clin Electrophysiol* 20: 1332−1341, 1997

Koskinen P, Virolainen J, Kuparo M. Acute alcohol intake decreases short-term heart rate variability in healthy subjects. *Clin Sci* 87: 225−230, 1994

Lombardi F, Malliani A, Pagani M, Cerutti S. Heart rate variability and its sympatho-vagal modulation. *Cardiovasc Res* 32: 208−216, 1996

Malliani A, Pagani M, Lombardi F, Cerutti S. Cardiovascular neural regulation explored in the frequency domain. *Circulation* 84: 1482−92, 1991

Mizoi Y, Ijiri W, Tatsuno Y. Relationship between facial flushing and blood acetaldehyde levels after alcohol

intake. *Pharmacol Biochem Behav* 10: 303−311, 1979

Mizoi Y, Tatsuno Y, Adachi J, Kogame M, Fukunaga T, Fujiwara S, Hishida S, Ijiri I. Alcohol sensitivity related to polymorphism of alcohol-metabolizing enzymes in Japanese. *Pharmacol Biochem Behav* 18: 127−133, 1983

Montano N, Ruscone TG, Porta A, Lombardi F, Pagani M, Malliani A. Power spectrum analysis of heart rate variability to assess the changes in sympathovagal balance during graded orthostatic tilt. *Circulation* 90: 1826−1831, 1994

Mukai S, Hayano J. Heart rate and blood pressure variabilities during graded head-up tilt. *J Appl Physiol* 78: 212−216, 1995

Murata K, Araki S, Yokoyama K, Sata F, Yamashita K, Ono Y. Autonomic neurotoxicity of alcohol assessed by heart rate variability. *J Auton Nerv Syst* 48: 105−111, 1994

Norsk P. Gravitational stress and volume regulation. *Clin Physiol* 12: 505−526, 1992

Parati G, Saul JP, Di Rienzo M, Pmboni S, Pedotti A, Mancia G. Spectral analysis of blood pressure and heart rate variability in evaluating cardiovascular regulation. *Hypertension* 25: 1276−1286, 1995

Pomeranz B, Macaulay RJB, Caudill MA, Kutz I, Adam D, Gordon D, Kilborn KM, Barger AC, Shannon DC, Cohen RJ, Benson H. Assessment of autonomic function in humans by heart rate spectral analysis. *Am J Physiol* 248: H151−H153, 1985

Sagawa S, Miki K, Tajima F, Shiraki K. Cardiovascular responses to upright tilt in man during acute exposure to 3 atm abs air. *Undersea Biomed Res* 19: 97−106, 1992

Sagawa S, Shiraki K, Miki K, Tajima F. Cardiovascular responses to upright tilt at a simulated altitude of 3,700 m in men. *Aviat Space Environ Med* 64: 219−223, 1993

Sanderson JE, Yeung LY, Yeung DT, Kay RL, Tomlinson B, Critchley JA, Woo KS, Bernardi L. Impact of changes in respiratory frequency and posture on power spectral analysis of heart rate and systolic blood pressure variability in normal subjects and patients with heart failure. *Clin Sci* 91: 35−43, 1996

Sayers BM. Analysis of heart rate variability. *Ergonomics* 16: 17−32, 1973

Schmedtje JF Jr, Gutkowska J, Taylor AA. Reciprocity of hemodynamic changes during lower body negative and positive pressure. *Aviat Space Environ Med* 66: 346−352, 1995

Schuckit MA, Duby J. Alcohol-related flushing and the risk for alcoholism in sons of alcoholics. *J Clin Psychiat* 43: 415−418, 1982

Seals DR. Cardiopulmonary baroreflexes do not modulate exercise-induced sympatho-excitation. *J Appl Physiol* 64: 2197−2203, 1988

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation* 93: 1043−1065, 1996

Taylor JA, Hand GA, Johnson DG, Seals DR. Sympathoadrenal-circulatory regulation of arterial pressure during orthostatic stress in young and older men. *Am J Physiol* 263: R1147−R1155, 1992

Timmis GC, Ramos RC, Gordon S, Gangadhran V. The basis for differences in ethanol induced myocardial depression in normal sujects. *Circulation* 51: 1144−1148, 1975

Victor RG, Leimbach WN Jr. Effect of lower body negative pressure on sympathetic discharge to leg muscles in humans. *J Appl Physiol* 63: 2558−2562, 1987

Wall TL, Thomasson HR, Ehlers CL. Investigator-observed alcohol-induced flushing but not self-report of flushing is a valid predictor of ALDH2 genotype. *J Stud Alcohol* 57: 267−272, 1996

Wolff PH. Ethnic differences in alcohol sensitivity. *Science* 175: 449−450, 1972

Wolff PH. Vasomotor sensitivity to alcohol in diverse mongoloid populations. *Am J Hum Genet* 25: 193−199, 1973

Zeiner AR, Paredes A, Christiansen DH. The role of acetaldehyde in mediating reactivity to an acute dose of ethanol among different racial groups. *Alcoholism* 3: 11−18, 1979