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REVIEW

Antenatal Kratom Exposure: Literature Review and Clinical Management Recommendations

Alice Ordean[1,2]

[1]Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada; [2]Department of Family Medicine, St. Joseph's Health Centre, Unity Health Toronto, Toronto, Ontario, Canada

Correspondence: Alice Ordean, St. Joseph's Health Centre, Family Medicine Clinic, 30 The Queensway, Toronto, Ontario, M9A 1E6, Canada, Tel +1 416 530-6860, Fax +1 416 530-6160, Email alice.ordean@unityhealth.to

Abstract: In recent years, there has been a rapid interest in using kratom for the self-management of various chronic pain, anxiety and mood conditions, as well as, for the management of opioid withdrawal symptoms. The two main kratom alkaloids have stimulant and opioid-like effects that cause concerns during pregnancy. A literature review was conducted, and ten case reports relating to maternal kratom use were included consisting of 12 mother-infant dyads. Case reports indicated that regular use of kratom was associated with the presence of maternal kratom dependence and withdrawal. The route and amount of kratom use reported was highly variable. The majority of women were only identified in the postpartum period after infants displayed symptoms and signs of neonatal withdrawal. Management of maternal kratom use varied and included either opioid agonist treatment with buprenorphine or morphine or detoxification. Most of the exposed infants were described to develop neonatal abstinence syndrome and more than half required pharmacological treatment with morphine. All neonates were discharged home in the care of their mothers. Clinicians should be aware of the possible clinical effects of perinatal kratom exposure and be able to implement appropriate maternal and neonatal management strategies.

Keywords: *Mitragyna*, pregnancy, opioids, neonatal abstinence syndrome, opioid agonist treatment

Introduction

Kratom products are being increasingly used for the self-management of chronic pain, psychiatric conditions, as well as, as an opioid substitute for the management of opioid withdrawal.[1–3] The estimated lifetime prevalence in the United States (US) ranges between 0.9% and 6.1% with higher penetrance among those with concurrent psychiatric and substance use-related conditions.[3–6] The US Food and Drug Administration (FDA) has regulated kratom as a dietary supplement and has not approved any medical uses; however, more recently, following a significant increase in kratom-related calls to poison control centers, the FDA has been warning consumers about possible risks associated with its use.[1,4]

Kratom contains over 40 alkaloids with both stimulant and opioid-like effects.[4,5,7] Mitragynine (MG) and 7-hydroxymitragynine (7-HMG) are the two main psychoactive alkaloids and mediate the pharmacological effects of kratom.[4,8] MG makes up 1–2% of the dry plant mass by weight and constitutes 60% of the total alkaloid content, whereas, 7-HMG is present at much lower levels. The pharmacological effects are the result of interactions of both MG and 7-HMG with adrenergic, serotonergic and opioid receptors leading to the development of physical dependence and withdrawal with abrupt cessation.[4,9,10] Routine urine drug screening does not detect the presence of kratom metabolites, and specific chromatography testing is required to identify the presence of this substance in urine samples.[11]

Among women of childbearing age, kratom use is especially concerning during pregnancy due to possible adverse effects including neonatal abstinence syndrome (NAS). A systematic review involving only five case reports indicated that antenatal kratom exposure was associated with maternal and infant withdrawal resulting in the need for further management.[11] However, limited data was provided in that review article about the extent of pharmacological treatment.

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Therefore, the aim of this article is to provide an updated review of the literature on both maternal and neonatal clinical outcomes associated with maternal kratom use, as well as, to summarize clinical management recommendations.

Materials and Methods

MEDLINE, Embase and Psych INFO databases were searched from their inception until April 2023 using the following keywords: pregnancy, kratom (*Mitragyna*), and neonatal abstinence syndrome. A manual review of the reference lists was also performed to ensure that all relevant studies were located. Inclusion criteria consisted of the following: 1) English language publications, 2) Studies involving kratom use during pregnancy and 3) Studies that reported data on maternal and/or neonatal outcomes.

Twelve unique articles were identified. Of these, five were excluded after abstracts were reviewed due to the following reasons: review article (n = 2), no clinical outcome data provided (n = 2) and study not focused on pregnancy (n = 1). The full text of the remaining 7 articles were reviewed which resulted in 2 additional studies being identified in their reference lists for a total of 9 reports being located from this literature search. An additional case report from Unity Health Toronto was included representing 10 case reports in total for the final literature review. Consent from the hospital Research Ethics Board and the patient were obtained for inclusion of this unpublished case report in this review.

Results

Ten case reports described maternal kratom exposure and associated outcomes for 12 mother-infant dyads. Five reports originated from the US, 3 from Canada and 1 each from Thailand and Switzerland (Table 1).[12–20]

Maternal Demographics, Kratom Use, and Comorbid Conditions

Although not uniformly reported, demographic data indicated that women ranged between 28 and 37 years of age (n = 6) and at least half (n = 6) were multips (Table 1).[15,16,18,19] Three of these women were identified during pregnancy and the remainder during the postpartum period. Maternal kratom use was reported as daily use by 9 women (75%)[12,15–20] and most women had used regularly for months prior to pregnancy (Table 1). Data on maternal kratom use was only provided for 7 women.[15–20] Formulations and administration routes varied between consumption of oral powder (n = 2), tablets (n = 1), tea (n = 3) or smoked (n = 1). Case reports indicated that women reported physical dependence with regular kratom use, difficulty weaning off kratom use prior to and during pregnancy, as well as, opioid-like withdrawal

Table 1 Summary of Published Case Reports of Maternal Kratom Use

Author, Year, Country	Study Type, Number of Cases	Maternal Demographics	Maternal Substance-Related and Associated Conditions
Trakulsrichai S et al[12] 2013, Thailand	Case report n = 1	N/A	Chronic Kratom use
Bosch A. et al[13] 2017, Switzerland	Case report n = 1	N/A	Daily Kratom use Polydrug use during pregnancy: cocaine, Ritalin, alcohol, cannabis, benzodiazepines
Cumpston KL et al[14] 2018, USA	Case report n =1	N/A	Kratom use during pregnancy
Mackay L, and Abrahams R.[15] 2018, Canada	Case report n =1	29 year old, G4P1A3 Postpartum day 2 Stable partner Supportive family Adequate housing	Daily Kratom use during pregnancy 18–20 grams powder tid Maternal opioid withdrawal Multiple failed attempts to taper Hx of opioid use disorder, chronic back pain and anxiety

(*Continued*)

Table 1 (Continued).

Author, Year, Country	Study Type, Number of Cases	Maternal Demographics	Maternal Substance-Related and Associated Conditions
Smid MC et al[16] 2018, USA	Case report n=2	Case 1: 32 year old, G4P2 22 weeks GA	Case 1: Daily Kratom use for 7 months until 16 weeks GA Maternal opioid withdrawal and self-weaned Hx of chronic pain and anxiety
		Case 2: 28 year old, G5P3 19 weeks GA	Case 2: Kratom smoked for 4 months Maternal opioid withdrawal Hx of intravenous drug use (heroin, methamphetamine), AUD, BAD, suicide attempts
Eldridge WB et al[17] 2018, USA	Case report n =1	N/A Postpartum day 2	Daily Kratom tea during pregnancy Hx of past opioid use
Davidson L et al[18] 2019, USA	Case report n =1	29 year old Single G2Px	Daily Kratom use during pregnancy 5g oral tablets od – tid Hx of chronic pain, fibromyalgia and anxiety, chronic smoker
Murthy P and Clark D.[19] 2019, Canada	Case report n =1	37 year old G2P2	Daily Kratom tea tid-qid Hx of restless legs syndrome, anxious depression
Love JS et al[20] 2020, USA	Case series n = 2	N/A	Case 1: Daily Kratom tea
		N/A	Case 2: Daily Kratom use
Ordean A. 2021, Canada	Case report n = 1	37 year old, G2P1 30 weeks GA Stable partner, Supportive family, Adequate housing, Employed	Daily use of Kratom powder 4–9g during pregnancy, intermittent use x 8 years Hx of ADHD, depression

Abbreviations: ADHD, attention deficit hyperactivity disorder; N/A, Not available; G, gravidity; P, parity; od, once daily; tid, three times daily; qid, Four times per day; USA, United States of America.

symptoms on past attempts to discontinue its use.[15–17] Comorbid conditions were reported for 7 women and consisted of a history of chronic pain (n = 4), anxiety or mood disorders (n = 6), ADHD (n = 1), and other substance use (n = 5) (Table 1).[15–19] For these women, initiation of kratom use was related to the self-management of chronic pain, uncontrolled anxiety or possible opioid use disorders.

Neonatal Outcomes and Associated Management

Birth parameters were reported for 10 neonates (Table 2).[13,15–20] All were born at term with Apgar scores within normal range. Birth weights were only mentioned specifically for 3 babies and ranged between 2773 and 3680 grams.[16,19] Small for gestational age (SGA) was mentioned for 3 additional neonates indicating possible intrauterine growth restriction in at least 25% of exposed newborns.[17,18,20] No neonatal deaths were reported.

All neonates had a history of prenatal exposure to kratom and as a result, all required assessment and monitoring for NAS. Ten neonates were found to display symptoms of NAS with mean onset of NAS on day 2 of life with a peak by day 4.[12–20] Seven out of ten neonates diagnosed with NAS required morphine treatment (Table 2).[13–19] Morphine treatment started on average on day 2 and lasted for 5 to 10 days. Neonates were discharged home by day 12 to 14 of life. One neonate required a more prolonged morphine weaning period of 2 months and was reported to have been experienced a more sustained in utero kratom exposure.[18] No follow-up data was available once neonates were discharged home in the care of their mothers. The

Table 2 Maternal and Neonatal Outcomes

Author, Year	Maternal Outcomes and Management	Neonatal Outcomes and Management
Trakulsrichai S. et al[12] 2013	No information	NAS onset on day 2 Symptoms: diaphoresis, increased tone Supportive treatment only
Bosch A. et al[13] 2017	No information	Term neonate Born with neonatal acidosis and global respiratory insufficiency required intubation and ventilation for 2 days NAS increased by day 4 Morphine treatment
Cumpston KL et al[14] 2018	No information	NAS onset on day 2 Symptoms: diarrhea, tachypnea Morphine and benzodiazepines treatment
Mackay L, and Abrahams R.[15] 2018	History of opioid withdrawal (diaphoresis, rhinorrhea, myalgia, anxiety, nausea, diarrhea, piloerection) Morphine substitution treatment postaprtum Morphine IR 10mg tid and kratom reduced to 10g tid Both tapered by 4 weeks	Term neonate 37+5 wks GA NAS onset on day 2 Symptoms: feeding intolerance, irritability, jitteriness, emesis Morphine treatment for 5 days
Smid MC et al[16] 2018	Case 1: History of opioid withdrawal Buprenorphine maintenance treatment – initiated at 8mg and reduced to 2mg for remainder of pregnancy	Case 1: Term neonate 39 wks GA BW 2773g, breastfed No NAS D/C home on day 3
	Case 2: History of opioid withdrawal Buprenorphine/naloxone maintenance treatment – 16mg until 36 wks GA then increased to 20mg	Case 2: Term neonate, 39 wks GA BW 2895g, breastfed NAS onset on day 4 Morphine treatment Weaned and d/c home on day 12
Eldridge WB et al[17] 2018	No information	Term neonate SGA NAS onset on day 2 Symptoms: tremors, irritability, hypertonia, high-pitched cry Morphine treatment from day 2 to 3 Clonidine treatment from day 3 to 5 D/C home on day 8 Child protection services involved
Davidson L et al[18] 2019	No information	Term neonate SGA NAS onset on day 2 Morphine treatment from day 2 to 12 Required prolonged weaning 2 months
Murthy P and Clark D.[19] 2019	Kratom rapid taper D/C home after 7 days off Kratom	Term neonate BW 3680g, formula fed NAS onset on day 2 Symptoms: feeding intolerance, jitteriness, hypertonia, sneezing, excessive crying Morphine treatment from day 2 to 12 D/C home from day 14

(*Continued*)

Table 2 (Continued).

Author, Year	Maternal Outcomes and Management	Neonatal Outcomes and Management
Love JS et al[20] 2020	Case 1: No information	Case 1: Term neonate SGA breastfed NAS onset on day 1 No morphine D/C home on day 5
	Case 2: No information	Case 2: Term neonate Breast and bottle-fed NAS onset on day 1 No morphine treatment D/C home on day 4
Ordean A. 2021	Kratom dose taper	Term neonate No NAS No morphine D/C home on day 2

Abbreviations: BW, birth weight; D/C, discharge; GA, gestational age; NAS, neonatal abstinence syndrome; g, grams; mg, milligrams; tid, three times daily.

presence of NAS and requirement for pharmacological management indicated that antenatal exposure was likely due to transplacental transmission of kratom.

Management of Maternal Kratom Use During Pregnancy

Case reports described maternal physical dependence and both maternal and neonatal opioid-like withdrawal syndromes resulting from maternal kratom use. Furthermore, different management strategies for management of regular maternal kratom use during pregnancy and postpartum were reported by half of the reports (Table 2).[12–20] Mackay and Abrahams offered morphine substitution treatment postpartum while reducing kratom use and then tapered both substances over 4 weeks.[15] Smid et al described the use of buprenorphine maintenance treatment for 2 pregnant women who discontinued kratom use following induction on buprenorphine, which was then continued for the duration of their pregnancies.[16] Murthy and Clark admitted a woman postpartum for rapid detoxification over the course of 7 days.[19] Ordean also reported a gradual dose reduction with ongoing kratom use throughout the pregnancy. With no formal guidelines available, these approaches were based on kratom's pharmacological properties and principles associated with the management of opioid use disorders. Similarly, neonates were treated effectively with morphine, which is the same medication used for the management of neonatal opioid withdrawal syndrome.

Discussion

Screening and Intervening with Maternal Kratom Use

The complex pharmacology of kratom indicates the possibility of both stimulant and opioid effects; however, no clinical presentation of stimulant withdrawal was documented among this patient population. For chronic kratom users, case reports indicated multiple failed attempts to taper off this substance and maternal withdrawal associated with its sudden cessation consisting of diaphoresis, myalgias, anxiety, nausea and diarrhea, similar to opioid-like withdrawal syndrome.[15,16] These observations are consistent with another study which determined that the primary features of kratom use disorder associated with continued kratom use consisted of tolerance and withdrawal syndrome.[21]

Use during pregnancy is also concerning due to possible adverse pregnancy outcomes such as premature delivery, intrauterine growth restriction, fetal demise and neonatal withdrawal. This literature review included 12 mother-baby dyads which is twice as many as cases as in the systematic review by Wright et al.[11] The additional cases of maternal kratom exposure included in this current review provided a larger evidence base and a wider range

of possible effects. No history of premature delivery, congenital anomalies or fetal deaths were documented in this updated review. Intrauterine growth restriction was indicated in 5 case reports including those which mentioned SGA babies and birth weights less than the mean birth weight in the general population.[16–18,20] This represents a new finding which was not included in the previous review.[11] Findings related to NAS were similar to the systematic review.[11] Specifically, NAS was observed by day 4 in over 80% of neonates and of these, 70% required morphine treatment.

Management Recommendations for Antenatal Kratom Exposure

Screening for kratom use during early stages of pregnancy would enable earlier identification and interventions. In this review, only 3 women self-reported kratom use in the second and third trimesters of pregnancy.[16] The other maternal cases were only determined retrospectively in the postpartum period when neonates presented with withdrawal symptoms consistent with NAS. This delayed identification did not permit women to receive timely care during pregnancy such as medical detoxification or opioid substitution treatment.

Recommendations for the clinical management of kratom use disorder are based on a literature review involving 14 case reports and a survey of addiction medicine experts.[9] Researchers indicated that kratom users with concomitant opioid use disorder (OUD) were all initiated to buprenorphine maintenance whereas most of those without OUD still benefitted from the same treatment approach.[9] In this review of cases involving kratom use during pregnancy, only two women were inducted onto buprenorphine and continued on maintenance treatment for the duration of their pregnancies.[16] The use of morphine as an opioid substitution agent in the postpartum period was also reported.[15] In addition, tapering off kratom was also documented by two pregnant women who opted for reducing their kratom dose instead of opioid substitution therapy.[8] Given the current evidence base, maternal kratom use can be managed similar to OUD consisting of primarily opioid agonist therapy (OAT) followed by detoxification, in cases where OAT is declined or not tolerated. Similarly, women should be counselled about the possible association between maternal kratom use and NAS requiring a more prolonged neonatal length of stay and neonatal morphine treatment. Further research is required to determine the full extent of effects related to maternal kratom use and the implications of kratom withdrawal during pregnancy. This additional data would help to inform the optimal management of perinatal kratom use disorders.

Conclusion

As the prevalence of kratom use is increasing, clinicians will encounter women who are consumers of this product. This is of particular importance among women of childbearing age and therefore, clinicians providing antenatal care should screen routinely for use of non-prescription medications and natural products, especially among pregnant persons with a history of substance use disorders, chronic pain and mental health conditions. Available literature supports that regular kratom use places pregnant women and their fetus at risk for dependence and withdrawal upon cessation of use. Management strategies for maternal kratom use during pregnancy should be similar to those used for OUD including the use of OAT and counselling about neonatal risks of kratom exposure such as NAS. More research is needed to determine the implications of maternal kratom use to optimize screening and interventions for both mothers and their neonates.

Disclosure

The author reports no conflicts of interest in this work.

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