



Alcohol intake and the risk of hyperuricaemia: A 6-year prospective study in Japanese men

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KEYWORDS

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Abstract *Background and aims:* Since there is little information derived from prospective studies on the amount of alcohol drinking required to induce hyperuricaemia, we attempted to address this issue in a Japanese population.

Methods and results: A total of 3310 Japanese men aged 20–54 years that were free of hyperuricaemia were classified according to their alcohol intake per week at baseline. Incident hyperuricaemia, defined as >7.0 mg/dl and/or taking medication for hyperuricaemia, was assessed through annual health examinations for 6 years after the baseline examination. During follow-up, 529 incident cases of hyperuricaemia occurred. There was a positive, dose-response relationship between alcohol intake and the risk of incident hyperuricaemia. The hazard ratio (95% confidence interval) for hyperuricaemia in drinkers compared with non-drinkers was 1.10 (0.85–1.42) for <10.0 drinks/week, 1.40 (1.07–1.84) for 10.0–19.9 drinks/week, 1.64 (1.23–2.21) for 20.0–29.9 drinks/week and 1.98 (1.40–2.80) for ≥30.0 drinks/week (one drink contained 11.5 g of ethanol) after adjusting for age, baseline serum uric acid, body mass index, smoking habits, exercise habits, serum creatinine, blood pressure, serum cholesterol and blood glucose. The fraction of hyperuricaemia in the population attributable to alcohol intake was 21.6%. A clear dose-response pattern was

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observed for both beer and *sake*, when the consumption of these two beverages was analysed separately.

Conclusion: Habitual alcohol intake significantly contributed to the development of hyperuricaemia in Japanese men, regardless of type of alcoholic beverage consumed. Therefore, it is essential to reduce excessive alcohol intake to prevent and manage hyperuricaemia.

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Introduction

Elevated serum uric acid is a metabolic disorder that is associated with gouty arthritis [1,2], urolithiasis [3,4], kidney disease [5,6] and cardiovascular disease including coronary heart disease and stroke [7,8]. Epidemiological studies based mainly on cross-sectional observations or interventions have shown a causal relationship between habitual intake of alcoholic beverages and hyperuricaemia [9–18]. Alcohol-induced hyperuricaemia is caused by accelerated synthesis of uric acid from adenosine, which is produced by the degradation of adenosine triphosphate to monophosphate during alcohol metabolism, and/or the reduced urinary excretion of uric acid due to the elevation of blood lactate produced by the oxidation of ethanol [19–22]. In addition, a large amount of purine contained in beer [23–25] contributes to hyperuricaemia from the excessive intake of this beverage [13–18,26,27]. Importantly, alcohol intake increases serum uric acid more than the intake of common purine-rich foods such as meat and seafood [15,16,28]. Accordingly, a key strategy for preventing and managing hyperuricaemia is the reduction of alcohol consumption. However, there is little information derived from prospective studies on the amount of alcohol drinking required to induce hyperuricaemia [11,12]. In particular, no prospective studies have been conducted on this issue, taking into account the type of alcoholic beverage consumed. Such information is an important public health issue, especially in countries such as Japan where large amounts of alcoholic beverages are consumed [29–31]. Therefore, the present study attempted to determine the nature of the causal relationship between the amount of alcohol consumed and the risk of incident hyperuricaemia in Japanese men using 6-year longitudinal follow-up data.

Methods

Study design and population

The study population consisted of Japanese men who worked for a metal products factory in Toyama prefecture, Japan; this factory had approximately 4400 male and 2600 female employees. The Industrial Safety and Health Law in Japan requires all employers to conduct annual health examinations on all employees. The details of this study population have been reported previously [32,33]. Of all employees who underwent an annual health examination in 1996 (>90%), 4011 male employees aged 20–54 years were enrolled as potential participants and were followed-up for 6 years from 1996 to 2002 through annual health examinations. Female employees were not included, because of low prevalence of

drinking, especially heavy drinking [33]. In addition, employees aged ≥ 55 years were excluded, because they were required to retire by the end of the follow-up period. The present cohort study was approved by the Institutional Review Committee of Kanazawa Medical University for Ethical Issues.

Of the 4011 potential participants, 701 were excluded due to one or more of the following criteria: baseline hyperuricaemia, defined as serum uric acid >7.0 mg/dl on the basis of the Japanese guideline for the management of hyperuricaemia and gout [34], and/or taking medication for hyperuricaemia ($n = 529$); baseline renal dysfunction, defined as serum creatinine >1.3 mg/dl set as the upper normal limit for men in our laboratory ($n = 9$); missing information at the time of the baseline survey ($n = 44$); or failure to obtain information in the follow-up survey ($n = 119$). The remaining 3310 normouricaemic participants were included in the final analyses as the eligible study population.

Baseline examination

Data collected through a self-administered questionnaire at study entry included age, medical history, and alcohol drinking, smoking and exercise habits. In addition, data were obtained on serum uric acid, creatinine, total cholesterol, blood glucose, blood pressure and anthropometric indices.

Each participant was asked whether he was a drinker or a non-drinker including an occasional drinker who consumed alcoholic beverages a few times per year. Then, every drinker was asked to estimate the frequency of alcohol intake per week (or per month) during a typical week (or month). The quantity of alcoholic beverages consumed on each typical occasion was also reported, using the following units typically consumed in Japan: a bottle of beer (663 ml), one *gou* (a traditional Japanese drinking unit) of *sake* (Japanese rice wine) (180 ml), double shots of whiskey (70 ml) and half a glass of *shochu* (Japanese distilled spirits made from barley, sweet potato, rice or any combination of these) (110 ml). All of these drinks have roughly equivalent ethanol content (approximately 23 g). In this report, all the units listed in the questionnaire were converted to drink, defining half a unit as one drink (11.5 g of ethanol), which is nearly equal to one 'standard' drink in most countries [35]. The average weekly alcohol intake (drinks/week) was calculated for each participant using data on the frequency and quantity of alcohol intake. Smoking habits were evaluated as to whether a participant was a never, former or current smoker; exercise habits were evaluated in terms of the frequency and intensity of exercise (no, light, moderate and hard exercise).

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