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Kratom Abuse in Ramathibodi Poison Center, Thailand: A Five-Year Experience

Satariya Trakulsrichai, M.D.[a]; Achara Tongpo, M.Sc.[a]; Charuwan Sriapha, M.Sc.[a]; Sunun Wongvisawakorn, M.Sc.[a]; Panee Rittilert, M.Sc.[a]; Sming Kaojarern, M.D.[a] & Winai Wananukul, M.D.[a]

Abstract — Kratom (Mitragyna speciosa Korth), a native tree in Southeast Asia, is misused as an abuse drug and becomes legally widespread to several countries. Currently, it is available through the online market or by some shops. The clinical manifestations of Kratom's effects are not well-defined and the clinical studies are limited. This study was designed to identify the characteristics of Kratom poisoning and withdrawal cases from Kratom exposure cases in Ramathibodi Poison Center (RPC), Thailand, during a five-year period. We used a retrospective review of Kratom exposure cases from the RPC toxic surveillance system. A total of 52 Kratom exposure cases were identified. The trend of case consultations has been increasing. There were Kratom poisoning cases (76.9%) and withdrawal cases (23.1%). Common presenting symptoms in the poisoning group were palpitation (22.5%), followed by seizure (17.5%). For the withdrawal group, the common presenting symptoms were myalgia (33.3%), insomnia (16.67%), fatigue (16.67%), and chest discomfort (16.67%). There was a baby with withdrawal symptoms who was delivered from a chronic Kratom-abusing mother, suggesting possible exposure via the transplacental route. There were no deaths in either group. Kratom abuse can cause either poisoning or withdrawal. Most cases in both groups had good prognostic outcome.

Keywords — Kratom, outcome, poisoning, seizure, withdrawal

INTRODUCTION

Kratom, known botanically as Mitragyna speciosa Korth, belongs to the Rubiaceae family (Puff, Chayamarit & Chamchumroon 2005). Plants in the genus mitragyna can be discovered in tropical and subtropical regions of Asia such as Thailand and Malaysia (Harizal et al. 2010). Kratom is a native tree indigenous to Asia, especially in Thailand (Suwanlert 1975). It contains several alkaloids such as mitragynine, mitraphylline, and 7-hydroxymitragynine (León et al. 2009). Mitragynine, the most prevalent alkaloid isolated from Kratom, is thought to have opioid effects (Babu, McCurdy & Boyer 2008). Kratom's clinical effects are thought to be dose-dependent, with stimulant effects in lower doses and opiate-like effects in higher doses (Babu, McCurdy & Boyer 2008). The antinociceptive, antidiarrheal, and antitussive effects have previously been described (Babu, McCurdy & Boyer 2008). Recently, taking Kratom for opioid withdrawal treatment was reported (Boyer, Babu & Macalino 2007; Boyer et al. 2008; Vicknasingam et al. 2010). Kratom was also found to stimulate glucose transport in muscle cells,

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which supported its use as a folk medicine to treat diabetes (Purintrapiban et al. 2011). The acute toxicities in rats were increasing blood pressure, severe hepatotoxicity, and mild nephrotoxicity (Harizal et al. 2010). In humans, symptoms of toxicity include nausea, vomiting, diarrhea, nystagmus, and tremor (Babu, McCurdy & Boyer 2008). In animal studies, mice fed with mitragynine for a long period developed impairment of cognitive behavioral function (Apryani et al. 2010). However, anorexia, weight loss, hyperpigmentation, and psychosis were described in chronic abusers (Babu, McCurdy & Boyer 2008).

In Thailand, Kratom is used as a folk medicine to treat various diseases and also is used to mitigate and treat opioid withdrawal symptoms (Suwanlert 1975). However, the clinical effects of Kratom are not well-defined and studies related to Kratom poisoning are rather limited.

The objective of this study was to identify the characteristics of Kratom poisoning and withdrawal in Kratom-exposed patients who consulted Ramathibodi Poison Center (RPC) during a five-year period (2005–2009).

METHODS

This was a retrospective study. Patients' clinical data were from Ramathibodi Toxic Surveillance System from 2005-2009. The primary outcome was the clinical characteristics of Kratom-exposed cases suspected of developing poisoning or withdrawal. The study was approved by the Ethics Committee on Human Experimentation of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

The setting of the study was a poison center of a tertiary university hospital. The center serves public and health personnel nationwide 24 hours a day and seven days a week. The majority of calls are from physicians and related health personnel with more than 15,000 consultations per year.

The inclusion criteria were all Kratom-exposed cases which were consulted to RPC and suspected of developing poisoning or withdrawal. After all Kratom exposure cases were identified, some cases were excluded from further analysis if they involved other substances, conditions, or diseases.

The authors collected the clinical data for all Kratom exposure cases. The data included demographic data, medical history, medical outcome, final diagnosis, and clinical details during follow-up. SPSS version 11 was used for statistical analysis.

RESULTS

A total of 78 cases of Kratom exposure were identified. Twenty-six cases were excluded from further analysis because they involved infection (such as pneumonia, sepsis), neurologic disease (such as stroke), upper gastrointestinal bleeding, cardiovascular disease, or admission for surgical operations with history of chronic Kratom abuse.

TABLE 1
Demographic Data of Kratom Exposure Patients (N = 52 Cases)

Characteristics	%
Gender	
- Male	84.6
- Female	15.4
Age (median, range)	30.5 (2 days - 81 years)
Number of substances abused	
1 (Kratom only)	67.3
>1 (Kratom with others)	32.7
The presenting clinical syndromes	
- poisoning	76.9
- withdrawal	23.1
Area of habitats (in Thailand)	
- Northeast	3.8
- Central	38.5
- North	0
- South	51.9
- East	3.8
- West	1.9

TABLE 2
Substances Which were Reported to Use in Combination with Kratom (N = 17 Cases)

Agents	Number of cases
Amphetamine	1
Haloperidol	1
Diphenhydramine	1
Codeine	9
Cola beverage	1
Unknown	1
Cola beverage and diphenhydramine	1
Cola beverage and cough depressant	1
Cola beverage, cough depressant and unknown chemical substance	1

The number of cases has been increasing during the last few years. Among the 52 cases, 40 were Kratom poisoning and 12 were Kratom withdrawal cases. Demographic data are shown in Table 1. The most common route of administration was oral (98%). There was one case, a two-day-old baby, in which the mother used Kratom chronically, suggesting possible exposure via the transplacental route. There were 17 cases (33.7%) who ingested Kratom and other additional substances, as shown in Table 2.

TABLE 3
Symptoms and Signs of the Acute Kratom Poisoning Patients (N = 40 Cases)

Symptoms/signs	Frequency (%)
Palpitation	9 (22.5)
Seizure	7 (17.5)
Nausea	6 (15)
Abdominal pain	5 (12.5)
Alteration of consciousness	4 (10)
Contraction	3 (7.5)
Confusion	3 (7.5)
Headache	3 (7.5)
Dizziness	3 (7.5)
Nonspecific chest pain	3 (7.5)
Syncope	2 (5)
Myalgia	2 (5)
Dry mouth	2 (5)
Diaphoresis	1 (2.5)
High blood pressure	1 (2.5)
Diarrhea	1 (2.5)

TABLE 4
The Symptoms and Signs of Patients who Presented with Withdrawal Syndrome (N = 12 Cases)

Symptoms/signs	Frequency (%)
Myalgia	4 (33.33)
Insomnia	2 (16.67)
Fatigue	2 (16.67)
Chest discomfort	2 (16.67)
Diarrhea	1 (8.33)
Nausea	1 (8.33)
Loss of appetite	1 (8.33)
Agitation	1 (8.33)
Tremor	1 (8.33)
Ataxia	1 (8.33)
Dystonia	1 (8.33)
Hypotension	1 (8.33)
Dry mouth	1 (8.33)
Palpitation	1 (8.33)
Diaphoresis	1 (8.33)

For the poisoning group, all presenting symptoms are shown in Table 3. The most common presenting symptoms were palpitation (22.5%), followed by seizure (17.5%), nausea (15%), and abdominal pain (12.5%). For the withdrawal group shown in Table 4, the common presenting symptoms were myalgia (33.33%), insomnia (16.67%), fatigue (16.67%), and chest discomfort (16.67%).

There was one case in the withdrawal group, which was a baby born to the chronically abusing mother. The baby had tonic tone and diaphoresis when she was two days old. Her condition was uneventful after receiving supportive treatment. She was suspected as having Kratom withdrawal symptoms. However, the mother was not described as having any illness.

Seventy-five percent of both poisoning and withdrawal cases were followed until they were discharged from the hospitals. The rest were not followed because they had only mild clinical symptoms and no significant illness was expected. All of the cases followed had uneventful outcome and were discharged from hospitals. There was no mortality in this study.

DISCUSSION

In Thailand, Kratom has been used as a folk medicine and as a substitute for opium in addicted patients for decades (Suwanlert 1975). Our study shows an increase in the number of Kratom exposure cases reported to the RPC during the last few years, though it was banned and became illegal in Thailand in 1943 (Suwanlert 1975). This may be due to changing patterns of use. In the past, people who abused Kratom were mainly laborers or opioid addicts. Recently, Kratom is re-emerging as a substance of abuse. A new way to abuse Kratom, popular among teenagers, is to combine it with other substances. There are combinations which are called among Thai abusers "Four multiply one-hundred." These remedies are mixtures of Kratom, cola beverage, and cough suppressant—either codeine, dextromethorphan, or antihistamine.

According to the previous studies (Matsumoto et al. 1996a; Tsuchiya et al. 2002; Takayama 2004; Horie et al. 2005; Matsumoto et al. 2006; Babu, McCurdy & Boyer 2008; Boyer et al. 2008; Chittrakarn et al. 2008; Adkins, Boyer & McCurdy 2010), the alkaloids in Kratom such as mitragynine and 7-hydroxymitragynine are an opioid agonist. In the opiate poisoning case, the patients should develop alteration of consciousness, miosis, and respiratory depression. Besides opioid receptors agonist effect, some studies hypothesized that mitragynine may involve alpha-2 adrenergic receptors, 5-HT_{2A} receptors, other noradrenergic and serotonergic pathways (Babu, McCurdy & Boyer 2008, Matsumoto et al. 1996b). Therefore, the mechanism of Kratom toxicity might be more complex and not exactly similar to opioids. If the effects of Kratom are hypothesized to be dose-dependent as stimulant effects at lower doses but opiate effects at higher doses (Babu, McCurdy & Boyer 2008), it might need a higher dose to generate opioid toxicity. This is relevant to our observation that no Kratom abusers have been found with a clinical presentation of sedation or central nervous system depression, as we commonly observed in opioid abusers. It also suggested that the dose which most patients took might not be high enough.

The 17 cases of multiple substances abuse shown in Table 3 were cases who took the aforementioned remedies. Most of them were poisoning cases, although the possibility of toxicities to be caused by the additional substances were not excluded. The presentation of these patients was not fit with their toxicities. If the patients suffered from codeine or dextromethorphan, their clinical presentation would fit with opioid toxidrome. Taken together, the signs and symptoms found in this study should be presumptively caused by Kratom.

This study revealed that seizure was one common presenting symptoms of Kratom poisoning (17.7%). Three previous case reports found seizure in their patients (Boyer et al. 2008; Roche et al. 2008; Nelsen et al. 2010); however, other reports did not (Suwanlert 1975; Babu, McCurdy & Boyer 2008; Klasco 2012). For the cause of seizure in our study, two of them reported taking only Kratom; the others took Kratom in combined with other substances. Since codeine and cola beverage rarely induce seizure, the authors propose that seizure may be caused by Kratom, and considered as a manifestation of Kratom toxicity. Though it was not observed in an acute toxicity of rodent study (Harizal et al. 2010), the pharmacology, action, clinical effect, and toxicity in rats and humans may be different. The mechanism of seizure is also not yet known (Boyer et al. 2008). Thus, seizure activity in Kratom toxicity has to be further investigated.

For the withdrawal group, the common presenting symptoms were myalgia (33.33%), insomnia (16.67%), fatigue (16.67%), and chest discomfort (16.67%). Our findings were partly compatible with the previous study, which mentioned that Kratom withdrawal symptom is also an opioid abstinence syndrome which includes irritability, yawning, rhinorrhea, myalgia, diarrhea, and arthralgia (Babu, McCurdy & Boyer 2008). Chest discomfort, one of the withdrawal symptoms in this study, may be caused by other mechanisms. To the best of our knowledge, these were not cases of cardiopulmonary or metabolic disorders. A possibility of anxiety was not ruled out. The authors also found that cases of Kratom withdrawal symptoms were modest, and severe cases of withdrawal were not commonly found. One explanation for this finding may be that the amount of ingestion in our patients was not very high. All of our patients abused Kratom by taking Kratom leaves, and this may result in exposure to lower amounts of active ingredients when compared with Kratom taken by other formulations.

One case in the present study was of a two-day-old baby presented with tonic tone and diaphoresis two days after delivery from a mother who ingested Kratom chronically. This case improved with supportive treatment. Kratom may be able to cross the placenta to the fetus in the pregnant abuser. However, further studies are required to determine the possibility of transplacental exposure.

The present study was a retrospective study, so the details of history, physical examination findings, and investigations might be missing. The clinical laboratory test for mitragynine is available in only a few hospitals in Thailand; thus the diagnosis of Kratom exposure is obtained by the history of Kratom abuse only. To our knowledge, this present study is the largest case series of Kratom toxicity reported to date. However, the number of cases in our study remains small.

Conclusion

Kratom abuse has been increasing during the last few years. It can cause either poisoning or withdrawal. In our study, the two most common presenting symptoms were palpitation and seizure in poisoning patients, while myalgia was the most commonwithdrawal-presenting symptom. The transplacental transfers of Kratom have been reported. Most cases in both groups had good prognostic outcome.

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