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Cardiovascular and Some Biochemical Effects of High Alcohol Consumption

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ABSTRACT

A sample of 200 men from the general population was investigated concerning alcohol consumption in relation to cardiovascular and laboratory findings. Symptoms of alcoholism (subjective relative loss of control over drinking, blackouts and morning drinks) were found to be related to the alcohol consumption. The subjects were divided into three groups: (I) a group with low alcohol consumption without symptoms of alcoholism, (II) an intermediate group with low, moderate or high alcohol consumption and with different alcohol symptoms and (III) a "heavy-drinking" group with moderate or high alcohol consumption and two or more symptoms. Group III had, on an average, a higher heart rate and a larger heart volume, and significantly lower serum (S) levels of magnesium, creatinine and IgG than groups I and II. Ten of the 53 heavy drinkers used liver-metabolized drugs, because of illness. On the average the heavy drinkers who used drugs had a higher heart rate and diastolic blood pressure and a larger heart volume, and in this group there was a higher incidence of pathological ECGs and a lower peak flow. They had higher S-cholesterol and triglycerides and, especially, low S-creatinine. Elevated cholesterol and triglyceride levels showed no relationships to high alcohol consumption alone, but a combination of high alcohol consumption and liver-metabolized drugs was significantly correlated to such elevations. The finding of a combination of high alcohol consumption as reported in a standardized questionnaire and low S-creatinine may discriminate an interesting homogeneous subgroup with over-consumption of alcohol.

INTRODUCTION

In severe acute alcoholism and in the late stages of alcoholic liver disease, it is well known that serum electrolyte disturbances, hypocalcaemia (5) and hypoalbuminaemia (5) occur. Among alcoholics deaths from ischaemic heart disease are common (22, 24), but convincing epidemiological data also indicate that alcohol consumption may have a protective effect (21). Low serum creatinine concentrations have been observed in alcoholism. In a group with a high level of gamma-glutamyl transpeptidase in the serum,

Peterson et al. (16) noted low serum creatinine values. Klatsky et al. (7) found a clear relation between blood pressure and the daily number of drinks. Waern et al. (23) found that the mean systolic and diastolic blood pressures were somewhat higher among 60-year-old men showing various indications of alcohol consumption. However, increased alcohol intake also represented increased caloric intake, and thus the increased blood pressure might have been a function of increased body weight (23).

In an earlier study of the present material, the following haematological variables were investigated: B-haemoglobin, erythrocyte mean corpuscular volume, serum iron, transferrin saturation, alcohol-related liver enzymes and amylase (14).

The purpose of the present investigation was to elucidate the following questions:

1. Is heavy alcohol drinking in a population sample related to cardiovascular changes and deviating results of biochemical tests?
2. Can biochemical tests, in particular those performed in this study, be used for screening of drinking problems?
3. How do liver-metabolized drugs together with alcohol influence the laboratory findings?

MATERIAL

The present sample of 200 men was collected as a reference group for the KARTAD project which is being carried out at the Magnus Huss Clinic of the Karolinska Hospital in Stockholm. "KARTAD", stands for the KAROlinska project for research and Treatment of Alcohol Dependence. During 1976-1981 more than 700 consecutively admitted alcoholic in-patients living in the same geographical area as the random control sample of men in the present study took part in the KARTAD investigation. The same medical, social and psychological methods were used for examination of the random controls as for the KARTAD patients.

From the National Register covering all Swedish inhabitants, a random sample of 228 men was taken from the general male population living in the urban districts of Solna and Sundbyberg, with altogether 80.000 inhabitants, in the catchment area of the Karolinska Hospital. Forty men in each of the age groups 20-29, 30-39, 40-49, 50-59 and 60-65 years were sampled in order to achieve the same degree of precision for all age groups in the estimation of different variables. The initial sample drawn consisted of 209 men aged 20-65 years. Of this sample, two persons had died, five had moved more than 120 miles from Stockholm, and ten were living permanently abroad at the time of the investigation and were thus excluded from the sample. Eleven persons refused to be examined. Thus, of the

initial sample of 209 men 181 were investigated. To increase the sample of investigated men to 200, a supplementary sample was drawn in exactly the same way as before. All men in the supplementary sample could be included in the investigation, and the final sample was thus 200. The drop-out rate in the collection of the sample was less than 10 %. The drop-outs did not differ from the examined persons in social status, age, education, civil status, work status or with respect to entry in official registers (police, social register, local health insurance office, Temperance Board register)($p>0.05$).

METHODS

The subjects were examined at the Magnus Huss Clinic of the Karolinska Hospital in Stockholm. In studies of alcohol consumption, the consumption in the last week was recorded, as it was considered that the subjects' recall would be poorer for the period further back in time. Otherwise the compliance would have been less than 100 %. In the present study the occurrence of three symptoms related to heavy drinking was recorded: Inability to cut down or stop drinking, i.e. loss of control; morning shakes and malaise relieved by drinking, i.e., morning drinks; and alcohol amnesia or memory lapse after drinking of alcohol, i.e. blackouts. The 200 participants were first divided into three groups:

(I) A group with low alcohol consumption without symptoms of alcoholism (n=41);

(II) an intermediate group with low, moderate or high alcohol consumption and different alcohol symptoms (n=106); and

(III) a heavy-drinking group with moderate or high consumption and two or more symptoms (n=53)(Table 1).

Table 1. Prevalence of symptoms associated with different alcohol consumption quartiles. Groups I-III.

Quartiles of alcohol consumed in previous week	No symptoms	One symptom	Two symptoms	Three symptoms
Quartile I (n=50)	GROUP I 41	6	3	0
Quartile II-III (n=100)	GROUP II 57	23	GROUP III 17	3
Quartile IV (n=50)	6	11	17	16

GROUP I Low alcohol consumption without alcohol symptoms (n=41)
GROUP II Intermediate group with low, moderate or high alcohol consumption with different number of alcohol symptoms (n=106)
GROUP III Heavy drinking alcohol group with moderate or high consumption and two or more symptoms (n=53)

Four subgroups were then formed with respect to the use of liver-metabolized drugs. Thus groups I and II combined were subdivided into groups IA and IB, and group III was subdivided into groups IIA and IIB, as follows:

(IA) low or moderate alcohol consumption and no use of drugs (n=126);

(IB) low or moderate alcohol consumption with use of drugs (n=21);

(IIA) high alcohol consumption with no use of drugs (n=43); and

(IIB) high alcohol consumption with use of drugs (n=10).

For more detailed information see Mützell, Tibblin and Bergman (15). Subjects taking antihypertensive drugs (beta-adrenoceptor blocking agents, hydrochlorothiazide, thiazides and hydralazines) were assigned to the groups without any use of drugs. Thirteen of the 126 men in group IA and three of the 43 in group IIA used antihypertensive drugs.

The examination took an average of about nine hours and included a general medical examination, taking of a psychiatric and social history, blood and urine tests, X-ray of the heart and lungs, ECG and electroneurography (ENeG).

Sociological interview

The sociological interview comprised standardized questions pertaining to family conditions, education, smoking and physical exercise.

The amount of alcohol consumed and the pattern of "alcohol behaviour" were thoroughly assessed back to childhood and the first glass of alcohol, wine or beer. To obtain as accurate as possible an idea of the present alcohol consumption, the questions were detailed.

Medical history

The subjects answered a self-administered standardized questionnaire concerning their previous and present health, respiratory symptoms, blackouts, epileptic fits and delirious episodes. The questionnaire was constructed at the Magnus Huss Clinic and has been used many years for testing alcoholic in-patients. The questionnaire consisted of a general and a cardiovascular section. Questions concerning respiratory and cardiovascular symptoms were identical to those in the questionnaire designed and tested for several years at the Department of Thoracic Medicine of the Karolinska Hospital. An interview was then conducted with all subjects concerning these questions, by one and the same person (the author).

Anthropometric measurements and blood pressure

Weight was recorded to the nearest kilogram and included light underwear. Height was measured in centimetres. The blood pressure (BP) was measured with the same mercury manometer in all subjects, between 9 and 10 a.m. and after 15 min of rest in complete

quiet. This was done in the same room by the same person (the author), and noise and chilling were avoided. The pressure was measured in the right upper arm and mean values of two measurements were used. The cuff had a rubber bladder 12 cm wide and 35 cm long. Systolic BP (SBP) and diastolic BP (DBP) were recorded to the nearest 5 mmHg. DBP was recorded at the disappearance of the Korotkoff sounds (phase 5).

Laboratory tests

Blood samples were drawn in the morning after an overnight fast, and analysed for serum (S) potassium, albumin, calcium, magnesium, creatinine, cholesterol and triglycerides, and for ethanol and methanol. Protein analysis (electrophoresis) was performed with IgG and haptoglobin.

Chest X-rays

A chest X-ray with the patient standing was taken as described by Liljestrand et al. (8). The relative heart volume, expressed in ml per square metre body surface area (BSA), was calculated (6) by one and the same experienced radiologist at the Department of Thoracic Medicine of the Karolinska Hospital, who also examined the heart configuration and lung films without knowledge of the patient's clinical data.

Electrocardiographic examination

The clinical examination included ECG recordings at rest with the subject in the supine position. The following leads were used: I-III, aVR, aVL, aVF and leads V_1-V_6. The chart speed was 50 mm/s and the instrument was a direct-recording 6-channel electrocardiograph (Mingograf 61, Elema-Schönander AB, Stockholm). The ECG findings were coded according to the Goldman criteria (4) and to the Minnesota code (19). All ECG examinations were interpreted by the same two independent physicians at the Department of Clinical Physiology, and without any knowledge of the subjects' identity and clinical data.

Lung function

Lung function was measured in a peak expiratory flow meter (litres/min), (Wright), with recording of the mean value from three blows. All subjects performed this immediately after arrival at the hospital in the morning, when the blood sample had been taken.

Electroneurography

The peripheral nerve function was examined by ENeG as performed routinely in clinical practice at the Department of Neurophysiology of the Karolinska Hospital by the same observer. Four peripheral nerves (median, ulnar, peroneal and sural) were investigated with ENeG methods recommended at a Scandinavian meeting on health hazards in the use of solvents (2). Each nerve was evaluated with respect to the occurrence of

neuropathy. A laboratory age-matched material from the Department of Neurophysiology was used as a reference group.

STATISTICAL METHODS

In order to test the hypothesis of two means being equal against a two-sided alternative, the t test was used. As a measure of association between pairs of variables, Pearson's product-moment correlation (r) was chosen. Differences in pairs of non-continuous variables were tested for significance by the Chi-square test. Quartiles were used for grouping the sample into homogeneous groups with regard to alcohol consumption. For testing levels of significances, groups II and III were tested against group I, and groups IB, IIA, and IIB against group IA.

RESULTS

Characteristics of the groups with different drinking habits are presented in Table 2. There was no difference in age between these groups. Their height and weight were the same. Ethanol was found in the blood of five (9 %) of the 53 heavy drinkers and varied between 3-64 mmol/l. The attendance of these five subjects for examination was distributed equally over the different days of the week. The one subject who attended on a monday morning was the man with 3 mmol/l. The proportion of smokers among the heavy drinkers was 62 %. Actions from the Temperance Board (against drunken driving and alcohol abuse) had been made in 32 %. Characteristics of the four subgroups are presented in Table 3.

Table 2. *Characteristics of the three groups with different drinking habits.*

	GROUP I (n=41)	GROUP II (n=106)	GROUP III (n=53)
Age (yrs)	44 ± 14	46 ± 14	42 ± 13
Height (cm)	178 ± 7	178 ± 6	177 ± 6
Weight (kg)	77 ± 12	76 ± 9	78 ± 10
Alcohol in blood on arrival at hospital(%)	0	1	9*
Alcohol consumption 7 days before arrival at hospital (g)	0 ± 1	11 ± 10***	34 ± 31***
Smokers (%)	46	42	62
Actions by the Temperance Board (%)	2	8	32***

Significance levels tested in comparison with group I by Student's t test and Chi-square test.
* $p<0.05$
*** $p<0.001$

Table 3. Characteristics of the four groups with different drinking habits with and without drug use.

	GROUP IA Low alcohol No drugs (n=126)	GROUP IB Low alcohol Drugs (n=21)	GROUP IIA High alcohol No drugs (n=43)	GROUP IIB High alcohol Drugs (n=10)
Age (yrs)	45 ± 14	46 ± 15	41 ± 14	49 ± 5
Height (cm)	178 ± 7	177 ± 8	177 ± 7	179 ± 4
Weight (kg)	76 ± 9	76 ± 12	76 ± 10	85 ± 5****
Alcohol in blood on arrival at hospital (%)	1	0	5	30****
Alcohol consumption 7 days before arrival at hospital (g)	8 ± 9	6 ± 11	30 ± 28****	39 ± 29****
Smokers (%)	42	52	60*	70
Actions by the Temperance Board(%)	6	10	33****	30**

Significance levels tested in comparison with low alcohol - no drugs group by Student's t test and Chi-square test.
- * $p<0.05$
- ** $p<0.01$
- **** $p<0.0001$

The drug-using groups were older, but not significantly, and the ten heavy drinkers and drug users in group IIB had a significantly greater body weight. Ethanol was found in the blood of 30 % of group IIB.

Group IIA had significantly ($p<0.05$) higher percentage smokers than group IA. There were no differences in smoking habits between the other three subgroups. Thirty per cent of group IIB and 33 % of group IIA were registered at the Temperance Board.

Cardiovascular variables

The heavy-drinking group III had a significantly higher mean heart rate and a significantly larger mean heart volume than groups I and II. The mean blood pressures were the same in these three groups (Table 4).

Table 4. Cardiovascular and other variables: Mean values of heart rate, blood pressure, heart volume, peak flow and percentage numbers with pathological ECG and ENeG.

	GROUP I (n=41)	GROUP II (n=106)	GROUP III (n=53)
Heart rate (beats/min)	69 ± 9	70 ± 14	73 ± 12*
Systolic blood pressure (mmHg)	142 ± 19	147 ± 23	145 ± 19
Diastolic blood pressure (mmHg)	89 ± 10	88 ± 11	89 ± 10
Total heart volume (ml/m^2 BSA)	697 ± 165	729 ± 147	760 ± 145*
Relative heart volume (ml/m^2 BSA)	359 ± 68	377 ± 71	386 ± 66*
Pathological ECG (%)	7	7	11
Peak flow (l/min)	429 ± 112	506 ± 96	504 ± 88
Pathological ENeG (%)	23	16	23

Significance levels tested in comparison with group I by Student's t test and Chi-square test.

- * $p<0.05$

There was no difference in the occurrence of pathological ECGs. Six men in group III had pathological ECGs. Two had pathological T-wave changes without coronary heart disease and one of them also had atrial fibrillation, one man had arrhythmias and three had ST segment changes and also tachycardia. The heavy drinkers using drugs (IIB) had a significantly higher mean heart rate, a significantly higher mean DBP and a significantly larger total mean heart volume than the other three subgroups (Table 5).

Table 5. Cardiovascular and other variables: Mean values of heart rate, blood pressure, heart volume, peak flow and percentage numbers with pathological ECG and ENeG.

	GROUP IA Low alcohol No drugs (n=126)	GROUP IB Low alcohol Drugs (n=21)	GROUP IIA High alcohol No drugs (n=43)	GROUP IIB High alcohol Drugs (n=10)
Heart rate (beats/min)	69 ± 13	72 ± 12	71 ± 11	79 ± 15*
Systolic blood pressure (mmHg)	145 ± 22	149 ± 22	142 ± 18	159 ± 20
Diastolic blood pressure(mmHg)	88 ± 10	89 ± 12	87 ± 8	98 ± 13**
Total heart volume (ml/m^2BSA)	724 ± 150	697 ± 162	739 ± 138	868 ± 138**
Relative heart volume (ml/m^2 BSA)	374 ± 70	358 ± 72	379 ± 66	419 ± 60
Pathological ECG (%)	8	0	9	20
Peak flow (l/min)	506 ± 94	480 ± 135	514 ± 86	463 ± 88
Pathological ENeG (%)	18	14	19	40

Significance levels tested in comparison with low alcohol - no drugs group by Student's test and Chi-square test.

* $p<0.05$
** $p<0.01$

ENeG

No difference in ENeG was found between the three main groups. Forty per cent of group IIB had pathological ENeGs, compared with 14-19 % in the other subgroups, but the difference was not significant (Table 4, 5).

Peak expiratory flow

There was no difference in peak flow between groups I, II and III (Tables 4).

Blood lipids

There were no differences between groups I and III concerning blood lipids except for group II who had a significantly lower triglyceride value ($p<0.05$)(Table 6). Higher serum cholesterol and triglyceride levels were found in the subgroup of heavy drinkers using drugs (IIB) than in the other subgroups.

Serum electrolytes and protein concentrations

Participants in group III had significantly lower S-creatinine and S-magnesium than participants in group I. There were no significant differences in albumin and in haptoglobin between the three groups. IgG was significantly lower in group III. No differences in serum electrolytes or protein concentrations were found between the four

subgroups, except for a low S-creatinine value in group IIB and a significantly higher haptoglobin value in group IB (Table 6).

Table 6. *Mean values for serum magnesium, creatinine, cholesterol, triglycerides, protein IgG and haptoglobin. Reference values in parenthesis.*

	GROUP I (n=41)	GROUP II (n=106)	GROUP III n=53)	GROUP IA Low alcohol No drugs (n=126)	GROUP IB Low alcohol Drugs (n=21)	GROUP IIA High alcohol No drugs (n=43)	GROUP IIB High alcohol Drugs (n=10)
S-Magnesium (0.65-1.00 mmol/l)	0.82 ± 0.05	0.82 ± 0.08	0.80 ± 0.09*	0.82 ± 0.07	0.81 ± 0.07	0.80 ± 0.09	0.79 ± 0.10
S-Creatinine (60-120 umol/l)	99 ± 16	93 ± 13**	92 ± 14***	95 ± 13	97 ± 20	93 ± 11	84 ± 22*
S-Cholesterol (2.6-7.8 mmol/l)	5.8 ± 1.1	5.7 ± 1.2	5.8 ± 1.4	5.7 ± 1.1	5.9 ± 1.3	5.6 ± 1.4	6.7 ± 1.4**
S-Triglycerides (0.4-1.7 mmol/l)	1.6 ± 1.3	1.3 ± 0.7*	1.6 ± 1.1	1.3 ± 0.9	1.6 ± 0.9	1.4 ± 0.7	2.5 ± 1.8**
IgG (7.0-15.0 g/l)	13.0 ± 3.1	12.7 ± 2.5	12.0 ± 2.3*	12.9 ± 2.5	12.0 ± 3.4	12.1 ± 2.4	11.5 ± 1.8
Haptoglobin (0.4-2.5 g/l)	1.9 ± 1.0	1.9 ± 0.9	2.0 ± 0.8	1.8 ± 0.9	2.2 ± 1.2*	1.8 ± 0.7	2.2 ± 1.1

Significance levels tested in comparison with group I respectively group low alcohol - no drugs (IA) by Student's t test and Chi-square test.

* $p<0.05$
** $p<0.01$
*** $p<0.001$

DISCUSSION

It was found that 27 % of the studied population belonged to a heavy-drinking group. Waern (23) reported that in 28 % of all participants of the health survey of 60-year-old men in Uppsala, one or two indications of long-standing or casual alcohol intake were noted.

In a study by Klatsky et al. (7) a clear relationship was observed between blood pressure and the daily numbers of drinks.

The heavy-drinking group of the present investigation did not have a higher SBP or DBP than the groups with lower alcohol consumption, nor did they differ in body weight, which was somewhat unexpected (17). The higher heart rate and the larger heart volume were noteworthy findings, but the mean values were within the normal range and were not impressive, and the practical significance is therefore questionable.

The group of drug-using heavy drinkers had a higher DBP, a higher heart rate and a larger heart volume than the other subgroups. They were also older and significantly heavier. An increased intake of alcohol implies an increased caloric intake, and thus elevated BP might be a function of increased body weight. Waern (23) found that the mean SBP and DBP levels were somewhat higher ($p>0.05$) among 60-year old men showing various indications of alcohol consumption. In the present population study high blood lipids were found not to be related to heavy drinking as such but showed a relationship to heavy drinking combined with the use of drugs.

The drugs used by subgroups IB and IIB were prescribed by a physician in adequate doses and there was no misuse. Group IIB had a poorer laboratory status and deviating values compared with the other subgroups. The findings in subjects with combined alcohol and drug use support the idea that ethanol inhibits drug metabolism and interferes with the rate of disappearance of drugs from the blood and whole body (20).

In acute alcoholism hypoalbuminaemia is known to occur. In the present study the albumin concentration was not lower in the heavy-drinking group than in the less heavy drinkers. Low serum levels of albumin have been found in alcoholic patients (13) and have been attributed to reduced synthesis of albumin due to liver damage. Another finding in the present investigation was a significantly lower serum level of IgG in the heavy-drinking group than in the groups with a lower alcohol intake. Decreased blood levels of immunoglobulins in alcoholics have been reported by a few authors (5). The majority of studies in this area have been concerned with the diffuse hypergammaglobulinaemia found in chronic alcoholics and alcoholics with cirrhosis of the liver (1).

The occurrence of peripheral neuropathy is common in patients with chronic alcoholism (ethyl alcohol) and has been observed for many years (3, 10). There was no significant difference in ENeG between the three main groups. This was not unexpected, as these men had no nutritional-vitamin deficiency or history of poor dietary intake (3).

Hypomagnesaemia was observed in the heavy-drinking group. Magnesium acts as a cofactor for many enzymic reactions, particularly those involved in high energy phosphate metabolism. A magnesium deficiency syndrome has been observed in alcoholic patients, especially during alcohol withdrawal, and in patients with delirium tremens (9, 11, 12). Patients with this syndrome also have an increased urinary excretion of magnesium and low values for exchangeable magnesium. Studies involving the administration of alcohol to both healthy volunteers and alcoholic patients have indicated that alcohol is the cause of the hypomagnesaemia and magnesium diuresis observed in alcoholics. The magnesium excretion is reported to be greatest when the blood alcohol level is rising.

Low serum creatinine values have been noted in alcoholism, especially in connection with vomiting and dehydration or in the presence of renal impairment. In a group with a high serum level of gammaglutamyl transpeptidase, Peterson et al., (16) found a low serum creatinine value, and this was also observed in our heavy-drinking group. The mechanism of this finding is not clear, as the urinary creatinine excretion has been found not to be affected by ethanol ingestion (18).

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