<u>Case report</u>

Kratom Dependence in Adolescents: Is Methadone A Lifesaver?

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<u>Abstract</u>

Kratom dependence among adolescent, even though underreported, is increasing in prevalence in Southeast Asia. Kratom can be simply misused with a great possible addiction and subsequently cause serious undesirable physical and mental health consequences, which is not something to be taken lightly. We present three case series of late adolescents who consumed kratom for more than six months, which leads to poor school performance and had already developed withdrawal symptoms. This case series illustrates the effectiveness of treating adolescents with kratom dependency using combination of medical therapy - Methadone as Drug Substitution Therapy (DST) and supportive therapy from their family members. Therefore, it is crucial for primary care practitioners to screen the adolescents and alert the withdrawal symptoms as well as initiating early discussion with psychiatrist in order to start the prompt treatment since DST is available in primary care clinic.

Keywords: Adolescent health; kratom dependence; methadone; mitragyna speciose

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Introduction

Kratom (*Mitragyna speciose*) is a plant that grows naturally in Thailand, Malaysia, Indonesia, and Papua New Guinea and was found abundant in the northern states as well as the east coast of Peninsular Malaysia. In Malaysia, kratom has been controlled under the Poison Act since 2003. It is an offense to import, export, manufacture, sell, and possess of kratom. In Thailand, Australia and Myanmar, it is regulated under the Narcotic Acts of the respective countries. In Indonesia, kratom is legally cultivated and exported on a huge scale to Asia, Europe and North America. Meanwhile, in UK, US, and Germany, kratom is not a controlled substance but under surveillance.¹ The lifetime prevalence of kratom use among high school students in southern Thailand has been increased from 3.97% to 9.43% in 2002 to 2004.² However, at present, there is no systematic data on the prevalence of kratom use among adolescents in Malaysia.² According to the national drug report, seizure for kratom has increased markedly for the past few years. This reflects that kratom use is gaining popularity among Malaysian.³

Kratom possesses benefits as a stimulant, sedative, pain reliever, psychological euphoria, antidepressant and anxiolytic effects.^{1,3} People use their leaf to brew it and drink like a tea to manage the pain, as an energy booster and beat the tiredness and as a substitute for opioid addiction or withdrawal.³ Kratom is available

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in the form of tea, chewed, smoked or ingested capsule. But the most popular one among Malaysian is they boiled the kratom leaves and drunk it like a tea.³ Regular and extended kratom use can cause dependence while abrupt cessation from it use can cause adverse withdrawal effects.³

Here, we reported a case series by using Methadone as Drug Substitution Therapy (DST) in the management of adolescents with kratom dependence and withdrawal symptoms attending Addiction Clinic, Hospital Raja Perempuan Zainab II from July 2018 to January 2020. The goals of the therapy include preventing withdrawal symptoms, reducing craving and blocking the euphoric effect of kratom dependence. These cases highlighted the success and challenges of methadone therapy in kratom addiction among adolescents that can be implemented in methadone clinic of primary care clinic setting.

Case series

Case 1:

A 17-year-old Malay boy was referred to an addiction clinic in July 2018 because of kratom withdrawal and impaired in social functioning. He was brought by his mother because of his kratom dependence for 7 months that lead to poor school performance. He became dependent on kratom and exhibit withdrawal symptoms (runny nose, body ache, craving and sleeping difficulty) when he tried to stop kratom. Otherwise, he denied any psychotic or aggressive symptoms. He denied another substance abuse and the urine toxicology test on the initial visit was negative. His mother reported school absenteeism for 2 months because of kratom addiction. He was started with low dose syrup methadone 5mg/day and the dose was titrated up till 20 mg/day maximally. He was able to maintain a tolerable dose of 20 mg/day for 5 months. For the five months follow up, the patient was getting better, less usage of kratom, less withdrawal effects and attend school well. After five months follow up, he dropped out of the program therapy. We followed up the case by calling his mother. He was unable to attend an addiction clinic due to work obligations and he is currently kratom-free.

Case 2:

A 17-year-old Malay boy was first referred to an addiction clinic in June 2018 for kratom dependence with withdrawal symptoms. He attempted to reduce

he exhibited the withdrawal symptoms (runny nose, watery eyes, body ache, craving and sleeping difficulty). He was expelled from the school because of long absenteeism. He took kratom in the form of a drink almost daily for 3 years. Parents noticed he did not adhere to religious practice since he took kratom and not socialise well with other siblings. Otherwise, no psychotic symptoms reported. He was started with low dose syrup methadone 5 mg/day and titrated up till maximal tolerable dose 25 mg/day. He was able to maintain with the current dose for 2 months then the dose was tapered down gradually as since taking methadone, his functionality and productivity improve, able to attend school, better performance and fewer withdrawal symptoms. He was in Methadone Replacement Therapy (MRT) for 18 months before he succeeds to cease. Since he was started methadone, the craving towards kratom was reduced and the patient able to sit for a major exit exam for secondary school. Parents reported his son more cheerful, obedient to religious practice and able to socialise well with siblings. He is currently taking a culinary course at a college.

the dose and stop the kratom consumption however

Case 3:

A 17-year-old Malay boy was referred to an addiction clinic in July 2018 for kratom dependence and withdrawal symptoms. He took kratom for the past one year and denied any other substance abuse. The urine toxicology test was negative. Post consuming kratom, parents noticed he always skipped the school and reducing in school performance, exhibit withdrawal symptoms (runny nose, mood irritable, difficulty in sleeping) and less talkative toward family members. Otherwise, the patient denied any psychotic symptoms. He was started with low dose syrup methadone 5 mg/day and titrated up till maximal tolerable dose 22.5 mg/ day. He felt nauseated in the early treatment with methadone, however able to tolerate it later. He was able to maintain the current dose for 3 months then the dose was tapered down gradually after mother satisfied with the patient's clinical condition: no more addiction to kratom, no withdrawal symptoms alongside improved performance in school attendance and academic achievement. Patient selfreported no more withdrawal symptoms and craving after taking syrup methadone. He was in Methadone Replacement Therapy (MRT) for 12 months before he succeeds to cease. Now, he further studies in a local institute in engineering courses. The mother reported his son maintaining well in life and has good social engagement after succeeding in a methadone program.

Discussion

Kratom is a widely used psychoactive drug in Southeast Asia. Kratom has the effect that mimics the opioid drug. Psychoactive compounds of kratom, mitragynine and 7-hydroxy mitragynine display a high affinity to μ -opioid receptors.⁴ Regular kratom use can expose to drug dependence which is the condition when users unable to refrain from kratom use when they wanted.³ Hence, they will develop symptoms of profound withdrawal and subsequent drug craving.³

Kratom users can exhibit physiological and psychological withdrawal symptoms after abstaining abruptly from kratom. Physiological withdrawal symptoms encountered during withdrawal period include headache, hot flashes, sweating, fever, watery eyes and nose, nausea, vomiting, hiccups, diarrhoea, abdominal pain, decreased appetite, sleeping difficulty, muscle spasm and shakiness or tremors, body aches, severe muscle pain and cramps while the psychological withdrawal that is commonly reported are nervousness, sadness, restlessness, aggression, hostility, tension, and depressed mood.^{3,5}

At present, there are no specific or concrete guidelines on the management of kratom dependence and withdrawal.⁶ As kratom has the opioid mimic action, the best approach is to follow the opioid withdrawal management.⁶ However, there are few case reports in the literature of supervised detoxification and drug treatment for kratom dependence and withdrawal using opioid withdrawal protocol.⁶ Pizarro-Osilla reported a case, a 1-day old term infant who presented to the emergency department with opioid withdrawal syndrome and the mother used kratom as supplements.6 The infant was given methadone for presumptive opioid withdrawal syndrome. However, the outcome of the treatment was not elaborate further. Few other reported cases in previous literature addressed successful treatment of kratom addiction and withdrawal with buprenorphine.4,7

Methadone is a synthetic agent that has a similar effect

as opioid drugs. It works by conquering and filling the site of brain receptors that affected by opioid drugs. Methadone can prevent euphoric effects and sedation from opioid drugs. It can reduce dependence as well as relieve physical and psychological withdrawal symptoms. Methadone is taken only once daily due to its slow absorption and longer action duration in the body system.⁸

Malaysia started Methadone Maintenance Therapy (MMT) nationwide to fight opioid dependence patients since 2005. This program was implemented as a part of the National Harm Reduction Program besides condom distribution and needle & syringe exchange programs (NSEP). This program was offered in a tertiary hospital, primary care clinic, private clinic, National Anti-drug Agency (AADK) and Malaysian Prison Department.8 In a primary care clinic, methadone can only be prescribed by a registered medical practitioner that undergoing training in methadone treatment. It is given daily to the patient by Direct Observation Therapy (DOT). The client on methadone therapy will be monitored thoroughly their withdrawal symptoms, intoxication, the side effect of methadone, improvement of laboratory psychosocial wellbeing, relevant parameters such as liver function test and the dose of methadone also being adjusted to reach the patient's need.8

The side effect of methadone is common during early treatment. The most common side effects of methadone are nodding off after taking methadone, loss of appetite, nausea, vomiting, increase weight gain, constipation, lethargic, insomnia, a dental problem, rashes and itching, decrease libido and low sex drive and others.⁸ Therefore, awareness of the side effect of methadone should be the priority throughout the methadone therapy.

All our reported patients with kratom dependence only required short duration of therapy approximately one to two years and with a low dosage of methadone maintenance ranging from 20 to 25 mg/day compared to another opioid dependence (heroin/cocaine) which has higher methadone dosages ranging from 60 to 100 mg/day and longer duration as years for the effectiveness together with good family support.^{9,10}

In our cases, we measure the success of the outcomes by face-to-face interviews with the patient and parents. Self-reported symptoms (includes no craving or withdrawal symptoms and able to attend schools or programs), while from parent's perspectives, the patient started to develop good family relationships, improved social performance and able to stabilize their life and can reintegrate within the expanded community.

The challenges of this program are a feasible treatment option. Methadone is dispensed daily to the patient by Direct Observational Therapy (DOT) until a certain period they can take away the dose. The patient needs to attend the clinic daily for DOT and there is a high risk for drop out of the program. This dispensing rule makes treatment accessibility difficult for individuals living in areas that are far away from the methadone maintenance program. Like in our first case, when the patient getting a job, he defaulted follow up and drop out of the methadone program. Hence, effective strategies should be sought to retain patients in the program. Health care professionals must think about the best strategy to retain adolescents in treatment. There are very few studies that published evidence of methadone efficacy and safety in adolescents compared to the adult group. However, for patients at high-risk dropouts such as adolescents, treatment retention should take superiority over the clinical considerations. Methadone appears to be effective in promoting treatment in opioid use disorder among adolescents.11

Another challenge of these consultation is kratom use cannot be detected by routine urine toxicology screening tests. The initial urine toxicology tests for morphine, cannabis, methamphetamine, amphetamine, benzodiazepine and ketamine were conducted to exclude if the adolescent were tested positive for these drugs. Psychoactive compounds of kratom, mitragynine and 7-hydroxy mitragynine can be spotted using liquid chromatography.³ This test is not done routinely in Malaysia. Promising approaches to precisely identify kratom compounds are still ongoing. We depend based on clinically on patient's improvement to determine the success rate. Further research should be done to determine the important domain that should be assessed. Based on these case series, the use of Methadone Replacement Therapy not only confined to heroin/cocaine abuse but can expand widely to all substance that has opioid-like action such as kratom.

In summary, all our cases reported favourable outcomes with methadone. The efficacy of Drug Substitution Therapy (DST) has been recognised in many countries to fight opioid withdrawal and Methadone Maintenance Treatment (MMT) is the one that implemented in Primary Care Clinic in Malaysia since 2005 to combat opioid dependence. Recognising the clients with kratom dependence and early referral or discussion with the psychiatric team in considering Methadone therapy as one of the treatment options is vital. Therefore, greater awareness among primary care health professionals about kratom's potential risks and management of its associated withdrawal symptom is essential.

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References:

- Hassan Z, Muzaimi M, Navaratnam V, Yusoff NH, Suhaimi FW, Vadivelu R, et al. From kratom to mitragynine and its derivatives: physiological and behavioural effects related to use, abuse, and addiction. *Neurosci Biobehav Rev.* 2013;37(2):138-151. https://doi.org/10.1016/j.neubiorev.2012.11.012
- Cinosi E, Martinotti G, Simonato P, Singh D, Demetrovics Z, Roman-Urrestarazu A, et al. Following "the roots" of kratom (Mitragyna speciosa): the evolution of an enhancer from a traditional use to increase work and productivity in Southeast Asia to a recreational psychoactive drug in western countries. *BioMed Res Int.* 2015: 1-11 https://doi.org/10.1155/2015/968786
- Singh M, Singh D. Measuring dependence severity of ketum (Mitragyna speciosa) use among ketum leaf users in Malaysia: Penang: Universiti Sains Malaysia, 2013 http://eprints.usm.my/43275/1/Darshan%20Singh%20 AL%20Mahinder%20Singh24.pdf. Accessed 15 March 2020.
- 4. Boyer EW, Babu KM, Adkins JE, McCurdy CR. Halpern JH. Self-treatment of opioid withdrawal using kratom (Mitragynia speciosa korth). Addiction. 2008;103(6):1048-1050. https://doi.org/10.1111/j.1360-0443.2008.02209.x
- 5. Pizarro-Osilla C. Introducing kratom. *J Emerg Nurs.* 2017; **43**(4):373-374. <u>https://doi.org/10.1016/j.jen.2017.03.016</u>
- 6. Stanciu CN, Gnanasegaram SA, Ahmed S, Penders T. Kratom withdrawal: a systematic review with

case series. J Psychoact Drugs. 2019;**51**(1):12-18. https://doi.org/10.1080/02791072.2018.1562133

- Khazaeli A, Jerry JM, Vazirian M. Treatment of kratom withdrawal and addiction with buprenorphine. J Addict Med. 2018;12(6):493-495. https://doi.org/10.1097/ADM.00000000000435
- Polisi Dan Prosedur Operasi Piawai Program Rawatan Methadone. Putrajaya: Bahagian Kawalan Penyakit Kementerian Kesihatan Malaysia; 2016 https:// https:// www.pharmacy.gov.my/v2/ms/dokumen/polisiprosedur-operasi-piawai-program-rawatan-methadone. html. Accessed 20 March 2020
- Faggiano F, Vigna-Taglianti F, Versino E, Lemma P. Methadone maintenance at different dosages for opioid dependence. *Cochrane Database Syst Rev.* 2003; (3):1-38. https://doi.org/10.1002/14651858.CD002208
- Ahmad N, Mat K, Mohamad N, Husain R, Bakar NH, Zakaria N , et al. A review on opioid dependence, mechanism and treatments used: option of treatments: modern versus alternative medicine. *Bangladesh J Med Sci*, 2019;**18**(2):171-177. <u>https://doi.org/10.3329/bjms.v18i2.40681</u>
- Bell J, Bell J, Mutch C. Treatment retention in adolescent patients treated with methadone or buprenorphine for opioid dependence: a file review. Drug Alcohol Rev. 2006;25(2):167-171. <u>https://doi.org/10.1080/09595230500537670</u>