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Patterns of Kratom use and health impact in the US—Results from an online survey

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ABSTRACT

Background: Kratom preparations have raised concerns of public health and safety in the US. Investigation into the demographics, perceived beneficial and detrimental effects of Kratom as well as common doses and purposes of its use are important to properly evaluate its potential health impact.

Methods: An anonymous cross-sectional online survey was conducted in October 2016 of 10,000 current Kratom users through available social media and online resources from the American Kratom Association. A total of 8049 respondents completed the survey.

Results: Kratom is primarily used by a middle-aged (31–50 years), middle-income ($35,000 and above) population for purposes of self-treating pain (68%) and emotional or mental conditions (66%). Kratom preparations present with a dose-dependent effect with negative effects, which were primarily gastrointestinal related including nausea and constipation, mainly presenting at high (5 g or more/dose) and more frequent (22 or more doses/week) dosing.

Conclusions: Kratom shows a dose-dependent opioid-like effect providing self-reported perceived beneficial effects in alleviating pain and relieving mood disorders. Kratom was primarily used for self-treatment of pain, mood disorders, and withdrawal symptoms associated with prescription opioid use.

1. Introduction

Kratom preparations are extracts of the leaves of a tree (*Mitragyna speciosa* Korth., Rubiaceae) native to Southeast Asia (Shellard, 1989; Tanguay, 2011). The leaves are traditionally chewed in fresh or dried form to alleviate pain, decrease fatigue, and elevate mood (Warner et al., 2016). It has also been used to alleviate opioid withdrawal symptoms in opioid misuse or abuse such as heroin or morphine (Boyer et al., 2008; Hassan et al., 2013). Kratom extracts available in the US are primarily powders that can be dissolved in fluid or consumed with food. Most commercially available powdered Kratom products in the US are recommended in doses of 2–6 g depending on the Mitragyna strain used and the intended use. In most cases, users will titrate themselves starting with lower doses until they reach the desired effect.

Although Kratom has been available in the US for at least the past ten years as a dietary supplement, public attention has recently increased with a report by the Centers for Disease Control and Prevention (CDC) stating a significant increase in Kratom-related calls to poison control centers between 2011 and 2015 (Anwar et al., 2016). Among the 660 reported calls, 49 (7.4%) were classified as major, life-threatening with some residual disability.

Based on the CDC report, the Drug Enforcement Administration (DEA) issued the intent to place Kratom and its opioid-like active constituents mitragynine and 7-hydroxymitragynine in schedule I of the controlled substances act (DEA, 2016). This intent has since been withdrawn awaiting a final decision after a public commenting period that expired on December 1st 2016. An eight-factor analysis of Kratom as mandated by the FDA has been made available by Drs. Henningfield and Fant leading up to the deadline (Henningfield and Fant, 2016). Indeed, the alkaloids mitragynine and 7-hydroxymitragynine have been identified to interact with the opioid receptors although the interaction is not entirely elucidated with some researchers indicating a full agonist activity with lower potency than morphine and others suggesting a partial agonist activity with higher potency than morphine (Kruegel et al., 2016; Prozialeck et al., 2012). Receptor-binding studies identified both mitragynine and 7-hydroxymitragnine as partial agonists at the human μ-opioid receptor and a partial antagonist at human κ-opioid receptors with several other alkaloids present in Kratom only acting on μ-opioid receptors with lower potency (Kruegel et al., 2016). The oxidized alkaloid 7-hydroxymitragynine displays a stronger binding affinity towards the opioid receptors compared to the classical full opioid agonist morphine (Matsumoto et al., 2004). In addition, *in vitro*

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assays and animal studies indicate that mitragynine may also interact with several non-opioid receptors in the CNS including adrenergic and serotonergic receptors that may contribute to its antidepressant and mood-altering effects (Boyer et al., 2008).

1.1. Purpose of study

Irrespective of its pharmacology, little is known about the use pattern and potential health impact of Kratom preparations in the US. The research underlying this article was conducted to answer the following questions:

- Who is consuming Kratom and for what purpose?
- What perceived beneficial and detrimental effects are reported by Kratom users if dose and frequency of consumption are considered?
- Does Kratom present with an abuse potential and withdrawal symptoms?

2. Methods

2.1. Survey setting, approval, and data collection

An online anonymous cross-sectional survey was conducted in October 2016 of 10,000 current Kratom users. Qualtrics (Qualtrics, Provo, UT) was used to collect the data. The survey was made available as an announcement on the homepage of the American Kratom Association (http://www.americankratom.org/) and their various social media outlets (American Kratom Association Facebook page, website forums, and membership email distribution) with follow-up reminders in weekly intervals until 10,000 responses were reached. In addition, information about the survey was shared on various other websites frequented by Kratom users such as http://www.speciosa.org or http://www.drugs-forum.com. Participants were offered no incentive to complete the survey. The survey (supplementary material) was designed and classified based on common variables used by the CDC Behavioral Risk Factor Surveillance System (BRFSS) (Silva, 2014). The protocol was approved by the Institutional Review Board at the University of Florida (IRB #2016-01581). Participants had to acknowledge they were 18 years or older before starting the survey and that they participated of their own free will in the study. Collection of data started on October 2nd and concluded on October 26th 2016 once 10,000 responses were collected. Only completed responses (8049 or 80.5%) were included in the data analysis. Internet protocol addresses were not stored with the data but used to prevent multiple responses from the same device to ensure anonymity and prevent ballot stuffing. The recruitment method utilized for this study likely introduced selection bias because of the use of electronic distribution techniques that may skew towards a younger and economically fluent population that has access to such technology thus resulting in underrepresentation of other socio-demographic groups such as low income and those lacking online skills or accessibility to the internet (Brown et al., 2014).

2.1.1. Survey format

Demographic data (age, gender, marital status, ethnicity, location by ZIP code, employment status, insurance coverage, household income, and education), overall health status (weight, height, self-rated overall health, smoking status, alcohol and caffeine consumption, reasons for healthcare provider visit, self-rated pain level, and self-reported diagnosed health conditions), Kratom use experience (source of Kratom information, length of medical condition prior to Kratom use, reason(s) for Kratom use, treatment for substance use disorder, change in medical condition with use of Kratom, amount and frequency of Kratom use, Kratom preparation, beneficial effects with Kratom use, negative effects with Kratom use, Kratom withdrawal symptoms and severity, need for health care treatment because of Kratom use), opinion on Kratom legislation and regulation (disclosure of Kratom use with healthcare provider, effect of Kratom ban on user, regulation of Kratom product quality, access restriction to Kratom by state or federal government). The complete survey is attached as supplementary material.

2.2. Data analysis

The data were analyzed in Microsoft Excel 2013 (version 15.0, Microsoft, Seattle, WA) and GNU PSPP (http://www.gnu.org/software/pspp/, version 0.10.4-g50f7b7). The frequency of Kratom dosing was binned into seven equally spaced categories (Tables 3 and 4). Chi-square analysis was applied for level comparison among nominal and ordinal variables against expected values for goodness of fit (single variable Chi-square goodness of fit assuming equal counts for expected values). Binomial logistic regression was used to compare levels of variables against a reference level to obtain odds ratios and 95% confidence intervals. For each logistic regression, all pertinent independent variables were included in the same model comparing all levels against each other (no adjustment for specific comparisons among levels, post-survey power calculation resulted in at least 85% power and 93% confidence for all models).

3. Results

3.1. Demographics

The survey was completed by 8049 participants (completion rate: 80.5%) and only completed responses were included in the data analysis. A majority of respondents were male (56.91%), between the ages of 31–50 years (55.09%), married or partnered (54.25%), white non-Hispanics (89.39%), employed for wages (56.83%), with private insurance through their employer or self-insurance (61.31%), an annual household income of $35,000 or higher (63.24%), and had at least some college education (82.32%) (Table 1). Each variable indicated a significant difference among the levels as evaluated by chi-square statistics.

3.2. Reasons for Kratom use

Among those respondents who currently use Kratom, a majority have used it for more than 1 year but less than 5 years (56.59%) and a substantial percent (40.05%) discussed the use of Kratom with their healthcare provider (physician, nurse, or pharmacist). The primary source of initial Kratom information was through internet searches (45.8%) or recommendation by friends (27.4%) (Table 1). Kratom was most commonly consumed in powdered form with a beverage followed by taken in pill form or consumed in pure powder form (Table 2).

Self-reported necessity for treatment for a medical/physical or mental health issue related to Kratom use (“Have you ever needed medical or mental health care treatment because of your Kratom use?”) was low (51/7893 or 0.65%).

Kratom use related to an illicit drug dependency, i.e. relieving the withdrawal symptoms of current or prior use of an opioid or another illicit drug, was more likely in participants between the ages of 21–30 years (OR: 1.89, CI: 1.02–3.51), those with self-insurance (OR: 1.57, CI: 1.18–2.10), Medicaid (OR: 2.11, CI: 1.49–3.00), Medicare (OR: 2.41, CI: 1.53–3.79), or no insurance (OR: 1.97, CI: 1.51–2.59), while females (OR: 0.63, CI: 0.51–0.78), married participants (OR: 0.69, CI: 0.54–0.87), and retired (OR: 0.26, CI: 0.07–0.93) and unable to work (OR: 0.29, CI: 0.16–0.51) were significantly less likely to use Kratom for this purpose (Table 3). Participants who consumed Kratom for a prescription drug dependency, i.e. an initially legally prescribed opioid or other medication that led to a dependency to the medication with resulting misuse and associated withdrawal and overdose symptoms, were more likely to be ages 21 years and older (ORs: 2.32–3.6), being partnered (but not married) (OR: 1.37, CI: 1.12–1.68), having Medicare