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Association of Marijuana Use With Psychosocial and Quality of Life Outcomes Among Patients With Head and Neck Cancer

Han Zhang, MD, FRCSC,[1] Michael Xie, BSc,[2] Stuart D. Archibald, MD, FRCSC,[2] B. Stanley Jackson, MD, FRCSC,[1] and Michael K. Gupta, MD, MSc, FRCSC[1]

[1]Division of Otolaryngology–Head and Neck Surgery, McMaster University, Hamilton, Ontario, Canada
[2]Michael DeGroote Faculty of Medicine, McMaster University, Hamilton, Ontario, Canada
Corresponding author.

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Corresponding Author: Michael K. Gupta, MD, MSc, FRCSC, St Joseph's Healthcare Hamilton, G836, 50 Charlton Ave E, Hamilton, ON L8N4A6, Canada (michaelkgupta@hotmail.com).

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Study concept and design: Zhang, Archibald, Gupta.

Acquisition, analysis, or interpretation of data: Zhang, Xie, Jackson, Gupta.

Drafting of the manuscript: Zhang, Xie, Gupta.

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Key Points

Question

Is there a difference in quality of life and psychosocial outcomes between marijuana users and nonusers who have newly diagnosed head and neck cancer?

Findings

In this case-matched cohort study, 74 patients with newly diagnosed head and neck cancer who were marijuana users appeared to have quality of life differences compared with 74 who did not use marijuana, including decreased anxiety, pain, and depression and increased appetite and generalized feelings of well-being on the Edmonton Symptom Assessment System and the EuroQol-5D questionnaires.

Meaning

Recreational marijuana use potentially improves quality of life and psychosocial symptoms among patients with newly diagnosed head and neck cancer.

Abstract

Importance

Cannabis sativa, the most widely used illicit substance in Canada, has a unique ability to facilitate relaxation and relieve anxiety while reducing pain. However, no study to date has examined quality of life (QOL) and psychosocial issues in relation to the use of this drug among patients with newly diagnosed head and neck cancer (HNC).

Objective

To examine the differences in QOL and psychosocial outcomes between marijuana users and nonusers with newly diagnosed HNC.

Design, Setting, and Participants

This prospective cohort study was conducted at a tertiary care cancer center. Patients were enrolled consecutively and prospectively at the time of HNC diagnosis from January 1, 2011, to January 1, 2015. Seventy-four patients who were current marijuana users were case matched to 74 nonusers in a 1:1 scheme based on age, sex, and tumor subsite. All patient demographic and QOL data were collected prospectively, and data analysis was conducted from November 1 to December 1, 2017.

Main Outcomes and Measure

The QOL outcome was assessed using the EuroQol-5D (EQ5D) and the Edmonton Symptom Assessment System (ESAS) questionnaires.

Results

A total of 148 patients were included in this study: 74 in the marijuana user group (mean [SD] age, 62.3 [10.3] years; male sex, 61 patients [82%]) and 74 in the marijuana nonuser group (mean age, 62.2 years; male sex, 63 patients [85%]). There was no statistically significant difference in age, sex, tumor subsite, clinical TNM staging, treatment modality, or mean Karnofsky score between the 2 groups. On univariate analysis, there was no statistically significant difference in the mobility, self-care, and usual activities domains of the EQ5D. Marijuana users had significantly lower scores in the anxiety/depression (difference, 0.74; 95% CI, 0.557-0.930) and pain/discomfort (difference, 0.29; 95% CI, 0.037-1.541) domains. Wilcoxon rank sum test confirmed the results of the EQ5D with improvements in the pain/discomfort (*z* score, −2.60) and anxiety/depression (*z* score, −6.71) domains. Marijuana users had less pain, were less tired, were less depressed, were less anxious, had more appetite, were less drowsy, and had better general well-being according to the ESAS. A Wilcoxon rank sum test confirmed a statistically significant improvement in ESAS scores within the domains of anxiety (*z* score, −10.04), pain (*z* score, −2.36), tiredness (*z* score, −5.02), depression (*z* score, −5.96), drowsiness (*z* score, −5.51), appetite (*z* score, −4.17), and general well-being (*z* score, −4.43).

Conclusions and Relevance

This prospective case-matched study suggests that there may be significant QOL benefits, including decreased anxiety, pain, and depression and increased appetite and generalized feelings of well-being, associated with marijuana use among patients with newly diagnosed HNC.

This case-matched cohort study investigates differences in psychosocial and quality of life outcomes between marijuana users and nonusers among patients with newly diagnosed head and neck cancer.

Introduction

Receipt of a cancer diagnosis is a life-changing event. Studies have shown a high prevalence of stress and anxiety from the diagnosis as well as through the course of the illness. The enormous psychological impact of the diagnosis cannot be overstated, with 33% to 60% prevalence of distress among patients with cancer at different sites, including among patients with head and neck mucosal cancer (HNC).[1,2,3] Because of the critical role of the head and neck in function, body image, and socialization, patients who receive a diagnosis of this disease can have a high amount of associated psychosocial stress. As the treatment of HNC has evolved, the field has progressed toward patient-centered care and the increasing recognition of psychosocial factors and quality of life (QOL) factors as inherently important aspects of patient health.[4] To address increasing issues with psychosocial distress, routine screening and appropriate referral of all patients with cancer for psychiatric assessment is now considered to be the standard of care by the American College of Surgeons and the National Comprehensive Cancer Network.[5,6] Although the psychosocial effects of receiving a cancer diagnosis are now well recognized, treating HNC-related stress and anxiety remains challenging.

Cannabis sativa, also known as marijuana, is one of the most commonly used illicit substances in Canada, with 12.2% of Canadians 15 years or older having reported marijuana use within the past year and the lifetime prevalence of use reported to be as high as 42.5%.[7] Canada's imminent trend toward legalization of the recreational use of marijuana may well increase this already sizeable number. The unique ability of marijuana to facilitate relaxation, relieve anxiety, and decrease pain is well known and is the rationale behind its medicinal use in oncology, psychiatry, and the treatment of chronic pain.[8,9,10,11]

Patients with HNC therefore may be ideal candidates for treatment with marijuana. However, data are lacking both on the effects of recreational marijuana use among patients with HNC and on the use of marijuana to treat anxiety and stress among patients with HNC. Therefore, it was our objective to explore the effects of marijuana on psychosocial and QOL outcomes among patients with newly diagnosed HNC.

Methods

Patients and Data Collection

Patients were enrolled consecutively and prospectively at the time of their HNC diagnosis into a database. All patients were treated at a single tertiary care cancer center and were enrolled from January 1, 2011, to January 1, 2015. Patient demographic characteristics, tumor characteristics, treatment regimens, socioeconomic data, and QOL measurements were collected prospectively as part of the database. Karnofsky scores were also collected prospectively to assess for overall patient functional level.[12] Income quintiles were created from the Canadian Census of Population data for 2011,[13] which was linked to patient postal codes. The study was approved by the Hamilton Integrated Research Ethics Board. Patient consent was obtained for all patients included in the study.

Patients who were current marijuana users were self-identified from the database and were confirmed to be at least 17 years of age, to have head and neck squamous cell carcinoma diagnosed by means of pathologic testing, and to be undergoing treatment with curative intent. These patients were then case-matched with patients who were nonusers of marijuana from the database in a 1:1 scheme based on age, sex, and tumor subsite. All patients who were included within the marijuana nonuser group met the same inclusion criteria as those within the marijuana user group. Marijuana use was defined as current use of loose-leaf marijuana at least weekly. All patients within the marijuana user group were using marijuana at the time of the data collection.

QOL Measures

Two instruments were used as QOL measures: the Edmonton Symptom Assessment System (ESAS) and the EuroQOL-5D (EQ5D).[14,15] The ESAS is a 9-item validated questionnaire used commonly for cancer QOL measurement. It assesses domains of pain, tiredness, drowsiness, nausea, appetite, shortness of breath, depression, anxiety, and general well-being on a 10-point scale, where 0 represents absence of the symptom and 10 represents the worst possible severity. The EQ5D is a 5-item health utility instrument measuring 5 dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Scores of 1, 2, and 3 indicate no problems, some problems, and extreme problems, respectively. A unique health state is defined by combining 1 level from each of the 5 dimensions and converting to a single overall health index score. All patients were administered the QOL measures by a trained HNC research assistant at a clinical visit before the initiation of treatment.

Statistical Analysis

The data analysis was conducted from November 1 to December 1, 2017. Baseline characteristics were compared using standard modes of comparison between multiple groups. Continuous data were analyzed using a 2-sample independent test. Categorical data were compared using the χ^2 test. The Wilcoxon rank sum test was used as the test for nonparametric data to compare the QOL metrics. The effect size for the difference in various domains of the 2 QOL measures between subjects in the 2 groups was measured as the absolute difference, and the precision of the effect size was measured with the 95% CI. Analyses were performed with SPSS, version 19.0 (IBM).

Results

Patient Characteristics

Patient and tumor characteristics are shown in Table 1. All 74 patients who were identified as marijuana users met inclusion criteria. These patients were then case-matched to 74 nonusers of marijuana in a 1:1 fashion. Both groups had a QOL instrument completion rate of 100%.

The mean (SD) age for the marijuana user group was 62.3 (10.3) years, and most patients in this group were male (61 of 74 patients [82%]). The mean (SD) age for the marijuana nonuser group was 62.2 (10.4) years, and 63 of 74 patients (85%) were male. In the marijuana user group, the

oropharynx was the most common cancer subsite (47 of 74 patients [64%]), and the majority of these patients had p16-positive disease (45 of 47 [96%]). Most patients presented with T3 or T4 disease (24 of 74 patients [32%] and 28 of 74 patients [38%], respectively) and with N1 or N2a nodal burden (33 of 74 [45%] and 20 of 74 [27%], respectively). There were no statistically significant differences in age, sex, tumor site, p16-positive oropharyngeal disease, T and N stage, or treatment modality between the 2 groups.

The mean (SD) Karnofsky score was found to be 92.4 (11.4) for the marijuana user group and 90.8 (13.9) for the marijuana nonuser group. Income quintiles were evenly distributed among the 5 levels for the 2 groups. The majority of patients were fully employed or retired, and there was no statistically significant difference between the 2 groups in employment status.

QOL Metrics

As shown in Table 2, there was no statistically significant difference in the mobility (1.22 vs 1.26; difference, 0.04; 95% CI, −0.10 to 0.19), self-care (1.11 vs 1.12; difference, 0.01; 95% CI, −0.20 to 0.19), and usual activities (1.31 vs 1.36; difference, 0.05; 95% CI, −0.03 to 0.32) domains of the EQ5D between the 2 groups. There was, however, a significantly lower mean (SD) score in the anxiety/depression (1.34 [0.53] vs 2.08 [0.61]; difference, 0.74; 95% CI, 0.56-0.93) and the pain/discomfort (1.53 [0.58] vs 1.82 [0.66]; difference, 0.29; 95% CI, 0.04-1.54) domains of the EQ5D within the marijuana user group. These results were confirmed with the Wilcoxon rank sum test for the pain/discomfort (*z* score, −2.60) and anxiety/depression (*z* score, −6.71) domains (Table 3).

All domains of the ESAS showed improved QOL for the marijuana user group, including statistically lower scores for pain (mean [SD], 1.85 [2.49] vs 2.72 [2.59]; difference, 0.87; 95% CI, 0.04-1.69), anxiety (0.77 [1.31] vs 5.30 [2.06]; difference, 4.53; 95% CI, 3.97-5.09), and depression (0.72 [1.68] vs 3.19 [3.05]; difference, 2.47; 95% CI, 1.67-3.27) and a statistically higher score for general well-being (4.05 [2.29] vs 2.12 [2.65]; difference, 1.93; 95% CI, 1.13-2.74). The Wilcoxon rank sum test confirmed these results for all domains, including pain (*z* score, −2.36), depression (*z* score, −5.96), anxiety (*z* score, −10.04), and general well-being (*z* score, −4.43).

Discussion

The use of cannabis as a medicinal therapy has been proposed for its analgesic and antiemetic effects among patients with cancer, its antianxiety and antidepression effects among patients with posttraumatic stress disorder (PTSD), and as an adjunct for neuropathic pain in patients with chronic pain syndromes.[8,10,16,17,18,19,20,21] Access to and acceptance of medical marijuana has been increasing in the past decade, with more than 76% of physicians approving of its use for medical purposes within the United States according to a recent survey.[22] The use of cannabis is likely to increase during the next decade with the impending legalization of this illicit drug in several states within the United States and Canada. However, little is known of the effects of marijuana as a QOL adjunct among oncology patients, particularly among those with HNC, for whom the psychosocial distress associated with receiving a diagnosis and undergoing treatment can be a major burden.[2,3,4]

The 2 major neuroactive phytocannabinoids within marijuana are tetrahydrocannabinol (THC) and cannabidiol (CBD). Both THC and CBD have very distinctive pharmacological and behavioral effects. A central role is played by THC in the regulation of fear-related and anxiety-related behavior, whereas CBD activates receptors that constrain fear-related and psychological stress responses.[23] Although available data on treatment outcome with respect to the psychosocial effects of marijuana use are not robust, there are small uncontrolled studies that have examined the effect of marijuana use among patients with PTSD. A study by Greer et al[8] reported a 75% reduction in PTSD symptoms, including anxiety and psychological stress, in its outcome measures. Passie et al[24] mimicked the results from Greer et al[8] in a case report that documented decreased anxiety in a patient with sexual abuse–related PTSD. These results show a similar trend compared with our data set, in which a statistically significant decrease was found in the EQ5D anxiety/depression score and in the ESAS anxiety and depression domains. Longitudinal data examining the association of marijuana use with psychosocial effects have also been reported within the literature. Johnson et al[9] showed that, among a sample of 700 patients, those who used marijuana reported fewer PTSD symptoms, including decreased anxiety and decreased depression. Elliot et al[18] showed that, among a cohort of 15 patients who received radiotherapy or chemoradiotherapy for HNC, the use of marijuana was associated with a 67% reduction in depression and a 33% reduction in anxiety using a medical marijuana QOL questionnaire. This is similar to findings within our cohort of patients, in which patients who used marijuana reported less anxiety/depression on the EQ5D and less depression and anxiety on the ESAS. Our cohort of oncology patients used marijuana only recreationally; this may mean that our patients experienced a different psychosocial challenge compared with patients with PTSD. However, the similarities between the 2 cohorts within the specific domains of anxiety and depression are striking. Certainly, additional studies to examine the effects of marijuana use on the long-term psychosocial aspects of oncology patients from diagnosis to cure would be interesting.

In addition to being known for its effect on anxiety, cannabis is also known for its antiemetic and analgesic properties. The use of THC has been proposed to treat nausea via emetic reflex pathways by acting at receptors located in the nucleus tractus solitarii as well as by reversing the effects of serotonin type 3 receptor agonists.[25] Tramèr et al[26] completed a systematic review of 30 randomized comparisons of cannabinoids with placebo or other antiemetics among patients with cancer diagnoses. When all trials (a total of 1366 patients) were compared, cannabinoids were found to be significantly more effective than placebo or other antiemetics in decreasing nausea and vomiting. This finding is similar to the results found within our patient population, in which there was a decrease in nausea and drowsiness reported on the ESAS. Cannabinoids have also been studied for their neuropathic pain relief potential. Cannabinoid receptors within the central nervous system are found in high concentrations in areas of the brain that modulate nociceptive processing, with strikingly similar distribution to opioid receptors.[27] As a result, several clinical trials confirming the use of cannabinoid receptor agonists to relieve chronic pain associated with cancer have been published. Noyes et al[28] examined 10 patients with various cancer diagnoses in a double-blind placebo-controlled trial and found that the analgesic effect of THC was significantly superior to that of placebo. In a similar manner, Johnson et al[29] examined the effects of cannabis extract preparations containing THC and CBD among 177 patients with advanced cancer and uncontrolled pain associated with cancer despite long-term opioid use. The study showed a 30% re-

duction in pain among the THC/CBD group when compared with the placebo group. Our cohort of patients exhibited similar results, with decreased pain/discomfort reported on the EQ5D as well as decreased pain with an increased feeling of general well-being reported on the ESAS.

Limitations

Although the reduction in psychosocial distress and pain within our cohort of patients who use marijuana is encouraging, the limitations of the study cannot be discounted. This study was designed as a case-matched cohort study among a group of patients with HNC with prospectively collected QOL data at the time of their cancer diagnosis. As a result, several limitations exist within our patient population. Because all of our patients in the marijuana user group were recreational marijuana users, they may not be comparable to users of medicinal marijuana or patients who are participating in clinical trials in which the dosage of cannabis can be controlled. In addition, psychosocial and QOL data within our patient population, which were collected at the time of cancer diagnosis, do not provide insight into the effects of marijuana use while receiving treatment and after treatment for HNC. Additional investigations involving long-term follow-up of this cohort of patients are planned, which will no doubt provide thought-provoking insights into the effects of marijuana on the QOL challenges among patients who undergo treatment and among long-term survivors. However, because of the paucity of information on QOL and the lack of psychosocial data within the literature on the population of patients with HNC, the results of this study not only provide valuable insight but also create an impetus for additional research on the association of marijuana use with QOL in patients with HNC.

As the field of HNC treatment moves toward a holistic medical model, an increasing focus on the importance of patient psychosocial well-being and QOL rather than just survival is becoming more prevalent. Data on the association of cannabis use with psychological outcomes among patients with HNC is lacking. Although more multi-institutional prospective outcome studies with long-term follow-up would no doubt provide more evidence on the true results of marijuana use for patients with HNC, this study provides compelling insight into the potential role that cannabis plays in psychological and QOL factors among these patients.

Conclusions

Recreational use of *C sativa* potentially alleviates anxiety, depression, pain, and nausea and improves general well-being in patients with newly diagnosed HNC. Additional study of whether these effects are maintained throughout treatment and among long-term survivors is warranted and could provide interesting insight.

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Figures and Tables

Table 1.

Patient and Tumor Characteristics

Variable	Marijuana User Group (n = 74)	Marijuana Nonuser Group (n = 74)
Age, mean (SD) y	62.3 (10.3)	62.2 (10.4)
Sex, No. (%)		
Male	61 (82)	63 (85)
Female	13 (18)	11 (15)
Tumor site, No. (%)		
Oropharynx	47 (64)	47 (64)
Oral cavity	14 (19)	14 (19)
Hypopharynx	1 (1)	1 (1)
Larynx	12 (16)	12 (16)
Oropharynx p16 status, No. (%)		
p16 positive	45 (96)	46 (98)
p16 negative	2 (4)	1 (2)
T stage, No. (%)		
In situ	3 (4)	4 (5)
1	12 (16)	11 (15)
2	24 (32)	24 (32)
3	28 (38)	27 (37)
4	7 (10)	8 (11)
N stage, No. (%)		
0	6 (8)	7 (10)
1	33 (45)	32 (43)
2a	20 (27)	19 (26)
2b	6 (8)	7 (10)
2c	3 (4)	4 (5)
3	4 (5)	3 (4)
Treatment modality, No. (%)		
RT	18 (24)	17 (23)
CRT	29 (39)	30 (41)
S	8 (11)	7 (10)

Abbreviations: CRT, chemoradiotherapy; RT, radiotherapy; S, surgery.

[a]Karnofsky scores range from 1 (dead) to 100 (no evidence of disease).[12]

[b]Income quintiles were created from the Canadian Census of Population data for 2011,[13] which was linked to patient postal codes.

Table 2.

Quality of Life Metrics

Variable[a]	Marijuana User Group	Marijuana Nonuser Group	Difference in Scores (95% CI)
EQ5D score, mean (SD)			
Mobility	1.22 (0.41)	1.26 (0.47)	0.04 (−0.10 to 0.19)
Self-care	1.11 (0.16)	1.12 (0.37)	0.01 (−0.20 to 0.19)
Usual activities	1.31 (0.48)	1.36 (0.59)	0.05 (−0.03 to 0.32)
Anxiety/depression	1.34 (0.53)	2.08 (0.61)	0.74 (0.56 to 0.93)
Pain/discomfort	1.53 (0.58)	1.82 (0.66)	0.29 (0.04 to 1.54)
ESAS score, mean (SD)			
Pain	1.85 (2.49)	2.72 (2.59)	0.87 (0.04 to 1.69)
Nausea	0.22 (2.13)	0.71 (2.86)	0.49 (0.11 to 0.88)
Tiredness	1.66 (0.65)	3.88 (1.54)	2.22 (1.39 to 3.04)
Depression	0.72 (1.68)	3.19 (3.05)	2.47 (1.67 to 3.27)
Anxiety	0.77 (1.31)	5.30 (2.06)	4.53 (3.97 to 5.09)
Appetite	1.70 (1.39)	3.57 (2.90)	1.87 (1.00 to 2.73)
Drowsiness	0.56 (2.43)	2.68 (2.88)	2.12 (1.38 to 2.87)
General well-being	4.05 (2.29)	2.12 (2.65)	1.93 (1.13 to 2.74)

Abbreviations: EQ5D, EuroQOL-5D; ESAS, Edmonton Symptom Assessment System.

[a]The EQ5D and ESAS instruments and scoring are explained in the QOL Measures subsection of the Methods section.

Table 3.

Quality of Life Wilcoxon Rank Sum Nonparametric Analysis

Variable[a]	*z* Score
EQ5D	
Pain/discomfort	−2.60
Anxiety/depression	−6.71
ESAS	
Pain	−2.36
Nausea	−2.48
Tiredness	−5.02
Depression	−5.96
Anxiety	−10.04
Appetite	−4.17
Drowsiness	−5.51
General well-being	−4.43

Abbreviations: EQ5D, EuroQOL-5D; ESAS, Edmonton Symptom Assessment System.

[a]The EQ5D and ESAS instruments are explained in the QOL Measures subsection of the Methods section.