

Clinical Events in Mad Honey Poisoning: A Single Centre Experience

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Abstract The aim was to evaluate the clinical findings of patients who admitted to the hospital with the diagnosis of grayanotoxin/mad honey poisoning. Thirty-three patients were included in this study. Three patients were female (9%) and the others male (91%). Median age of patients was 52 (42–68). The most frequently observed findings were sinus bradycardia (91%), nausea-vomiting (81.8%), and dizziness (78.8%). Average heart rate was 55.35 ± 6.72 beats/min. Mean systolic and diastolic blood pressures were 77.86 ± 16.64 mmHg and 46.42 ± 12.30 mmHg, respectively. Mad honey poisoning is an important problem that is life-threatening in the Black Sea region of Turkey.

Keywords Mad honey · Grayanotoxin · Intoxication · Clinical event

Mad honey poisoning is a well known phenomenon in the Eastern Black Sea region of Turkey. It is caused by the

consumption of honey containing grayanotoxin from the pollen and nectar of rhododendron species (Gunduz et al. 2006). It is rarely reported outside of Turkey. In addition, mad honey poisoning presented as case reports in the literature (Gunduz et al. 2006, 2008; Yilmaz et al. 2006; Choo et al. 2008; Choi et al. 2007).

People usually consume the honey as a medicinal drug for gastric pain relief or as a sexual stimulant in this region of Turkey (Gunduz et al. 2006, 2008). The mad honey intoxication is frequently characterized by sinus bradycardia, dizziness, hypotension, nausea-vomiting in low doses and nodal rhythm and atrioventricular block, impaired consciousness, seizures in high doses (Yilmaz et al. 2006; Yavuz et al. 1991; Dursunoglu et al. 2007).

We investigated the clinical findings in patients who diagnosed with the mad honey poisoning-associated with grayanotoxin in the emergency department of hospital.

Patients and Methods

Between March 2008 and December 2008, 33 patients with diagnosis of the mad honey poisoning in emergency department of hospital were included in the study. On admission, all patients' physical examination was performed by cardiologist.

In addition, the questionnaire forms associated with the history of honey intake were noted for all patients. This questionnaire forms included the parameters such as patient's age and gender, time of onset of symptoms, systolic and diastolic blood pressure values, heart rate, nausea-vomiting, fainting, dizziness, blurred vision, sweating, mental confusion and duration of hospitalization.

On admission, the electrocardiogram and chest X-ray was taken for all patients. In addition, echocardiography

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was performed for all patients. The complete blood count (CBC) and serum biochemistry levels were studied for all patients. The patients with bradycardia and hypotension were followed through cardiac monitoring. All patients received parenteral fluid during the hospitalization. Atropine was given to all patients for their symptomatic sinus bradycardia and other reasons (i.e. prophylaxis).

Statistical Analysis

Statistical procedures were performed by using SPSS for windows version 11.5 software program. Variables in the study are evaluated for normal distribution using One-Sample Kolmogorov–Smirnov test. Normally distributed data were represented by arithmetic mean and standard deviation and data not normally distributed were represented by median (minimum–maximum) values.

Results and Discussion

Three patients were female (9%) and the others male (91%). Median age of patients was 52 (42–68). The most frequently observed findings during the admission to the emergency department were sinus bradycardia in 30 patients (91%), nausea-vomiting in 27 patients (81.8%), dizziness in 26 patients (78.8%) and mental confusion in 18 patients (54.8%). Average heart rate was 55.35 ± 6.72 beats/min. During the initial electrocardiogram examination in emergency department, sinus bradycardia was observed in 30 (91%) patients. Other rhythm disturbances were not shown during the follow up in emergency department of hospital. In addition, there were severe nausea-vomiting and hypotension in 3 (9%) patients without sinus bradycardia. For all patients, echocardiography revealed normal left ventricular systolic functions. The patient characteristics and clinical findings were shown in Table 1.

In first admission, systolic blood pressure was found lower than 95 mmHg for all patients. Mean systolic and diastolic blood pressures were 77.86 ± 16.64 mmHg and 46.42 ± 12.30 mmHg, respectively. The mean time to onset of symptoms was 1.64 ± 0.87 h. Average amount of consumed honey in patients was 43.88 ± 23.99 gr. Any death event was not observed. All patients were discharged after 3–8 h of follow up.

The beekeeping is common a job in the eastern Black Sea region of Turkey. The honey is widely used as alternative therapies for the reduction in the risk of coronary heart disease and the treatment of gastrointestinal diseases such as gastritis and peptic ulcer in this region of Turkey. Since it is believed that mad-honey has sexual stimulating

Table 1 The demographic and clinical findings of the patients who diagnosed the mad honey poisoning in the emergency department of hospital

Characteristics	Findings
Age, median (range)	52 (42–68)
Sex, n (%)	
Female	3 (9)
Male	33 (91)
Cardiac features (mean \pm SD), %	
Heart rate	55.35 ± 6.72 (beats/min)
Systolic blood pressure	77.86 ± 16.64 mmHg
Diastolic blood pressure	46.42 ± 12.30 mmHg
Sinus bradycardia (<60 beats/min)	30 (91)
Atrioventricular complete block	0
Noncardiac features, n (%)	
Nausea-vomiting	27 (81.8)
Dizziness	26 (78.8)
Mental confusion	18 (54.8)
Sweating	16 (48.5)
Blurred vision	4 (15.1)
Syncope or fainting	4 (15.1)
Amount of consumed honey (mean \pm SD)	43.88 ± 23.99 gr
Time to onset of symptoms (mean \pm SD)	1.64 ± 0.87 h
Death event (%)	0

effects, mad or black-beehive honey is especially produced in this region.

Mad-honey intoxication is caused by grayanotoxins, which are a polyhydroxylated cyclic diterpene that do not contain nitrogen. Also, the mad honey is commonly named as ‘black beehive honey’ by the rural populace (Gunduz et al. 2007). Grayanotoxin is found in the nectar and pollen of certain members of the family Ericaceae, especially *Rhododendron* L. species (*R. luteum* and *ponticum*) in the Black Sea Region of Turkey (Onat et al. 1991a, b). There are various types of grayanotoxin. Grayanotoxin I is the principal toxic form (Poon et al. 2008).

Grayanotoxin binds to specific sodium ion channels in cell membranes. This combination increases sodium channel permeability and inhibits repolarization. The modified sodium channels lack the inactivation process. Thus, excitable tissues including muscle and nerve cells are maintained in a state of depolarization during which entry of calcium into the cells may be facilitated (Maejima et al. 2003; Seyama et al. 1985; Gossinger et al. 1983). Finally, decreased action potential causes sinus node dysfunction (Seyama et al. 1985).

Onat et al. suggested that the cardiac and respiratory symptoms and findings are regulated via the central nervous system, and that the bradycardic effect of

grayanotoxin is mediated by vagal stimulation at the periphery. They investigated the grayanotoxin doses leading to the cardiac side effects are acting through the vagus nerve. They discovered that very small doses delivered intracerebroventricularly yielded the same physiological effects as well as larger doses administered intraperitoneally. They also discovered that bilateral vagotomy of the vagus nerve eliminated the bradycardic effect of grayanotoxin (Onat et al. 1991a, b).

Mad honey intoxication is a usually benign condition and is rarely fatal. Grayanotoxin may cause cardiac disturbances such as low blood pressure or shock, bradyarrhythmia, sinus bradycardia, nodal rhythm, second-degree or complete atrioventricular block (Yilmaz et al. 2006; Gunduz et al. 2008, 2007; Choo et al. 2008; Dursunoglu et al. 2007; Gossinger et al. 1983; Onat et al. 1991a, b, 2004). Moreover, it causes some complaints such as dizziness, nausea-vomiting, sweating, weakness, blurred vision, convulsions and loss of consciousness, extremity paresthesia, excessive perspiration and salivation (Yilmaz et al. 2006; Gunduz et al. 2008; Yavuz et al. 1991; Dursunoglu et al. 2007; Ozhan et al. 2004; Dilber et al. 2002).

In our study, the doses of atropine sulfate 1–2 mg and parenteral fluid was given to all patients with sinus bradycardia and they fully recovered within 3–8 h following the completion of treatment in emergency department. However, 3 (9%) patients who have severe nausea-vomiting with no sinus bradycardia received intravenous fluid and atropine treatment with recovery of symptoms during 3–8-h follow up. Death was not observed due to toxicity. The most common observed toxicities in our patients were found to be sinus bradycardia, nausea-vomiting, dizziness and mental confusion. Additionally, the majority of patients had low systolic and diastolic blood pressure. The death event associated with mad honey poisoning has not been reported so far in English Language Literature. All the complaints are usually temporary and can be treated with atropine, saline infusion and close observation of vital signs for 3–6 h (Gunduz et al. 2008; Choo et al. 2008; Dursunoglu et al. 2007). A temporary transvenous ventricular pacemaker placing was rarely reported (Dursunoglu et al. 2007).

There are still some unanswered questions about honey poisoning. First, the exact time necessary for intoxication is unknown. According to the literature, although it may be dose dependent, it varies from a few minutes to 2 or more hours (Yavuz et al. 1991; Dursunoglu et al. 2007). In our study, it ranged between 1 and 3 h. Second, the toxic dose of black beehive honey is unknown. All forms of mad honey or its ingredients are not same, so the toxic dose varies. In general, the severity of the honey poisoning depends on the amount ingested and the concentration of

grayanotoxin in the honey (Gunduz et al. 2008; Choo et al. 2008; Dursunoglu et al. 2007).

Because grayanotoxins are rapidly metabolized and excreted, patients generally regain normal consciousness and feel better within hours. Additionally, heart rate and blood pressure usually return to normal within 2–9 h (Onat et al. 1991a, b). Our cases monitored in the emergency department were discharged within 3–8 h. Therefore, in mild cases, if heart rate and blood pressure are within normal ranges, the patient may be discharged from the emergency department within the first 6–9 h.

The possibility of honey poisoning should also be considered in previously healthy patients who admitted with unexplained hypotension, bradycardia or other rhythm disturbances, as well as cardiovascular diseases or drug-related conditions (Kumral et al. 2005; Weiss et al. 2008; Eller et al. 2008). Moreover patients who have consumed honey in the Black Sea region of Turkey should be examined carefully because of the possibility of honey intoxication.

In conclusion, the mad honey poisoning may cause the important cardiac problems such as hypotension, bradycardia, atrioventricular block and other symptoms such as nausea-vomiting, dizziness, sweating, and blurred vision. Patients usually recover within 2–8 h with atropine and fluid treatment.

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