CASE REPORT

Parental Self Instrumentation of Kratom as Pain Substitute for the End-of-Life Care in a Malay Child

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ABSTRACT

Kratom has garnered controversies due to vague understanding of its pharmacology and often been associated with substitute for opioid withdrawal symptoms. In the East, it has been used for many reasons. Our case potentially is the first case report in paediatrics where parent self-instrumentation use of kratom as the substitute for morphine for their dying child. Despite short use of the substance, it was subjectively reported to positively control of the symptom without further need of morphine breakthrough. Kratom is controversially being banned in some countries due to lack of research evidence. It may potentially have a role in managing children with chronic pain, anxiety, and poor energy level at the end of their lives.
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INTRODUCTION

Kratom is a tropical plant native to Southeast Asia, which contain compounds such as mitragynine and 7-hydroxymitragynine (Figure 1). These elements interact with opioid receptors in the brain causing potential pain relief, energy boost, and alleviation symptoms of opioid withdrawal. It has been suggested that kratom helps in patients with chronic pain and mood disorders. However, due to concerns about safety and potential for abuse, kratom's medical use remains controversial and requires further investigation. Our study highlights the first case of parental self-instrumentation of kratom use for cancer pain among paediatric cancer patients.

Figure 1: Kratom leaves

CASE REPORT

1 ½ year old girl was diagnosed with rare recurrent ovarian germ cell tumour. She had tumour debulking operation, but the tumour recurred. She was given a few months to live. Parents have opted to return to home state for the end-of-life care. Upon review by the palliative care paediatrician, her parent complained that she was not sleeping, difficult to settle at night and having had partial relieved from oral morphine. Her recent CT scan showed a heterogenous cystic mass causing mass effect to the diaphragm and aorta with moderate ascites. She had trouble with nighttime sleep, reduced mobility, and labile emotion. She has been commenced on opioid for the last 4 months without dose adjustment, and since then she has been on regular opioid for her pain relief. The pain control was gradually achieving a stable state after starting on fentanyl 75mcg/hr for background pain, and oral morphine 15mg as needed. Her disease

had shown further progression restricting her breathing, energy level and causing uncontrolled oedema of her legs. She would require twice breakthrough oral morphine daily (total 30mg/day). Her parents wished to try kratom (locally known as ketum) as the morphine substitute for pain, anxiety and ascites. The patient was switched to kratom drink 10ml twice per day without consultation the managing team. Following this, she demonstrated marked clinical improvement, without the need for breakthrough morphine. However, she still required similar dosage of fentanyl patch. After 9 days on daily kratom use, her parents reported of satisfactory symptoms controlled throughout her terminal stage until she peacefully passed away.

DISCUSSION

Kratom or locally known as 'ketum' in Malaysia is an indole opioid with scientific name as Mitragyna speciosa. It is grown naturally in the tropics of Malaysia, Thailand and Myanmar. Traditionally, it is used as stimulant after hard labour or commonly among the school age adolescent. Some of the stated benefits are for treating pain, anxiety, opioid dependence, weight loss, anti-microbial, anti-diabetic, and muscle relaxant.

Kratom has more than 40 alkaloids and 2 most important one is mitragyna (66%), which is a partial agonist for mu opioid receptor and 7-hydroxy mitragyna (2%), which is 46 times more potent to mu receptor with competitive antagonist to kappa and delta receptors (1). Other alkaloids are present in much lower concentration. These 2 compounds are considered atypical opioid due to similar effect but arresting the beta arestin pathway leading to lesser action of constipation and respiratory depression. It is also important that these alkaloids may also act on different receptors such as dopaminergic, serotonin and adrenergic which lead to mixed mechanism of action. Low dose of kratom (1-5g) has stimulant effect and higher dose (>5g) could potentially lead to opioid like side effect such as constipation, hypotension, dry mouth, and tachycardia. Mitragyna in research has the onset of 5-10 minutes and the half-life for mitragyna was 3.85 hours and for 7-hydroxymiragyna was 2.5 hour (2).

There is paucity of data on the use of kratom in palliative care. Previous case reports in paediatrics were related to neonatal abstinence and adolescent chronic pain (3,4). This is the first case report of using kratom in a child at the end of life. The purpose of palliation is to ensure comfort care, reduce suffering and controlling symptoms such as pain. Our patient was not an opioid naïve and her oral morphine equivalent was a staggering 210mg/day (Fentanyl 75mcg/hr for background pain with oral morphine 30mg/day for breakthrough pain). Our patient was reported to consume only 20ml/day of kratom drink which eliminated the need for oral morphine. Subjective report from the parents revealed that she had a good sleep time and possessing better energy level as parental wishes. This formed part oftheir goals of care.

It is known that morphine works on the mu receptor to promote intracellular changes in to achieve pain control. This works after the process of glucuronidation to produce metabolites such as M3G and M6G. Similarly, fentanyl acts on the same receptor but is 50–100 times more potent than morphine, producing supraspinal analgesic effects. Kratom has different mechanism of action due to different alkaloid properties.

The formation of 7-hydroxymitragynine as a hepatic metabolite is thought to mediate the analgesic effect from the activation of mu opioid receptors. The analgesic properties induced appears to depend on this metabolite rather than the parent compound. Mitragynine is converted to the potent mu-opioid receptor agonist and this conversion is mediated by cytochrome P450 3A isoforms. This explains on the opioid-receptor-mediated analgesic activity of mitragynine.

The pain symptom was subjectively reported as good by parents for morphine substitute in the breakthrough pain episodes. We need to be aware that parents were trained to utilize morphine in pain control and able to gauge the safety use of the drugs accordingly. Secondly, despite kratom drink introduction, fentanyl remained a required drug to control the background pain. It is difficult to titrate equianalgesic for the opiate to the mitragyna compounds. However, experimentally it was thought that 630g of mitragyna would be equivalent to 5 mg of intravenous morphine (ie equivalent to 10 mg of oral morphine). Both fentanyl and mitragyna have potent compound for mu receptor, thus symptom control may be achieved through combination of analgesic, anxiolytic, relaxant and better sleep pattern for the child. Kratom effects have also been described as psychostimulant at small dosages of up to 5 g of plant material and similar to opioids at higher doses of approximately 5 to 15 g (5).

Drug instrumentalization is referred to the use of a psychoactive drug by a non-addicted individual to reach non-drug related goals in life. Instrumentalization goal is prevalent in Southeast Asian because kratom is considered a medication for traditional consumption. Potential benefit would be considered in view of parental desperation to seek for curative approach or trying to improve quality of life using kratom. There is incongruent of decision making, on one hand parents are the best person to select on the route of treatment albeit end-of life care. On the other hand, despite lack of clinical evidence, vulnerable parents are exposed to external influences, testimonies and experimentation to their beloved and dying child.

CONCLUSION

Although this case highlighted the first self-instrumentation by parent to substitute morphine using mitragyna

compound in children with palliative care needs, there are many issues related to adequacy of mitragyna dose, subjectivity of patients' symptom control, the legality of kratom in Malaysian context and experimentation ethical conscience by the managing paediatrician. The use of kratom as personal use in palliative care needs to be cautiously monitored, similar to the trend of cannabis as there is no concrete evidence to utilize the compound at this stage.

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