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Original article

Population blood pressure and low to moderate alcohol intake in an untreated population followed over 20 years. Copenhagen City heart study

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ABSTRACT

The aim of this study is to evaluate whether a changing population alcohol intake is capable of setting off a shift in the blood pressure distribution in the untreated part of a population. The focus is on subjects with an alcohol intake well below the limits of alcoholism because these subjects make out the majority of the population. The Copenhagen City Heart Study is a prospective longitudinal epidemiological study. The untreated study population was followed over 20 years. Specially trained technicians using a blinded sphygmomanometer measured BP once with the subject in the sitting position. The BP measurement was fully standardised and the measurement method was unchanged throughout the observation period. A questionnaire concerning drinking habits was completed by the participants and double-checked by the technicians. The results were a decreasing population systolic BP and an increasing self-reported alcohol intake. The population increase was based on an increasing proportion of light to moderate drinkers. There was no effect of a moderately increasing alcohol intake as a covariate in a multivariate analysis of population systolic BP. Conclusion: A moderately increasing population alcohol intake cannot explain the observed changes in population systolic blood pressure.

1. Background

Population blood pressure (PBP) is the mean value of all BPs in a population. It is a significant marker of a population's risk of cardiovascular death and strokes [1]. Consequently, it is important to know the determinants for PBP. PBP is particular for a population and for a time, so PBP will change with environmental factors that are in a state of flux. The association between alcohol and BP has been studied in several cross-sectional studies using different statistical models. Univariate and age-adjusted ANOVA and regression models were applied to show a positive linear relationship between alcohol intake and BP [2–5].

The association between PBP and alcohol intake may also be evaluated in a comparison of two populations separated geographically, culturally or in time. Geographically separated populations were analysed in China where ethnic groups were compared without finding any link between alcohol and BP [6]. Populations separated in time are analysed when the same population is examined at twice or more occasions (within-population study).

Alcohol intake is not a stable lifetime characteristic. Throughout a lifetime, people may start drinking or stop drinking. They may increase or decrease their intake due to alterations in social life, health, family life or economy [7–9]. If alcohol intake is a true determinant, then population BP will change with changing population alcohol intake. Random effects (longitudinal) analyses [10] are designed to study time-varying variables across the life span. The reason for this is that unlike cross-sectional studies, longitudinal studies track the same people, and therefore the differences observed in those people are less likely to be the result of cultural or socio-economic differences across generations. The aim of the present study is to evaluate, by means of a random effect analysis, whether a changing alcohol intake in the population is a determinant factor for changes in population systolic BP (SBP). The results are important in primary prevention where an identification of significant determinant factors for elevated BP is essential in order to prevent hypertension and its associated diseases.

2. Methods

2.1. Subjects

The Copenhagen City Heart Study (CCHS) is a longitudinal epidemiological study in a random sample of subjects of both genders

Abbreviations: BMI, Body mass index; CCHS, Copenhagen City Heart Study; DBP, Diastolic blood pressure; PBP, Population blood pressure; SBP, Systolic blood pressure.

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aged 20 and above. The sample was randomly selected from the civil register of people living in a defined area of Copenhagen. The subjects were invited to four examinations carried out from 1976 through 1978, from 1981 through 1983, from 1992 through 1994, and from 2001 through 2004, respectively. Middle-aged subjects were in majority to ensure significant results concerning cardiovascular diseases. Younger subjects (age 20–30 years) joined the survey as new entrants in surveys 2–4. Total response rates were 74%, 70%, 61% and 50%. The sex distribution was the same in all four surveys. Details of the selection procedure, a description of the eligible non-participants, the complete examination program, and information on the subjects have been presented elsewhere [11].

Observer bias and bias related to the device (i.e. last digit preference) are important issues in the methodology of PBP measurement and must be dealt with before planning a PBP study. Any possible source of measurement error has been evaluated in the CCHS [12]. Prior to analysing BP, the surveys were checked for non-responder bias. There was a small but significant difference in the fraction of male smokers when comparing survey 3 and survey 4. There was no non-responder bias in the other explanatory variables or in BP.

The CCHS was approved by the Regional Ethical Committee for Medical Research in Copenhagen.

2.2. Procedures

2.2.1. BP measurements

The WHO guidelines recommended by Rose and Blackburn [13] were observed. Specially trained technicians using a London School of Hygiene sphygmomanometer [14] measured BP once on the non-dominant arm after a 5-min rest with the subject in the sitting position. The single-measurement strategy is advantageous in a large-scale population study with a large number of measurements on each subject. The single-BP-results from the Copenhagen Heart Study have been validated by several authors [1,15–18]. The result is, that the association between single-measurement-BP and outcome parameters as e.g. all-cause-death, myocardial infarction and stroke is strong and highly significant. The fall of the mercury column was set to 2 mm/s. During this time, the Korotkoff sounds were measured through a stethoscope placed over the brachial artery. The first Korotkoff sound signified systolic BP (SBP). The fifth Korotkoff sound (the sounds disappear) signified diastolic BP (DBP). In all four surveys the technicians were instructed in the same way, and all conditions during the measurements were identical in the four surveys. All equipment was examined at regular intervals.

2.2.2. Weight and height

Height was measured without shoes on a scale fixed to the wall, to the nearest 0.5 cm. Weight was measured with indoor clothing on, but without shoes, on a Seco digital scale, to the nearest 0.1 kg. The scales were calibrated daily. Body mass index (BMI) was calculated (kg/m^2).

2.2.3. Plasma cholesterol

Non-fasting venous blood samples were analysed for plasma cholesterol (mmol/l). Analyses were performed enzymatically in a Gilford 3500 autoanalyser, with "Precicet" (Boehringer Mannheim, Mannheim, Germany) for standardisation (Gilford Laboratories, Oberlin, OH, USA), and a pooled plasma control and "Precilip" for accuracy control.

2.2.4. Questionnaire

A self-administered questionnaire concerning family life, socio-economic status, smoking status, diabetes, physical exercise, medicine and drinking habits was completed by participants. The questionnaire has been validated by its authors [13]. Questions on alcohol habits were added and these questions were validated by Grønbaek [19]. Questionnaires were completed by the participants and double-checked by the technicians.

The subjects were asked in multiple choice formats about the average number of drinks consumed per week. One bottle of beer contains 12 g of alcohol, and this may be considered the average for the other types of drinks. The subjects were classified into four alcohol groups by their total weekly alcohol intake of <1, 1–6, 7–13, or 14 or more drinks. The questionnaires concerning alcohol habits were identical in surveys 2–4. Survey 1 was excluded from the alcohol habit analysis.

The subjects were also asked about antihypertensive medication. All subjects that at some point during the observation period reported use of antihypertensive medicine were excluded from this study. The exclusion of subjects on antihypertensive medication was based on the fact that the treatment effect on BP would bias the possible association between alcohol and BP. Untreated individuals and individuals that are treated with antihypertensive medicine cannot be compared in the same statistical models because the treated individual may have a BP that is – say – 20 mm Hg below an untreated counterpart. The achieved treatment effect blurs the relationship between BP and determinant factors in any statistical analysis. Thus, the study population consisted of 11 261 (Survey 2), 8529 (Survey 3) and 4927 (Survey 4) subjects. Altogether 33 607 BP measurements were reported in this analysis. 12 726 (38%) were SBP ≥ 140 mm Hg. The results from the present analysis were therefore based on both low SBP-values and high SBP-values. More and more hypertensives were taken into treatment during the observation period, but the level at which hypertension is pharmacologically treated has not changed [20].

The subjects were asked about their habitual physical exercise, and based on the answers, the population was subdivided into four physical activity groups: Group 1: sedentary subjects or less than 2 h of light activity. Group 2: subjects with less than 4 h of light physical activity in the leisure time. Group 3: light physical activity in more than 4 h per week or more strenuous activity for 2–4 h per week. Group 4: More than 4 h of strenuous activity per week.

2.2.5. Statistics

Trends were analysed by mixed linear models with extension for random subject effect [10]. Random effect models allow for the inclusion of time-varying and time-invariant covariates. Random effects analyses enable a description of the trend over time while taking into account the correlation that exists between successive measurements.

Therefore the final analysis of the SBP trend was performed by random effect analysis with alcohol, age, gender and cardiovascular risk factors as variables. The adequacy of models in a stepwise selection procedure was tested by means of a residual likelihood ratio test. SBP was log transformed in these models. The final model was determined by a restricted/residual likelihood ratio test.

Model diagnostics were used to check if the final model captured all systematic effects in the data and fulfilled all other model assumptions.

The calculations were carried out using the statistical software SAS 9.1. A value of $P < 0.05$ was considered statistically significant.

3. Results

Descriptive data on the three surveys are given in Table 1. There was an increased self-reported age-adjusted alcohol intake (Fig. 1) in the study population. Women almost doubled their alcohol intake from 4.3 drinks (St error: 0.08) a week in survey 2 to 8.6 drinks (St error: 0.12) ($p < 0.0001$) in survey 4. The abstainer group comprised 42.2% of the women in survey 2. The ratio of abstainers was reduced to 2.6% in survey 4, whereas the number of drinks in groups 2, 4 and especially 3 increased (Table 2). Men increased their intake from 13.4