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Alcohol consumption and type 2 diabetes

Meta-analysis of epidemiological studies indicates a U-shaped relationship

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Abstract To clarify the relationship between alcohol consumption and type 2 diabetes we conducted a meta-analysis of published epidemiological studies. Data from 13 cohorts were included in the analysis. The results of these studies are consistent with regard to moderate alcohol consumption, indicating a protective effect in the order of 30% (relative risk $[RR]_{meta}=0.72$, 95% CI=0.67–0.77). The reduced risk is seen in men as well as in women, although few studies investigated women. No protective effect of high alcohol consumption was seen and one cannot rule out that large intakes of alcohol may increase the risk of type 2 diabetes. Results from published studies suggest a U-shaped relationship between alcohol and type 2 diabetes, but this is based on rather few studies with heterogeneous design and definitions. It seems important to further investigate if, and to what extent, high alcohol consumption increases the risk of type 2 diabetes. Aspects of moderate alcohol consumption also need further investigation; these include type of drink, frequency of drinking, sex and ethnic differences.

Keywords Alcohol · Epidemiology · Meta-analysis · Review · Type 2 diabetes

Abbreviations RR: relative risk

Introduction

It is becoming increasingly clear that alcohol consumption is a factor of importance for the risk of type 2 diabetes. Data from epidemiological studies suggest a protective effect of moderate alcohol consumption (reviewed in [1]). However, the strength of these data with regard to different aspects of alcohol exposure has, to our knowledge, not been evaluated in detail. Important aspects include the influence of high versus moderate alcohol consumption, different susceptibilities for men and women and the magnitude of any protective effect of alcohol consumption. The purpose of this commentary is to provide a better understanding of the epidemiological literature, including the aspects mentioned, by using meta-analysis.

Material and methods

By Medline search we identified 25 epidemiological studies on the relationship between alcohol and type 2 diabetes (search strategy and keywords available from authors) [2–26]. These were published between 1988 and March 2004. All studies except three [5, 6, 14] were prospective cohort studies with a follow-up time of up to 20 years [24]. The majority of studies concern men, but some included women [2, 4, 5, 7, 8, 11, 16, 17, 19, 20, 22, 24–26]. Nine studies were not included in the meta-analyses since the authors analysed alcohol consumption continuously [5, 8] or dichotomised [3, 11, 19], did not provide confidence intervals [4] or analysed men and women together [7, 20, 22] (complete information on the strategies behind the pooling is available from the authors). Furthermore, the British Regional Heart study [9, 21], the US Health Professionals Follow-up Study [10, 18] and the Nurses Health

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Fig. 1 Moderate alcohol consumption and type 2 diabetes. Moderate consumption is defined as approximately 5–30 g of alcohol per day. This corresponds to about 0.5–2.5 drinks per day. Abstainers (Todoroki, Tsumura, Ajani, Wei, Wannamethee 2003, Saremi, Hu) or low consumers (approximately <5 g of alcohol per day) (Carlsson 2000, Conigrave, Kao, Nakanishi, Wannamethee 2002, Carlsson 2003) are used as reference category

Study [2, 17] were reported twice. Of these papers, only the more recent of the two were included in the meta-analysis [17, 18, 21]. The meta-analysis was performed with Episheet [27] and the pooled estimate was calculated using methods described by Fleiss [28].

Results

Moderate alcohol consumption

Moderate alcohol intake, corresponding to about 5–30 g of alcohol per day, was associated with a reduced risk of type 2 diabetes in the order of 30% (relative risk $[RR]_{meta}=0.72$, 95% CI=0.67–0.77) compared to low consumption or abstinence (Fig. 1). The magnitude of this risk reduction corresponds to the reduced risk of cardiovascular disease

reported in moderate drinkers (reviewed in [29]). There are few studies in women, but available data seem to indicate that moderate alcohol consumption is equally beneficial in women as in men (RR_{meta} in women=0.68, 95% CI=0.61–0.75). Most of these studies were based on Caucasians, but the results were consistent across other ethnic groups such as Japanese [6, 12, 23], African-Americans [16] and Nauruans [5]. Similar results were seen in most [3, 5, 7, 8, 11, 19, 20, 22], but not all [4] of the studies excluded from the meta-analysis due to differences in methodology.

Moderate consumers of alcohol have a reduced risk compared to low consumers [14, 16, 18, 21, 23, 24] and to abstainers [6, 13, 15, 17, 25]. Thus it does not seem likely that inclusion of people who did not drink because of disease or previous high alcohol consumption as reference can explain a protective effect in moderate consumers. Moreover, the reduced risk persisted after adjustment for a

Fig. 2 High alcohol consumption and type 2 diabetes. The definition of high consumption varies from ≥ 20 g of alcohol per day [Carlsson 2003 (in women)] to >69 g of alcohol per day (Nakanishi), but in the majority of studies a cut-off of ≥ 30 g per day (corresponding to about three drinks per day or more) was used. Abstainers (Todoroki, Tsumura, Wei, Wannamethee 2003) or low consumers (approximately <5 g of alcohol per day) (Carlsson 2000, Conigrave, Kao, Nakanishi, Wannamethee 2002, Carlsson 2003) are used as reference category

number of potential confounders such as age, body mass index, smoking, physical activity, family history of diabetes, socioeconomic group and diet (see for example [18] or [21]).

High alcohol consumption

The relationship between high alcohol consumption (corresponding to about 30 g of alcohol per day or more) and type 2 diabetes is inconsistent across studies (Fig. 2). In all studies except two [6, 18], high consumers have an increased risk of type 2 diabetes compared to moderate consumers, but whether they have an increased risk compared to low consumers or abstainers is less clear. This was suggested in two studies [14, 16] but not confirmed by others. Notably, in women an increased risk of diabetes has been found in subgroups of high consumers such as lean women, (RR=2.8, 95% CI=1.1–7.3) [24], and women with high consumption of spirits (RR=2.5, 95% CI=1.0–6.2) [25].

Discussion

Since the effects of long-term alcohol intake can hardly be investigated in an experimental setting, research largely has to rely on epidemiological methods. Two major methodological problems are evident in all epidemiological studies on alcohol and type 2 diabetes: how to obtain accurate exposure information and how to identify all cases of diabetes. Bias resulting from misclassification of exposure and/or disease may be one reason for the inconsistent results on high alcohol consumption and type 2 diabetes. Questionnaire information on alcohol was used in all but one of the studies [4] we investigated. Such information is often under-reported [30] and as a consequence, some high consumers may have been classified as moderate or low consumers. This will not produce a spurious risk reduction in moderate consumers, but rather it may make it difficult to observe a relationship between high alcohol intake and type 2 diabetes. In addition, under-reporting implies that the cut-off levels used to define low, moderate and high alcohol intake cannot be interpreted as a measure of absolute consumption. With regard to identification of cases, self-reported diabetes information is often used in epidemiological studies and will be sufficient for many purposes. However, in studies of alcohol, such information may introduce bias since the likelihood of having your diabetes diagnosed may depend on your level of alcohol consumption. Some of the larger studies included in our meta-analysis were based on self-reported diabetes and the results may hence be afflicted with such bias [13, 17, 18, 21, 25]. Another potential reason for the inconsistent results on high alcohol intake and diabetes could be chance, since the number of cases among high consumers of alcohol was very small in most studies.

The results of any meta-analysis are limited since they involve pooling of risk estimates from studies that may have more-or-less-pronounced differences in methodology

and, probably, setting. Some of the differences that need to be kept in mind while considering the pooled risk estimates include (1) different reference categories were used to calculate the relative risks, some have used abstainers for comparison whereas other have used low consumers; (2) the definition of low, moderate and high alcohol consumption varies between the studies; (3) the relative risk estimates are not adjusted for the same confounders; (4) different questions are used to measure alcohol intake; and (5) it was not possible to include all studies of alcohol and diabetes in the pooled analyses, due to differences in methodology and publication bias.

Conclusions

The results of published studies on alcohol consumption and type 2 diabetes consistently indicate that moderate alcohol consumption reduces the risk of type 2 diabetes. The risk reduction is in the order of 30%. This is comparable to what has been reported for cardiovascular disease [29]. The reduced risk is seen both in men and in women, although it should be noted that few studies investigated this issue in women. From a mechanistic point of view, a protective effect of moderate alcohol consumption is compatible with findings that alcohol can enhance insulin sensitivity [31, 32].

As to the effect of high alcohol intake on the risk of type 2 diabetes, it is difficult to draw any conclusions. The most consistent finding is that no beneficial effect can be attributed to high alcohol consumption. Whether high alcohol intake actually increases the risk of type 2 diabetes is unclear. Methodological problems such as difficulties in measuring alcohol consumption, underdiagnosing of diabetes cases and small numbers may contribute to partially inconsistent results.

Should one then recommend alcohol to the general population in order to reduce the risk of type 2 diabetes? It seems premature to formulate any such recommendations. Further investigations are needed to decide to what extent high alcohol consumption may increase the risk of diabetes and what moderate and high alcohol consumption means in absolute terms. The possible protective effect of moderate alcohol consumption also needs further attention, considering influence from type of beverage, frequency of drinking and interaction with other risk factors such as overweight and family history of diabetes. More studies in women and different ethnic groups are also warranted.

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