Epidemiology and inflammatory bowel diseases

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Abstract

The role of alcohol in causing or aggravating the pathogenesis of inflammatory bowel disease is unclear. For finding a conclusive answer for this valuable question we conducted this review. Only two studies were identified that successfully fulfilled our inclusive criteria. Usual consumption of alcohol reduced the risk compared with less frequent use (odds ratio = 0.57, 95%CI: 0.37-0.86). Light alcoholic drinking has protective effects against development of ulcerative colitis. But this inverse association disappeared when smoking was included.

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Key words: Epidemiology; Inflammatory bowel diseases; Crohn's diseases; Ulcerative colitis; Alcohol

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INTRODUCTION

Alcohol is widely consumed in the Western part of the globe where inflammatory bowel diseases are prevalent. However, the role of alcohol in the pathogenesis of inflammatory bowel diseases is not clear. The question is "what the role of alcohol in the pathogenesis of inflammatory bowel disease is?"

METHODOLOGY

For finding this (these) answer(s), we conducted search throughout Medline, EMBASE, Current content, CINAHL, DARE, the Cochrane Central Register, the Cochrane Database of Systematic Reviews, Joanna Briggs Institute's website, the Campbell Collaboration, the Centre for Evidence-Based Medicine, the NHS Centre for Reviews and Dissemination, ISI web of knowledge, TRIP database, INTUTE and Bandolier were searched from inception to July 2009. The search terms: alcohol (use, drinking, utilize, consume, consumption, ingestion and intake), and beverages were matched against Crohn's disease, ulcerative colitis and inflammatory bowel disease for identifying all published articles. Also, the search included reviewing the published abstracts in online journals for unpublished reports. References from relevant articles were checked as well.

Our criteria for selection were: (1) the study should be of good quality: A. the hypothesis/aim/objective of the study should be clearly described; B. a case-definition and the sources for patients and controls should be clearly described and both cases and controls were representative of their entire population; C. the selected cases should fulfill Leonard-Jones criteria (the diagnosis was confirmed by at least two investigations of these three: Barium studies, colonoscopy and/or biopsy); D. the selected controls should have no family background of inflammatory bowel diseases (Crohn's disease and ulcerative colitis). This is the minimum safest way to ensure that the selected controls had not conducted inflammatory bowel disease by excluding a hereditary genetic factor; E. clear definitions of different "alcohol drinking" categories should be plainly mentioned in the article; F. the main findings of the study should be clearly described; G. the published studies in non-English language would be excluded; (2) the study should be unbiased; (3) patients and controls should be
randomly selected and were recruited from the same population and over the same period of time; (4) the studies should not be based on long term historical recalls; (5) the statistical tests used for assessing the main outcomes should be appropriate; (6) the outcome measures should be clearly described; and (7) the outcome measures should have sufficient statistical power.

**FINDINGS**

Only nine studies examining the association between alcohol intake and inflammatory bowel diseases were identified. The nine studies were published in six peer review journals\(^1\) (Gastroenterology, American Journal of Gastroenterology, American Journal of Epidemiology, Journal of Clinical Gastroenterology, Nippon Enigaku Zaishi and Gastroenterology). Three of them were excluded because they were written in non-English language (Brandes et al\(^7\), Katschinski et al\(^6\) and Higashi et al\(^9\)). Another two were excluded because of lack of controls (Jowett et al\(^8\) and Zatashi et al\(^9\)). A further study was excluded because the authors did not examine the association before the onset of the disease (Samuelsson et al\(^5\)). The study of Boyko et al\(^3\) was also excluded because of the lack of addressing the family background of the selected controls and the types of their diseases were not explained in the article. Therefore, only two of the nine articles fulfilled our inclusion criteria. The validated studies came from Asia with none from Europe and United States. An association between Crohn's disease and alcohol intake was not examined in either of the two studies (Table 1).

**Study design**

**Nakamura et al\(^4\) study:** A. It was a case-control study; B. Patients selection (inclusion criteria): patients were residents of areas covered by 93 selected public health centers. Patients who had begun to receive financial aid for treatment of ulcerative colitis during the period of the study were asked to participate in this survey. Three hundred and eighty-four out of the 490 randomly selected patients with ulcerative colitis (78.4%) agreed to participate in the study; and C. Controls were healthy fit volunteers who were pair matched by age and sex to patients. They were selected randomly among those included in the schedules of health checkup programs.

**Jiang et al\(^7\) study:** Patients selection (inclusion criteria): 177 inpatients with ulcerative colitis were recruited prospectively from 5 major hospitals in a specified city in central China. Controls were healthy volunteers who were randomly selected among those who were neighbors and colleagues to patients. Patients and controls were matched by sex and age.

**Instrument for data collection**

Two studies used questionnaires for data collection. It was a self-administered questionnaire in the study by Nakamura et al\(^4\); and the participants were interviewed to complete a detailed questionnaire in the study by Jiang et al\(^7\).

**Details of alcohol consumption**

(1) No indication of the level of alcohol consumption among participants in their samples was provided in either of the two studies; (2) In the study of Nakamura et al\(^4\), alcohol consumption was categorized by three levels of drinking frequency: daily alcohol drinkers: "who drank alcoholic beverages 5 d or more a week"; moderate alcohol drinkers: "who drank alcoholic beverages 1-4 d a week"; and non-drinkers: "who had drank alcoholic beverages less than a day per week". This classification was also used in the former drinkers; and (3) But in the study by Jiang et al\(^7\), 4 categories were determined. Frequent drinking was defined as "alcoholic drinking 3 d or more per week for continuous 6 mo before the diagnosis of ulcerative colitis"; light drinking was defined as "drinking alcoholic beverages less than 3 d a week"; non drinking was defined as "never or rarely drinking"; and former drinking was defined as "patients who had quit drinking for more than 6 mo before the diagnosis of ulcerative colitis". No information was provided about either the duration of alcohol drinking or the type of alcoholic beverage.

**Outcome measures**

**Alcohol consumption and time to onset of the disease:**

Onset of the disease was defined as "the time when the related symptoms first appeared". This timing was used to discriminate between pre- and post-illness in the two acknowledged studies. No specified period before the first appearance of symptoms was determined in either.

**Alcohol consumption and probability of ulcerative colitis:** Nakamura et al\(^4\) demonstrated that usual consumption of alcohol reduced the risk of developing the disease compared with less frequent use (odds ratio = 0.57, 95%CI: 0.37-0.86). But there was no significant association between ulcerative colitis and alcohol use was found by Jiang et al\(^7\).

**Identification and adjustment for confounding factors:**

Cigarette smoking was considered as a confounding factor by the two studies. Jiang et al\(^7\) revealed that light alcoholic drinking had protective effect against development of ulcerative colitis. But this inverse association disappeared when smoking was included.

**DISCUSSION**

Thousands of reports examining possible role of environmental factors in the development of inflammatory bowel disease were published. However, the outcome was trivial. It was just smoking was beneficial in patients with ulcerative colitis but was aggressive in subjects with Crohn's disease. But no reason was given. It is likely due to the use of the time of diagnosis for differentiating between pre- and post illness. But in the case of inflammatory bowel diseases as in other chronic-non-infectious diseases, the time interval between onset of the disease (conduction of the disease without symptomatic presentation) and time of diagnosis (symptomatic presentation) may be ten years
or more. Therefore, it is likely that the majority of these studies compared between two conditions of post-illness. Yet it is still possible by following this policy to assess the effect of different environmental factors on the progress of the disease.

As it can be seen from the above results, a correlation between the progress of ulcerative colitis and consumption of alcohol was investigated in only two studies. However, it was not possible to mix the results of the two studies up due to the existence of heterogeneity (different definitions on the consumption of alcohol). It is also noticeable that Nakamura et al[6] failed to include light (mild) drinking in their categorization. This error was avoided by Jiang et al[3]. This is likely the reason for achieving this constructive conclusion about the protective effect of light drinking in subjects with ulcerative colitis.

The reason for this beneficial effect is likely due the existence of different phenols (rich in antioxidants) in alcoholic beverages[11]. Antioxidants have inhibitory effect against the production and function of pro-inflammatory cytokines[12].

Yet, this beneficial action is contradicted by the activity of other contents in alcohol. Ethanol and its metabolite, "the acetaldehyde", both stimulate the production of reactive species[13,14]. This destructive activity is dose and strength related. This may explain the reason for discovering the useful activity in only light alcohol consumers. However, it is interesting to observe that despite of the fact that both of smoking[18] and light drinking could solely have protective effects in subjects with ulcerative colitis this advantage disappeared when both combined together. This evidently proves that the pathogenesis of inflammatory bowel disease is quite complex and the conduction of experimental studies on animal models and linking the outcome to the pathogenesis of inflammatory bowel diseases do not do any useful help but it might hurt.

Table 1  The outcome of the study

| The study       | The outcome                                                                 |
|-----------------|-----------------------------------------------------------------------------|
| Nakamura et al  | Regular consumption of alcohol reduced the risk of ulcerative colitis compared with less frequent use (odds ratio = 0.57, 95%CI: 0.37-0.86) |
| Jiang et al     | Light alcoholic drinking had protective effect against ulcerative colitis and this effect disappeared when smoking associated with the light drinking of alcohol |

OUTCOME AND IMPLICATIONS OF THE REVIEW FOR PRACTICE AND RESEARCH

People who drink regularly were at less risk for developing ulcerative colitis. Light drinking had protective effect but this effect could be abolished by smoking.

Further research studies are needed for confirming these conclusions and to assess the existence of possible correlation between different concentrations of alcohol and severity of the disease.

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