

REPORT ON THE WOMEN & ALCOHOL SYMPOSIUM (Stockholm, Sweden, 30 October 1998)

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Introduction

In 1994, a group of doctors from Denmark, Norway and Sweden founded the Scandinavian Medical Alcohol Board (SMAB) with the purpose to inform factually and comprehensively about new research results regarding the health effects of moderate alcohol use. This SMAB symposium about 'Women & Alcohol' was attended by about 75 people. An abstract of each presentation is presented here.

Sensitivity to alcohol of the female body (Alan W. Jones)

Women are more prone to alcohol-related disease than men because of physiological differences in alcohol metabolism. The most important factor appears to be the distribution volume for alcohol, total body water (TBW). The main determinants of TBW are age, weight and height. Human pharmacokinetic studies have revealed that women reach an 1.26 times higher blood alcohol concentration (BAC) than men after alcohol ingestion, standardized for alcohol dose and body mass. Female hormonal status seems also to be involved. Testosterone levels are inversely associated with ADH activity in the liver. Therefore, low testosterone levels in women result in faster elimination of alcohol, coinciding with higher blood acetaldehyde levels. Sex differences exist in the distribution and activities of ADH. Women have less gastric ADH activity, which increases the availability of alcohol.

New trends in alcohol use among Swedish women (Ylva Arnhof)

Between 1980 and 1989, alcohol use among Swedish girls and women aged 16-24 increased. This increase is mainly attributable to increased wine consumption. A significant contribution also comes from (partly illegally produced) spirits. Between 1994 and 1996, there has been no change in drinking level among girls. Questionnaire surveys indicate that girls are more concerned about alcohol use and misuse than boys, and one third of girls consider alcohol as a major public health problem. Furthermore, the experience of drunkenness (quantified by asking: how often do you feel drunk?) has been found to be higher among students from Nordic countries than among those from southern European countries.

Relation of alcohol to coronary heart disease, stroke and total mortality in women (R. Curtis Ellison)

Moderate alcohol consumption, defined as 5-20 g alcohol per day, has been associated with a reduced

coronary heart disease (CHD) risk for women. Data from the Framingham Heart Study have shown that this risk reduction was at least equally strong for women as for men. This association is mainly explained by an increase in HDL-cholesterol. Women showed similar or even greater increases in HDL-cholesterol levels than men and also a slight decrease in LDL-cholesterol. The HDL-cholesterol raising effect of alcohol was much stronger than for physical activity. In addition, inhibition of platelet aggregation may be involved in female CHD prevention, which is illustrated by a lower risk for acute myocardial infarction and cardiac death in moderate drinkers than in abstainers, when alcohol consumption is defined as consumption 24 h prior to the event (1). A similar inverse association is found between alcohol consumption and ischaemic stroke. Haemostatic stroke is positively associated with alcohol use, but the net effect on stroke risk is J-shaped. In an ongoing project the risk of death over a 10-year period in relation to life-style is being estimated and used to predict effects of life-style changes. Ellison and colleagues have found that abstaining women aged 55-75 who start to drink one drink per day live longer than teetotalers on average, even longer than women at low risk for CHD and at high risk for breast cancer (unpublished data). The take-home message for women should be 'Don't drink too much, but not too little either'.

Alcohol and dementia (Luc Letenneur)

Results of the PAQUID cohort study were presented (2). In this study 3675 mentally healthy subjects aged over 65 were followed for 8 years. End-points were dementia and Alzheimer disease as diagnosed by accepted biomedical criteria. In this red wine-drinking population age was identified as an important risk factor and moderate drinkers (3-4 drinks/day) appeared to have a significant (40%) decrease in risk for dementia relative to abstainers. For light drinkers (1-2 drinks/day) no significant effect on risk was found (0.89, $P = 0.13$). For women a similar trend was observed. This trend was, however, not statistically significant, probably due to the low proportion of moderately drinking women in the study population (53 out of 1700).

Alcohol and diabetes (Calle Bengtsson)

Unpublished data were presented from a Swedish cohort of 1317 women aged 38-60 at baseline. Associations between diabetes incidence, fasting insulin and alcohol use were evaluated during 24 years of follow-up. Light, moderate and heavy

This issue of Alcohol Research contains several abstracts related to the same topic. The following topics were identified: moderate alcohol consumption, cancer, alcoholic liver disease, GABA-related events, screening for alcohol use, treatment for alcoholism and withdrawal, and adolescents.

Moderate alcohol consumption

Six abstracts address various aspects of moderate alcohol consumption. Hendriks et al. (3306) report on the effects of moderate consumption of beer, wine and spirits on postprandial lipoprotein metabolism in middle-aged men. A decrease in wine consumption to moderate levels may have contributed to a decline in CVD mortality in Spain (Artalejo et al., 3302). Fecundability is reduced in women drinking 5 or fewer drinks weekly (Kold Jensen et al., 3308). An acute moderate dose of alcohol induces echocardiography and auscultatory signs suggestive of mitral valve prolapse in healthy women (Kelly et al., 3322) and may also contribute to lowered immunity and host defence in healthy men and women (Szabo, 3342).

Cancer

Four abstracts concern the relation between alcohol use and cancer. In the USA, no association was found between alcohol use and male breast cancer mortality (Hsing et al., 3307). Lumey et al. (3312) could not confirm a previously reported association between prostate cancer and alcohol use in a population of US white men. Alcohol use is associated with colorectal cancer risk in a dose-dependent fashion in an Argentinean population (Munoz et al., 3313). In Japanese alcoholics, the presence of the *ALDH2**2 allele (strongly) increases the risk for cancers of the digestive tract and lung cancer but not for liver cancer and other cancers (Yokoyama et al., 3330).

Alcoholic liver disease: genetic aspects

Individual variation in susceptibility to alcohol's hepatotoxic effects may have a genetic basis. Grove et al. (3318) report that the rare mutant *c2 CYP2E1* allele in combination with the *ADH3**2 allele is a risk factor for alcoholic liver disease (ALD) in Caucasians. In a case-control study no association was found between polymorphism of apolipoprotein E and the development of alcoholic cirrhosis (Giraud et al., 3317). Iron overload, common in the liver of alcoholics, may be attributed to a gene, *HFE*, that is mutated in most patients with hereditary haemochromatosis. However, patients heterozygous for *HFE* mutations did not have an increased risk for advanced ALD (Grove et al., 3319).

GABA-related events

Alcoholics have reduced GABA-benzodiazepine receptor levels in the absence of grey matter atrophy in some cortical regions (Lingford-Hughes and Acton, 3324). Predisposition to alcoholism may be related to benzodiazepine-induced changes in cerebral blood volume (Streeter et al., 3328). Female and male rats differ in GABA_A receptor gene expression in cerebral cortex elicited by alcohol dependence (Devaud et al., 3332). Rat lines selectively bred for alcohol sensitivity differ markedly in GABA-mediated events which correlate with the sedative effects of alcohol (Liu and Deitrich, 3336). Morales et al. (3340) provide anatomical evidence that GABAergic neurons of the

central nucleus of the amygdala are responsive to acute alcohol exposure.

Screening for alcohol use

Three abstracts concern the use of biomarkers for detection of alcoholism. Schmitt et al. (3325) report that carbohydrate-deficient transferrin (CDT) has insufficient specificity and sensitivity for the detection of alcohol abuse in an unselected population. CDT appears to be a poor indicator of heavy drinking in women, but sensitivity increases when CDT and GGT are used in combination (Yeasted et al., 3329). Both laboratory markers and brief questionnaires (CAGE and MAST) have too low a sensitivity to be useful to detect alcoholism in patients admitted to a general hospital (Wetterling et al., 3315).

Treatment of alcoholism and withdrawal

The results of a preliminary study by Kranzler et al. (3323) support the potential clinical utility of an injectable sustained-release preparation of naltrexone for treatment of alcohol dependence. In an open pilot study, infusional application of caroverine for treatment of patients with an alcohol withdrawal syndrome was well tolerated without adverse side-effects (Geretsegger and Fartacek, 3334). Burman (3346) searched for perceived changes since abstinence in alcoholics who recovered from alcoholism without treatment or support of a self-help group. Connors et al. (3348) studied factors associated with the onset and termination of specific relapse events in male and female alcoholics. As a first step in a cost-effectiveness analysis of a randomized alcohol treatment matching trial (MATCH), the relative costs of three manual-guided, individually delivered treatments were examined (Cisler et al., 3347).

Adolescents

The Sociology/psychology section includes seven studies focusing on adolescents. Motivations young people have for drinking are complex and alcohol use has linkages to both social context and perceived norms (Thombs et al., 3356). Family bonding characteristics (Kirby Forgays, 3351) as well as social activities with peers (Vicary et al., 3357) relate to adolescent alcohol use. Knowledge of adolescents' social skills competence and alcohol expectancies jointly can help predict alcohol involvement (Gaffney et al., 3351). Sutherland and Willner (3355) reveal data on the relationship between cigarette, alcohol and drug use in adolescents in the UK. Surveys in Canada indicate that bush party attendance is a popular recreational activity among adolescents; drinking-driving at these events is common and warrants community action (Stoduto et al., 3354). A study by Rounds-Bryant et al. (3353) provides information on important sex differences and similarities in adolescents who enter adolescent-oriented substance treatment programmes.

We hope you will enjoy reading the abstracts included in this issue. In addition, we announce that we will make Alcohol Research available through the Internet. More information will be provided in the next issue of this journal.

Marian R.T. van Haaren and Henk F.J. Hendriks (editor-in-chief)

drinkers were defined as drinking one or more drinks per month, week and day, respectively. Diabetes incidence was higher in abstainers and light drinkers than in moderate drinkers, but this association was significant for spirits only. Higher fasting insulin levels, a risk factor for developing diabetes, were seen in abstainers relative to moderate and heavy drinkers, but this effect was only significant for beer. Body mass index (BMI), a strong predictor of diabetes, was higher for abstainers than for drinkers, but the inverse association between moderate drinking and diabetes persisted after adjustment for BMI. Similar findings have been reported in the literature, albeit some publications are conflicting. The biological mechanism is unclear, but the speaker philosophized that an alcohol-induced increase in peripheral uptake of glucose could be an explanation.

Alcohol and female body mass (Klaus Jung)

In western countries alcohol provides over 10% of total energy. The waist-to-hip ratio (which correlates positively with risk for coronary heart disease) is inversely associated with wine consumption but positively with consumption of beer or spirits (3). Moderate drinking (up to 50 g/day) is associated with a lower BMI relative to abstinence in men and even more so in women (4). Classical experiments by Lieber's group have shown that substitution of alcohol for carbohydrates does not result in an increased BMI. Proposed mechanisms are (1) suppressed fat oxidation and (2) increased resting metabolism (women) and increased energy expenditure (men). Lean women metabolize alcohol-derived energy less efficiently than fat women (5). From a review on alcohol and obesity (6) it has been concluded that this association is inconclusive because of many potential confounders. From the audience it was proposed that leptin could be involved in the population variance in energy utilization of alcohol. Bengtson answered that he had tested this hypothesis in his cohort but had not found any interaction.

What level of alcohol consumption endangers the female liver? (Ulrik Becker)

One of the risk factors for alcoholic liver disease (ALD) is being female. Results from two cohort studies (7, 8) have shown that women have a higher risk of developing ALD than men at any given level of alcohol intake. It has been proposed that a safe intake level of alcohol is less than 21 drinks/week for men and less than 14 drinks/week for women. The results of several cohort studies from the Copenhagen area (7) suggest that a higher wine consumption as a percentage of total alcohol consumption can markedly decrease the risk for cirrhosis in both men and women. At a share of 31-50% for wine the risk was found to be lowered by about 60%, taking no wine consumption as reference. No experimental evidence is available yet. Wine could be a marker of a healthier life-style, which might explain the effect. Before public health recommendations can be made, more research has to be done.

Facts, myths and problems concerning alcohol use during pregnancy (Jørn Olsen)

Heavy drinking during pregnancy is associated with growth retardation, poor mental development and a characteristic pattern of facial abnormalities in offspring (foetal alcohol syndrome, FAS). Only few pregnant women in Europe are heavy drinkers (more than 4 drinks per day), but many continue to drink small to moderate amounts of alcohol during pregnancy. Most research on low to moderate drinking during pregnancy has shown reassuring results. Recently, however, one study (9) found a reduction of female fecundability for women having only 1-5 drinks/week. Furthermore, children exposed to low levels of alcohol prenatally (corresponding with 1 drink/week) are vulnerable to develop behavioural problems. Olsen expects that there is a dose-effect relationship: 5 drinks/week disturbs foetal growth, 10 drinks/week results in a lower head circumference, 15 drinks/week causes lower placental weight, preterm birth and behavioural problems and 20 drinks/week decreases APGAR scores as well as fecundability. There are still questions to be answered, for example: are there sensitive time periods during pregnancy, what is the effect of binge drinking and what is the interaction between medication and alcohol?

The female problem drinker (Moiria Plant)

Female problem drinkers are considered an unpopular group by physicians and may therefore be underexposed. The barriers to treating female problem drinkers are: shame, powerlessness, helplessness, feeling of inadequacy, fear of losing the children, lack of support and inadequacy of health insurance. In Project MATCH, a large-scale study evaluating treatment programmes (10), women performed better than men. The strongest predictors of success were readiness to change and self-efficacy. Female problem drinkers are not harder to treat than men, but a different approach is needed.

Alcohol, oestrogen and breast cancer (Judith S. Gavalier)

After the menopause oestrogen levels of women drop. Five drinks per week or less can increase oestradiol levels by 100% as compared to abstainers, but above a level of 5 drinks per week there is no further benefit and the risk of alcohol-related problems increases. Oestrogen replacement therapy (ERT) is often given to alleviate menopausal symptoms as well as to protect against osteoporosis and CHD. In a sample of 170 postmenopausal women the effect of alcohol consumption on hormone levels during ERT (treatment with conjugated equine oestrogens, CEE) was evaluated. The proportion of drinkers was higher in the group of responders to ERT (54.7% of the total sample) than among non-responders. Among moderate drinkers the hormonal effect was higher for a low dose of CEE (0.625 mg/day or less) than for a high dose (0.9 mg/day or more) (odds ratio relative to non-responders 4.2 and 1.06 respectively). Thus, irrespective of treatment with ERT, moderate drinking increases oestrogen levels, which may have implications for breast cancer risk.

Does alcohol consumption raise the risk of breast cancer? (Klim McPherson)

Many epidemiological studies have found alcohol use to be associated with no elevated risk, or a slightly increased risk, of breast cancer. The aetiology of breast cancer is largely unknown and there may be confounding factors such as diet and stress. At a level of 1-2 drinks/day, there is little to worry about, and only one study has found an association between alcohol and breast cancer for a level higher than 6 drinks/day. Ischaemic heart disease (IHD) is prevented by alcohol rather than that alcohol causes breast cancer. Thus, probably only cutting excessive drinking levels to a moderate level would reduce the attributable risk for breast cancer. However, because most women are moderate drinkers, they probably need not give up a pleasurable habit.

Bone and alcohol (Olof Johnell)

Osteoporosis and its clinical consequences (fractures) are a major health care problem in the western world. One of the risk factors is alcohol. Most epidemiological studies have found that light to moderate drinking decreases fracture risk compared to abstinence, but there are several possible confounders. In alcoholics the number of fractures increases, partly due to reduced bone mass but probably also to an increased falling tendency. There is probably a J-shaped relation between alcohol and bone density in women. In men no such relationship has been found. This may indicate a positive effect of moderate drinking on female bone density.

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