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Review

Head and neck cancer among marijuana users: A meta-analysis of matched case–control studies

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ABSTRACT

Objectives: The scientific literature presents conflicting data on a possible causal relationship between marijuana users and the development of head and neck cancer.**Design:** This study performed a systematic review with meta-analysis. Articles were selected from various electronic databases using keywords obtained from the Medical Subject Headings (MeSH). After reading by three reviewers and scoring of methodological quality, six articles (totaling nine case–control studies) were assessed with Comprehensive Meta-Analysis[®] software. The value of effect (odds ratio) was calculated, which represented the chance of developing head and neck cancer between individuals who had smoked marijuana in their lifetime in models controlled for age, gender, race, and tobacco consumption.**Results:** Approximately 12.6% of cases and 14.3% of controls were marijuana users. The meta-analysis found no association between exposure and disease (OR = 1.021; IC 95% = 0.912–1.14; $p = 0.718$).**Conclusion:** No association between lifetime marijuana use and the development of head and neck cancer was found. The different methods of collection/presentation of results in the selected articles prevented other analyzes from being conducted. Additional studies are needed to assess for long-term effects.

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1. Introduction

Marijuana (*Cannabis sativa*) is a drug of vegetable origin that contains more than 60 compounds known as cannabinoids (Berthiller et al., 2009; Liang et al., 2009; Versteeg, Slot, van der Velden, & van der Weijden, 2008). The smoke generated by combustion of these compounds is recognized as a potential carcinogen (Rosenblatt, Darling, Chen, Sherman, & Schwartz, 2004). Cannabis affects cardiovascular, respiratory and immune systems, and a chronic use can cause premalignant changes with chance of developing into head and neck cancer (HNC) (Hashibe et al., 2005; Rosenblatt et al., 2004; Versteeg et al., 2008). The scientific literature to date has presented limited and conflicting data regarding the possible causal relationship of marijuana in the development of HNC (Aldington et al., 2008). There are several differences between these studies, including the criteria used for age, affected site, stage, and etiology, thus making it challenging to compare findings (Llewellyn, Linklater, Bell, Johnson, & Warnakulasuriya, 2004a). Previous publications are contradictory: some indicate that marijuana use increases the risk of developing HNC (Aldington et al., 2008; Feng et al., 2009), while others suggest that moderate marijuana use can have a protective effect (Liang et al., 2009). These differences may be related to methodological differences, target population, choice of controls, low response rate, sample size, and inefficiency in quantifying drug use.

A consortium of research groups on the epidemiology of HNC recently published a pooled analysis of five case-control studies (Berthiller et al., 2009). The results indicated that infrequent marijuana smoking does not confer increased risk of developing HNC. This study aimed to update the subject and conduct a systematic literature review and meta-analysis among nine case-control studies to answer the following question: Does marijuana use favor the development of HNC? Given the contradictory findings to date, it is important to assess studies with strong methodological consistency in order to develop a consensus on this question.

2. Methods

2.1. Search strategy and selection criteria

The following databases were used to search for original articles: The Cochrane Library, Pubmed, Lilacs, Embase, BBO, and Bireme SciELO. Articles published in English before July 2015 were included. This study was conducted according to the criteria of the PRISMA Statement guide to systematic reviews and meta-analysis (Moher, Liberati, Tetzlaff, & Altman, 2009).

The search strategy included keywords obtained from the Medical Subject Headings (MeSH). All possible combinations of the following terms were used: hashish; marijuana; bhang; ganja;

Table 1

Description of criteria for evaluating the quality of the selected articles. Scale adapted for this study from Vilani et al. (2012), constructed based on STROBE criteria for case-control studies.

| Components | Classification | Score | Definition |
|---|----------------|-------|---|
| 1. Recruitment | Adequate | 1.0 | Describes local and relevant dates, including periods of recruitment and data collection |
| | Inadequate | 0.5 | Insufficient data |
| | Not described | 0 | Data not clearly presented in the article |
| 2. Eligible criteria for participants described | Adequate | 1.0 | Displays eligibility criteria (inclusion/exclusion) of the cases and the proportion of controls per case |
| | Inadequate | 0 | No description of criteria for selection |
| 3. Presence of a control group | Yes | 1.0 | Presence of a control group |
| | No | 0 | Absence of a control group |
| 4. Variables | Adequate | 1.0 | Clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers (tobacco, alcohol) |
| | Inadequate | 0.5 | Insufficient data |
| | Not described | 0 | No description |
| 5. Data collection | Adequate | 1.0 | Specifies the form of research (questionnaire / interview) and presents key questions |
| | Inadequate | 0 | Not described |
| 6. Study size | Adequate | 1.0 | Explains how we arrived to the sample size |
| | Inadequate | 0 | Does not describe/present/communicate conducting sample calculation |
| 7. Statistical analysis | Adequate | 1.0 | Statistical treatment fully described and adequate |
| | Inadequate | 0.5 | Statistical treatment not fully described |
| | None | 0 | No statistical treatment applied |
| 8. Reported dropouts | Explained | 1.0 | Dropouts reported with explanation |
| | Not explained | 0.5 | Dropouts reported with no explanation or description of complete or incomplete data retrieved |
| | None | 0 | No description of dropouts or data retrieved |
| 9. Potential bias and trial limitations addressed | Fully | 1.0 | Description of potential bias and trial limitations acknowledging them |
| | Partially | 0.5 | Description of potential bias and trial limitations without acknowledging them |
| | None | 0 | No description of potential bias or trial limitations |

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