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Alcohol consumption and later risk of hospitalization with psychiatric disorders: Prospective cohort study

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ABSTRACT

The potential effects of alcohol intake upon the risk of psychiatric disorders have not often been investigated. The purpose of this study was to investigate, in a population sample, the association between self-reported amount of alcohol intake and the later risk of being registered in a Danish hospital with a psychiatric disorder. The prospective cohort study, the Copenhagen City Heart Study ($n = 18{,}146$), was used, containing three updated sets of alcohol intake and lifestyle covariates and up to 26 years follow-up. Alcohol intake was measured by self-report while psychiatric disorders were measured through registers. For women, the overall pattern showed that drinking above the sensible limits increased the risk of psychiatric disorders in general, especially for anxiety disorders where women drinking above the sensible drinking limits had a risk of 2.00 (confidence interval: 1.31–3.04) compared to women drinking below the sensible drinking limits. For men, the risk functions were slightly U-shaped; thus, a weekly low or moderate alcohol intake seemed to have a protective effect towards developing psychiatric disorders. The findings suggest sex differences in the association between alcohol consumption and risk of psychiatric disorders.

1. Introduction

Denmark and several other countries have sensible drinking limits of 14 and 21 drinks per week for women and men, respectively (Webster-Harrison et al., 2001; Mørch et al., 2005). These limits are primarily based on the risk of alcohol-related physical morbidity and mortality, but although 14 and 21 drinks per week may be a large amount of alcohol in relation to the physical influences of alcohol on the body, it does not necessarily affect social and mental functioning, and results concerning the relationship between alcohol intake and risk of psychiatric disorders have not been consistent (Hartka et al., 1991; Lipton, 1994; Schutte et al., 1995; Patten and Charney, 1998; Graham and Schmidt, 1999; Dixit and Crum, 2000; Rodgers et al., 2000; Alati et al., 2005; Graham et al., 2007). In addition, due to lack of longitudinal studies, the causality of this potential association is unknown. Therefore prospective studies in which information on alcohol use is collected before development of psychiatric disorders are needed to provide relevant evidence. However, such studies have not been conducted.

Exposure to alcohol is a necessary factor for the development of alcohol use disorders (AUD) and it has been shown that the risk of AUD increases dose-dependently with increased alcohol intake (Flensborg-Madsen et al., 2007). In addition, a substantial co-morbidity of AUD with psychiatric disorders has been documented: A high prevalence of co-morbid psychiatric disorders in individuals with AUD has been demonstrated in a number of large epidemiological studies (Regier et al., 1990; Penick et al., 1994; Tomasson and Vaglum, 1995; Kessler et al., 1997; Farrell et al., 2001; Kringlen et al., 2001; Grant et al., 2004a; Hasin et al., 2007), and it has been shown that AUD is more prevalent among individuals with psychiatric disorders than in the general population (Kessler et al., 1996; Dixon, 1999; Spak et al., 2000; Hasin et al., 2005). Finally, it has recently been found that AUD is registered before the co-morbid psychiatric disorder more often than the reverse temporal order (Flensborg-Madsen et al., 2009). It is therefore reasonable to assume that alcohol is an important risk factor for the

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development of psychiatric disorders, and this hypothesis will be investigated in the present study, using a Danish longitudinal cohort study with linkage to Danish hospital registers. The aim of the present study was to investigate in a large population sample the prospective association between self-reported amount of alcohol intake and the later risk of being registered at a hospital with mood disorders, psychotic disorders, anxiety disorders, personality disorders, drug abuse and psychiatric disorders in general. The results will be stratified according to sex in order to investigate possible sex differences.

2. Method

2.1. Study population

Data from the Copenhagen City Heart Study (CCHS) were used. CCHS is an ongoing series of studies conducted in the Danish population and initiated in 1976, when a random sample of men and women above 20 years of age and living in the Copenhagen area was invited to participate. The sample was randomly drawn from the Central Population Register, by use of the unique personal identification number, and invited by letter to answer self-administered questionnaires in the years 1976–1978. The number of participants was 14,223, with a response rate of 74%. This examination was followed by three follow-up examinations in the years 1981–1983 (CCHS II) (number of participants 12,698; response rate 70%), 1991–1993 (CCHS III) (number of participants 10,135; response rate 61%) and 2001–2003 (CCHS IV) (number of participants 6,238; response rate 50%). Data from the last examination, CCHS IV, were not used in these present analyses since the register follow-up only included data until the end of 2002. All follow-up examinations were supplemented with younger participants in order to keep the population large and representative. Detailed descriptions of the study have been published elsewhere (Appleyard et al., 1989; Schnohr et al., 2001; Thygesen, 2008). A total of 18,146 individuals answered questionnaires on their alcohol intake and other lifestyle factors in three waves of the Copenhagen City Heart Study (CCHS I–III).

2.2. Assessment of alcohol consumption

Information on amount and frequency, and type of alcohol intake was obtained from CCHS I–III where participants were asked in multiple-choice format to describe their alcohol habits. In CCHS I, however, the weekly alcohol intake had to be calculated: As in CCHS II and III, participants in CCHS I were asked whether they "hardly ever/never," "monthly," "weekly," or "daily" drank alcohol, but only if this intake was daily, was the average daily intake recorded. Thus, an absolute amount of consumed alcohol was obtainable only for persons stating a daily alcohol intake. Therefore the weekly intake in CCHS I was calculated by means of a series of regression models estimated from CCHS II. These were previously constructed by Becker et al. (1995) and include the explanatory variables age, sex, alcohol intake patterns and weekly alcohol intake. In all three waves, CCHS I–III, the average weekly intake of beer, wine and spirits was summed to the total alcohol intake (with one bottle of beer being approximately equivalent to the alcohol contents of one glass of wine or one glass of spirits, assuming each drink contains 12 g of alcohol).

Results are illustrated based on two different categorizations of alcohol: First, we divided individuals into five alcohol-drinking groups (Fig. 2a and b) using non-drinking individuals as the reference group. Then, we divided the study sample into those drinking below and those drinking above the sensible drinking guidelines and using the former category as the reference group (Table 1a and b).

2.3. Assessment of psychiatric disorders by linkage to national registers

All persons invited to CHHS I–III were followed by linkage with Danish registers using the unique personal identification number. The Danish Hospital Discharge Register (Jurgensen et al., 1986) contains information on dates of hospital admissions and discharge diagnoses from Danish hospitals since 1976; the Danish Psychiatric Central Register (Munk-Jorgensen and Mortensen, 1997) contains information on dates of hospital admissions and discharge diagnoses from Danish psychiatric hospitals since 1969; and the Danish Causes of Death Register (Juel and Helweg-Larsen, 1999) contains information on causes of death of all Danish residents who died in Denmark since 1943. Diagnoses in the registers are classified according to the World Health Organization's International Classification of Diseases (ICD) using the eighth revision until 1994, and the 10th revision from 1994 and onwards.

Psychiatric disorders were in this study divided into the following categorizations: mood disorders, psychotic disorders, anxiety disorders, personality disorders, drug abuse, and all psychiatric disorders in general (except for individuals with only AUD). Individuals that were registered with the outcome disorder before their entry into the study were eliminated from the analyses. Many individuals had several diagnoses and a non-hierarchical approach was taken, meaning, that all individuals with a given diagnosis were included in the analysis of this specific outcome disorder. The following diagnostic categories were used:

- Mood disorders: ICD-8 (296, 300.4, 298.0), ICD-10 (F30-34, 38, 39)
- Psychotic disorders: ICD-8 (295, 297, 298.1-9, 299), ICD-10 (F20-29)
- Anxiety disorders: ICD-8 (300.0, 300.2, 300.3), ICD-10 (F40-43)
- Personality disorders: ICD-8 (301), ICD-10 (F60)
- Drug abuse: ICD-8 (304), ICD-10 (F11-19 – for only harmful use and dependence)
- Any psychiatric disorder: ICD-8 (28, 30, 31), ICD-10 (F1, F2, F3, F4, F5, F6, F7, F8, F9), minus AUD diagnoses

2.4. Assessment of possible confounding factors

A number of covariates were considered putative confounders in the association between alcohol intake and psychiatric disorders. The following were available in all three data collection follow-ups: sex, smoking (current smoker, previous smoker, and never smoker), cohabitation status (living alone, living with someone), and educational level (less than 8 years, 8–12 years, and more than 12 years). All results were adjusted for these factors.

2.5. Statistical analysis

The analyses used to estimate the risks of psychiatric disorders were Cox proportional hazard regression (Collett, 2008). By including age as the time variable the estimates were adjusted for confounding by age. Subjects were followed from their date of entry, when they answered their first questionnaire between 1976 and 1993, to the date of the first registration of the psychiatric outcome disorder, death, disappearance, emigration, or until the end of follow-up (January 2002), whichever occurred first. The assumption of proportional hazards was tested for the main exposures by adding a time-dependent covariate (log t) to the regression model and testing the significance of this interaction with significance defined as $p<0.05$. No violations were detected.

In contrast to time-fixed covariates, both the alcohol intake and the possible confounding factors from CCHS were time-dependent variables as they were measured repeatedly over time in 1976–1978, 1981–1983, and 1991–1993, with the number of observations and the time between the observations varying between subjects. The presented analyses were based on updated measures of alcohol consumption and confounders. In these analyses we prospectively assessed the risk of psychiatric disorders in between examination increments based on determinations of covariates derived from the preceding questionnaire. Technically, this means that several observations were analyzed for each individual who was characterized anew in each of the consecutive examinations and that information from all observation intervals was pooled as if the information recorded at each interval were a new observation. In case of missing data the last observation was carried forward. All analyses were performed using SAS software package SAS 9.1.

3. Results

Fig. 1 shows the distribution of the amount of alcohol intake in CCHS I, illustrating that 13.8% of the study population drank above 21 drinks of alcohol per week. The study population was followed for up to 26 years in Danish registers in order to capture diagnoses of psychiatric disorders. Among the 18,146 individuals completing at least one of the three questionnaires in CCHS I–III, 965 (5.3%) individuals were registered with mood disorders, 382 (2.11%) with psychotic disorders, 333 (1.84%) with anxiety disorders, 602 (3.32%) with personality disorders, 295 (1.63%) with drug abuse, and 2092 (11.53%) were registered with some kind of psychiatric disorder other than AUD.

The patterns of risks of psychiatric disorders according to alcohol intake were different for men and women. For women, the overall pattern showed that large amounts of alcohol increased the risks of psychiatric disorders up to 2 times that of non-drinking women, mainly for anxiety disorders and psychiatric disorders in general (Fig. 2a and Table 1a). Hence, the risk of anxiety disorders for women drinking 15–21 drinks per week was 1.92 (95% confidence interval (CI): 1.10–3.33) compared to women who did not drink alcohol