Letters

Medical Oncologists' Views on the Utility of Medical Marijuana Across the Cancer Trajectory

To the Editor:

Medical marijuana (MM) is nonpharmaceutical, herbal (typically unrefined) cannabis that health care providers recommend therapeutically in line with state law. Federally illegal, it is legal on a state level in 33 states.[1] Unlike most illnesses, cancer is a qualifying condition for MM in almost every state law.[1] Although cancer patients frequently use cannabis to treat symptoms—or even cancer itself—few empiric studies have examined the efficacy of MM in oncology.[2] In 1979, Chang et al. randomized 15 patients to receive unrefined cannabis versus placebo to treat chemotherapy-induced nausea and vomiting.[3] A few state-run trials tested MM for this indication as well and published results in governmental reports without undergoing formal peer review.[4] To our knowledge, clinical trials have not tested whether MM improves other cancer-related symptoms (i.e., pain, cachexia, poor sleep) or oncologic disease status.

Moreover, little is known about medical oncologists' views on MM.[2,5] To address this lack of data, we examined oncologists' beliefs about the utility of MM for treating symptoms along the cancer continuum. We hypothesized that oncologists would favor MM as a strategy for palliative symptom management because, at the end of life, the importance of effective symptom management would outweigh the potential risks of MM use (i.e., addiction).

Methods

We surveyed by mail a nationally representative sample of 400 medical oncologists drawn from SK&A Healthcare Databases. We queried their MM knowledge, attitudes, and practices, including beliefs about cannabis' utility at various points along the cancer continuum.[5] Methodological details are presented elsewhere.[5] The present analysis focused on oncologists' perceptions of MM's utility in early-stage cancer, during survivorship, and at the end of life; MM's effectiveness compared with standard treatments for common symptoms (e.g., nausea, pain, cachexia); its risks compared with opioids; and its potential antineoplastic effects.

Outcome Variables

Utility of Medical Marijuana Across the Cancer Continuum

To assess when oncologists perceived MM use might be beneficial, we asked: "In your opinion, how often is MM beneficial for 1) those near the end of life, 2) those with early-stage cancer, 3) cancer survivors?" Response options included "never beneficial," "rarely beneficial," "sometimes beneficial," "usually beneficial," "always beneficial," and "I don't know." Responses were categorized as at least some benefit ("sometimes," "usually," "always") versus no benefit/don't know ("never," "rarely," "don't know").

Comparative Effectiveness

To assess MM's comparative effectiveness, we asked oncologists who reported MM had at least some benefit: "Compared to treatments you typically use, how would you rate the effectiveness of MM for the following cancer-related conditions?" Conditions included pain, poor appetite/cachexia, nausea/vomiting, depression, anxiety, poor sleep, and general coping. Responses included "much more effective," "somewhat more effective," "equally effective," "somewhat less effective," "much less effective," and "I don't know." Responses were categorized into at least as effective as standard treatments ("much more," "somewhat more," "equally"), less effective than standard treatments ("somewhat less," "much less"), and don't know.

Perceived Risks of MM Compared With Opioids

We examined oncologists' beliefs about the risks of MM relative to prescription opioids with: "In your opinion, how do the risks of MM compare to the risk of prescription opioids?" Risks listed included paranoia/psychosis, anxiety, depression, confusion/impaired mentation, falls, addiction, and overdose

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death. Response categories included "much higher than opioids," "somewhat higher than opioids," "comparable to opioids," "somewhat lower than opioids," "much lower than opioids," and "I don't know." Responses were categorized as comparable to or worse than opioids ("much higher," "somewhat higher," "comparable"), lower than opioids ("somewhat lower," "much lower"), and don't know.

Perceived Antineoplastic Activity

As some preclinical studies have suggested that cannabis/cannabinoids slow tumor growth, we asked: "To what extent do you think MM has antineoplastic effects?[6] Response categories included "to a great extent," "to some extent," "to a very little extent," "none at all," and "I don't know."

Predictors

Prespecified variables included personal characteristics such as age, years since medical school graduation (based on a question, "When did you graduate from medical school?"), and gender; and medical practice characteristics such as whether the oncologist treated adults, children, or both; and whether their area of focus included "solid" tumors, "liquid" tumors, or both. The latter variable was based on responses to the question: "Which of the following cancers do you treat?" Options included breast, gastrointestinal, genitourinary, gynecologic, head and neck, hematologic, neurological, sarcoma, melanoma or cutaneous, thoracic or other. Responses were categorized as solid (breast, gastrointestinal, genitourinary, gynecologic, head and neck, neurological, sarcoma, melanoma or cutaneous, thoracic or other), liquid (hematologic), or both.

Analysis

Using Fisher's exact and Wilcoxon rank-sum tests, respectively, categorical and continuous sociodemographic and professional variables were compared between groups. *P*-values were two sided and significant at <0.05 level. R version 3.4.4 was used for all statistical analyses.[7]

Results

Among the 237 survey respondents, 232 (98%) completed the question assessing perceived benefit of MM along the cancer continuum. Among responding oncologists, 192 (82.8%, 95% CI 77.3%−87.4%) reported MM to have at least some end-of-life benefit, whereas 11 (4.7%) indicated it was rarely or never beneficial at the end of life, and 29 (12.5%) reported not knowing. By contrast, only 77 oncologists (33.2%; 95% CI 27.2%−39.6%) reported MM to have at least some benefit, 113 (48.7%) reported that it was rarely/never beneficial, and 42 (18.1%) reported not knowing the benefit for MM in patients with early-stage cancers. Similarly, only 60 oncologists (25.9%; 95% CI 20.3%−32.0%) reported some benefit, 124 (53.4) reported that it was rarely/never beneficial, and 48 (20.7%) reported not knowing its benefit for cancer survivors. There were no significant associations between oncologists' beliefs about the utility of MM use at end of life and sociodemographic and professional variables including clinician age, years since graduation from medical school, gender, type of patients treated (adults only, children only, both), and type of tumors treated (liquid tumor, solid tumor, both).

Most oncologists who felt MM to be beneficial at the end of life believed that the agent was at least as effective as standard treatments for common symptoms including poor appetite/cachexia ($n = 140$; 74.5%), nausea/vomiting (105; 55.8%), and anxiety (99; 53.2%; Fig. 1a). The majority also reported that MM had lower risk for addiction (104; 55.0%) and overdose (151; 79.5%), compared with prescription opioids. Most reported that risks of MM were comparable to prescription opioids for paranoia (106; 55.8%), confusion (103; 53.9%), and driving difficulties (120; 63.5%; Fig. 1b). Of oncologists indicating at least some benefit for MM at the end of life, 136 (70.8%) denied MM possessed antineoplastic effects, 44 (22.9%) did not know whether MM possessed antineoplastic effects, 9 (4.7%) believe MM to have antineoplastic effects to some extent, and three (1.6%) declined to answer.

Comment

In this nationally representative sample of oncologists, 83% reported MM to be potentially beneficial near the end of life. By contrast, only a minority reported MM to be beneficial during early-stage cancer (33%) or cancer survivorship (26%). These findings are noteworthy because oncologists who reported MM to be potentially beneficial at the end of life also reported MM to be as effective as standard treatments for symptoms frequently experienced by patients throughout the cancer continuum (e.g., poor appetite/cachexia, nausea/vomiting, and anxiety). Although the survey was not designed to answer why this might be the case, the findings may reflect oncologists' beliefs that, at the end of life, the potential benefits of cannabis outweigh perceived risks (identified in this study as driving liabilities, paranoia, and confusion comparable or worse than those with opioids) and that, by contrast, the risk/benefit ratio is reversed in early-stage disease and survivorship. Alternately, oncologists may simply be more attuned to symptom

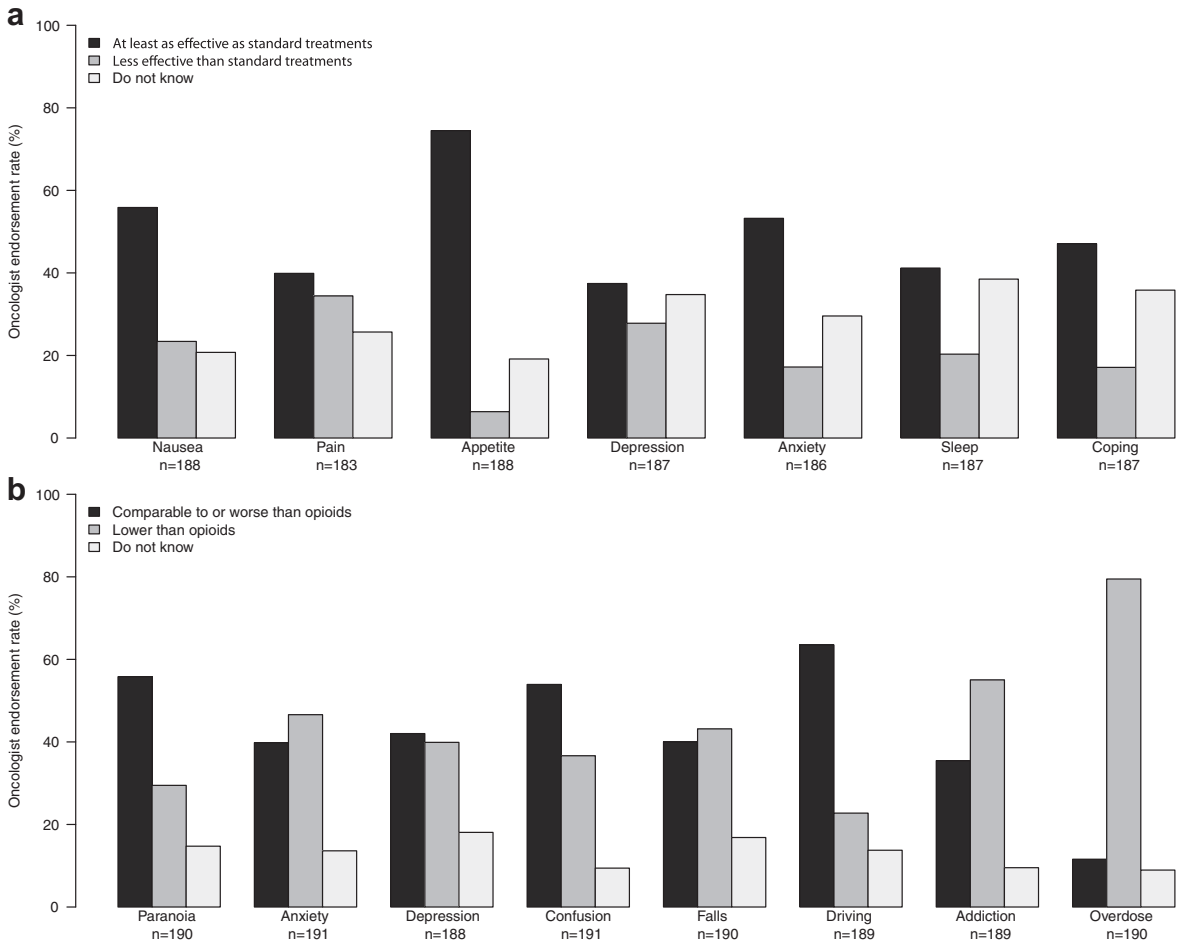

Fig. 1. a) Perceived effectiveness of medical marijuana as compared to standard treatment and b) perceived risks of medical marijuana as compared to prescription opioids among participants indicating at least some benefit to medical marijuana use near the end of life.

management at the end of life than at other stages of disease. Future studies should test these hypotheses. Of note, oncologists favoring cannabis at the end of life did not view the agent as a powerful antineoplastic. This finding renders it less likely that these oncologists considered cannabis a "last ditch" antineoplastic option.

Although, to our knowledge, this study is the only nationally representative survey of oncologists' attitudes and beliefs about MM since the advent of such laws, it has limitations. For instance, the 63% response rate, while impressive for survey research of practicing physicians, somewhat limited our ability to look at subgroup analyses. In addition, it focused only on the views of oncology providers, and future studies are needed to better understand the views of oncology patients and their families.

We believe our finding that a nationally representative sample of oncologists regarded MM as a potential strategy for palliative symptom management is clinically meaningful and hope that it will encourage oncologic clinical trials with cannabis at the end of life, particularly for symptoms including poor appetite/cachexia, nausea/vomiting, anxiety. Our findings may also encourage hospice and palliative care professional organizations, many of which do not have MM position statements or clinical guidance statements, to increase their attention to MM as an area for education and further study.

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Predatory Publishing in Palliative Care

We read with interest the letter *Predatory Open-Access Publishing in Palliative and Supportive Care*.[1] The authors report that, to the best of their knowledge, this is the first attempt to analyze predatory publishing in palliative and supportive care. They did not find our paper *Open Access Journals and Predatory Publishing in Palliative Care*,[2] published in the journal *Medicina Paliativa*. It was accepted for publication in March 2017, was available online in January 2018, and was finally printed in July 2018. We addressed predatory publishing in palliative care from a different perspective to distinguish between legitimate open-access journals and predatory publishing in palliative care. We analyzed 32 palliative care journals with full or partial open access. Nine of these 32 journals came from publishers, such as *BMJ Journals*, *LWW*, *Liebert*, *Elsevier*, *Taylor & Francis and Cambridge Core*, that allow the possibility of publication with open access; five of the nine had recognized Impact Factors in Journal Citation Reports. Seven of the 32 journals had the profile of open-access scholarly journals, that is, journals that only accept open-access publications and are usually indexed in recognized directories such as the Directory of Open Access Journals (DOAJ) or the directory of the Open Access Scholarly Publishers Association (OASPA) and do not share other relevant characteristics of predatory publishing.

In total, 16 of the 32 palliative care journals could be designated as "suspected" predatory journals. This designation is appropriate because there are no strict criteria to define a journal as predatory.[2,3] Although the Beall list is sometimes used as a reference, it has been criticized[4] for its potential to stigmatize publications. All 16 journals designated as "suspected" in our publication were included in the December 2016 version of the Beall list, and none appeared in the DOAJ or directory of OASPA. There were many concerns noted in this group of 16 journals, including a lack of indexing in PubMed, the use of e-mails asking for new papers, request for papers when the journal is not yet active, the offering of membership (payment not for every paper but for the option of publishing during a period), and the possibility of becoming a member of the Editorial Board or a reviewer.

At the last meeting of the Spanish Society of Palliative Care,[5] there were abstracts about the easy access to the Editorial Board of suspected predatory journals and the proportion of predatory journals that stop publishing after a few years There also was discussion about the presence in palliative care of predatory conferences[6]—meetings that follow the model of predatory publishing, appearing as legitimate scientific