

Clinical and laboratory findings in mad honey poisoning: A single center experience

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Abstract

Objective: This study is aimed at analyzing the demographic and clinical characteristics, as well as the hematological-biochemical parameters of patients who admitted to the hospital with the diagnosis of mad honey poisoning.

Materials and Methods: A total of 16 patients who were admitted with mad honey intoxication symptoms and treated in Emergency Department of Sakarya Education and Research Hospital between January 2009 and December 2012 were included in the study. Demographic and clinical characteristics of the patients and hematological, biochemical parameters were obtained from hospital records. Heart rate, systolic and diastolic blood pressure on admission and at discharge were obtained retrospectively.

Results: Sixteen patients (10 males and 6 females, mean age 58.5 ± 10 years, range between 41 and 79) were included in our study. Heart rate was 42 ± 6 beats/min, systolic blood pressure was 73 ± 19 mmHg, and diastolic blood pressure was 45 ± 17 mmHg on admission. In the evaluation of the patients' heart rhythms on admission to the emergency room, nine (56.3%) patients had sinus bradycardia, three (18.8%) patients had nodal rhythm, two (12.5%) patients had first degree atrioventricular block, and two (12.5%) patients had atrial fibrillation. Atropine 1.1 ± 0.4 mg and saline 1125 ± 465 ml were used to treat patients. Patients were discharged with a stable condition after an average 27.7 ± 7.2 h of follow-up. Heart rate was 75 ± 8 beats/min, systolic blood pressure was 132 ± 7 mmHg, and diastolic blood pressure was 82 ± 6 mmHg at discharge. Mortality was not observed. Hematological and biochemical parameters measured at the time of admission were within normal ranges.

Conclusion: Mad honey poisoning should be considered in previously healthy patients with unexplained symptoms of bradycardia, hypotension, and cardiac dysrhythmias. Therefore, diet history should carefully be obtained from the patients admitted with bradycardia and hypotension, and mad honey intoxication should also be considered in the differential diagnosis, as well as primary cardiac, neurologic, and metabolic disorders. Mad honey poisoning may be presented with life-threatening symptoms without any hematological and biochemical disorder.

Key words: clinical and laboratory findings, mad honey, poisoning

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Introduction

Mad honey intoxications are caused by the consumption of honey containing grayanotoxin (GT), which is produced by bees fed from the nectar of *Rhododendron* species (especially *Rhododendron ponticum* and *luteum* species in Turkey).^[1] A typical course of poisoning consists of the gastrointestinal system irritation, cardiac arrhythmias, and neurological

symptoms.^[2] These symptoms include a burning sensation in the throat, itching in the mouth and nose, redness on the skin and eyes, vertigo and headaches, nausea, vomiting, salivation, cramping style abdominal pain, weakness, blurred vision, fever, seizures, bradycardia, hypotension, and changes in consciousness.^[2-5] There are also reports

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of patients with hepatotoxicity,^[6] asystole,^[7] myocardial infarction,^[8] and atrioventricular complete block^[9] caused by mad honey poisoning in rare cases.

The toxic effects are caused by the GT contained in the honey.^[1] GTs are nitrogen-free polyhydroxy cyclic hydrocarbons and are lipid-soluble toxins. Eighteen different GT types have been identified.^[10,11] The main toxin responsible for the cardiac effects of mad honey poisoning is GT I. In addition, GT II has the ability to suppress spontaneous beating from the sinoatrial node. GTs effect by binding to the sodium channels in the cell membranes.^[1,4,5,10,11]

This study is aimed at analyzing the demographic and clinical characteristics, as well as the hematological-biochemical parameters of mad honey intoxication.

Materials and Methods

In our study, 16 patients who were admitted with mad honey intoxication symptoms to Sakarya Educational Research Hospital and treated in the emergency department between January 2009 and December 2012 are included and evaluated, retrospectively.

The mad honey intoxication diagnosis was made through the presence of the findings, such as a history of consumption of regionally prepared raw honey, and the typical symptoms of mad honey poisoning, such as fatigue, nausea, dizziness, bradycardia, and hypotension.

Physical examinations were performed by an internal medicine and a cardiologist. Information related to mad honey intoxication, such as patients' age, gender, time between honey consumption, and onset of symptoms, blood pressure and heart rate at the time of hospital admission, total cardiac rhythm periods in the electrocardiography taken on admission, applied treatment and intensive care requirements, and whether a temporary pacemaker was applied or not were determined. The complete blood count and serum biochemistry levels measured at the time of admission of the patients were obtained from hospital records.

Inclusion and exclusion criteria

The patients with history of consumption of regionally prepared mad honey and the typical symptoms of mad honey poisoning were included in the study. The patients with previous cardiac, renal and thyroid disorders, using any medication effects cardiac rhythm were excluded from the study. Two patients with coronary artery disease, one patient with chronic renal failure and hyperpotassemia, one patient with hypothyroidism on levotiron therapy and two patients with known valvular heart disease were excluded in the study.

Statistical analysis

Data were analyzed with the SPSS 17 software package (SPSS Inc., Chicago, IL). The continuous data of the patients were presented as mean \pm SD, the numbers indicating frequencies were presented as numbers (*n*) and percentages (%).

Results

Of the 16 patients of mad honey poisoning followed-up in our clinic, 10 (62.5%) were male and 6 (37.5%) were female. The mean age of our patients was 58.5 ± 10 years, range between 41 and 79. The mean length of delay of the symptoms of the patients was found to be 95.6 ± 64 min following consumption of the honey. In the analysis of the amount of honey consumed by the patients, it was found that the intoxication symptoms presented after consumption of approximately 2.9 ± 1.2 tablespoons of honey. As the presenting symptoms, 15 patients (93.8%) had nausea and vomiting, 15 patients (93.8%) had dizziness, three patients (18.8%) had syncope, two patients (12.5%) had vision loss, and another two patients (12.5%) had impaired consciousness. Fundoscopic examination was not performed in patients with vision lost because the recovery was rapid. The average heart rate of the patients on admission was found as 42 ± 6 beats/min. The patients' mean systolic blood pressure was 73 ± 19 mmHg, and mean diastolic blood pressure was 45 ± 17 mmHg at the time of admission. In the evaluation of the heart rhythms of the patients on admission to the emergency room, nine (56.3%) patients had sinus bradycardia, three (18.8%) patients had nodal rhythm, two (12.5%) patients had first degree atrioventricular block, and two (12.5%) patients had atrial fibrillation. Atropine 1.1 ± 0.4 mg and saline 1125 ± 465 ml 0.9% was used in treating patients. It was found that all of the patients achieved normal sinus rhythms and normal blood pressure values after treatment, and were discharged approximately after 27.7 ± 7.2 h of follow-up and monitoring. Heart rate was 75 ± 8 beats/min, systolic blood pressure was 132 ± 7 mmHg, and diastolic blood pressure was 82 ± 6 mmHg at discharge. Demographic, clinical characteristics and treatment outcome of patients with mad honey intoxication are given in Table 1. In our study, there were no mortalities due to mad honey intoxication. Hematological and biochemical data are given in Table 2.

Discussion

It is worth noting that most of the patients examined in this case series of mad honey poisoning were middle-aged and elderly males.^[3,12] Gunduz *et al.* in their study have reported in their studies that 85% of patients were male and the mean age was 56.3 ± 12.2 years.^[12] Demircan *et al.* noted in their studies that 85.7% of patients were male and the mean age was 55 ± 11 years.^[13] Ozhan *et al.* have reported in their studies that 63% of patients were male and the mean age

Table 1: Demographic, clinical characteristics and treatment outcome of the patients with mad honey intoxication

| Parameter | N (%), mean \pm SD |
|--|----------------------|
| Gender | |
| Female | 6 (37.5) |
| Male | 10 (62.5) |
| Mean age (years) | 58.5 \pm 10 |
| Onset of symptoms (min) | 95.6 \pm 64 |
| Mean duration of symptoms (min) | 203.4 \pm 120.6 |
| Mean duration of admission (h) | 27.7 \pm 7.2 |
| Mean systolic blood pressure (mmHg) | 73 \pm 19 |
| Mean diastolic blood pressure (mmHg) | 45 \pm 17 |
| Mean pulse rate (beat/min) | 42 \pm 6 |
| Mean quantity of mad honey <i>n</i> (spoons) | 2.9 \pm 1.2 |
| Symptoms (%) | |
| Nausea/vomiting | 15 (93.8) |
| Dizziness | 15 (93.8) |
| Syncope | 3 (18.8) |
| Vision loss | 2 (12.5) |
| Impaired consciousness | 2 (12.5) |
| Cardiac rhythm (%) | |
| Sinus bradycardia | 9 (56.3) |
| Nodal rhythm | 3 (18.8) |
| Atrial fibrillation | 2 (12.5) |
| First degree atrioventricular block | 2 (12.5) |
| Atropine (mg) | 1.1 \pm 0.4 |
| Saline (ml) | 1125 \pm 465 |

SD=Standard deviation

was 40 \pm 10 years.^[3] Furthermore, in our study, 62.5% of the 16 cases examined due to mad honey poisoning were male with a mean age of 58.5 \pm 10 years, similar to the literature. As explanatory factors for gender and age distribution, it was suggested that the middle-aged and elderly male patients use mad honey as a traditional treatment for diabetes mellitus and chronic hypertension, and also prefer it to increase sexual performance.^[13]

The symptoms of toxicity may occur with the consumption of a small amount of honey in these mad honey intoxications. Gunduz *et al.* have reported that in many cases, the symptoms could occur with one tablespoon (15 g) of honey consumption, and emphasized that the symptoms when smaller quantities are consumed.^[12] However, various studies have reported that symptoms may be seen with the consumption of various amounts (5–180 g) of honey.^[3,4,13] In our study, the honey consumption was found as 2.9 \pm 1.2 tablespoons.

Gunduz *et al.* have reported that the symptoms began approximately 2.8 \pm 1.8 h after consuming honey.^[12] Demircan *et al.* emphasized that the symptoms began within 1 \pm 0.5 h after consuming honey.^[13] The length of delay of the symptoms was found as 95.6 \pm 64 min in our study and these findings were consistent with the literature.

Table 2: Hematological and biochemical parameters of the patients with mad honey intoxication

| Parameter | Mean \pm SD | Minimum-maximum |
|--------------------|-----------------------|-----------------|
| WBC (K/uL) | 8,806.2 \pm 2458 | 5,000-13,300 |
| RBC (M/uL) | 4.5 \pm 0.6 | 3.3-5.8 |
| Hemoglobin (g/dl) | 12.9 \pm 2 | 9.6-17.9 |
| HCT (%) | 39.6 \pm 5.6 | 29.3-55.2 |
| Platelets (K/uL) | 283,750 \pm 141,188 | 152,000-751,000 |
| MPV (fl) | 7.7 \pm 1.3 | 6.3-11.4 |
| Neutrophil (K/uL) | 6,073.3 \pm 2,473.7 | 2,600-10,000 |
| Neutrophil (%) | 64.8 \pm 13.0 | 48.3-88.2 |
| Lymph (K/uL) | 2,200 \pm 849.3 | 300-3,500 |
| Lymph (%) | 26.2 \pm 11.7 | 3.2-40.5 |
| Mono (K/uL) | 553.3 \pm 226.3 | 300-1,000 |
| Mono (%) | 6.2 \pm 2.0 | 3.5-9.9 |
| Eosinophil (K/uL) | 161.3 \pm 116.4 | 0-300 |
| Eosinophil (%) | 2.0 \pm 1.6 | 0-5 |
| Baso (K/uL) | 60 \pm 50.7 | 0-100 |
| Baso (%) | 0.58 \pm 0.38 | 0-1 |
| Glucose (mg/dl) | 114 \pm 28.8 | 79-174 |
| Urea (mg/dl) | 36 \pm 11.9 | 20-73 |
| Creatinine (mg/dl) | 0.9 \pm 0.2 | 0.6-1.5 |
| ALT (U/L) | 19 \pm 11 | 9-56 |
| AST (U/L) | 20 \pm 5 | 14-32 |
| Na (mmol/L) | 141 \pm 3 | 133-145 |
| K (mmol/L) | 4.1 \pm 0.5 | 3.5-5.1 |

WBC=White blood cell; RBC=Red blood cell; HCT=Hematocrit; MPV=Mean platelet volume; ALT=Alanine aminotransferase; AST=Aspartate aminotransferase; SD=Standard deviation

In mad honey poisoning, presenting symptoms of hospitalized patients are mostly bradycardia and hypotension. Gunduz *et al.* reported the mean heart rate as 46.6 \pm 12.1 beats/min, systolic blood pressure value as 79.86 \pm 19.4 mmHg, and diastolic blood pressure value as 51.6 \pm 15.2 mmHg on admission to hospital. Ozhan *et al.* reported the mean heart rate as 41 \pm 4 beats/min, systolic blood pressure value as 78 \pm 9 mmHg, and diastolic blood pressure value as 44 \pm 10 mmHg.^[3] Demircan *et al.* stressed that the mean heart rate was 45 \pm 9 beats/min, systolic blood pressure value was 79 \pm 19 mmHg, and diastolic blood pressure value was 58 \pm 13 mmHg.^[13] Similar to previous studies, bradycardia and hypotension were also the primary symptoms of our patients on admission in our study, and the mean heart rate was 42 \pm 6 beats/min, systolic blood pressure value was 73 \pm 19 mmHg, and diastolic blood pressure value was 45 \pm 17 mmHg.

Various cardiac dysrhythmias have been reported related to mad honey poisoning.^[7-9,14-16] It has been reported in case reports and studies that non-specific bradyarrhythmias or sinus bradycardia have been observed in the majority of patients.^[2-4] Heart blocks and conduction disturbances in varying degrees have also been observed, in addition to sinus bradycardia in mad honey intoxication. In a review in which mad honey cases were analyzed, it was reported that

70.5% of the patients had sinus bradycardia or nonspecific bradycardia, and 11% of the patients had nodal rhythm, 8.7% of the patients had complete heart block, 2.9% of the patients had second-degree heart block, 1.4% had Wolff–Parkinson–White syndrome, and 1.4% of the patients had asystole.^[17] Gunduz *et al.* reported that 78.7% of the patients had sinus bradycardia, 12.8% of the patients had nodal rhythm, 6.4% of the patients had normal sinus rhythm, and 2.1% of the patients had complete atrioventricular block.^[12] In the evaluation of the heart rhythms in our study, nine (56.3%) patients had sinus bradycardia, three (18.8%) patients had nodal rhythm, two (12.5%) patients had first degree atrioventricular block, and two (12.5%) patients had atrial fibrillation. In our case series, the rate of atrial fibrillation was considered frequent in comparison to the literature.

Despite the worrying symptoms in the cases of mad honey poisoning, supportive care of electrocardiographic monitoring, normal saline infusion, and intravenous atropine treatment are sufficient for the improvement of symptoms in many patients.^[3,4,12,13] Gunduz *et al.* returned most of the patients to normal rhythm with 0.5–2 mg of intravenous atropine and with sufficient intravenous fluid therapy.^[12] Demircan *et al.* have reported that they used approximately 0.4 ± 0.4 mg of atropine in the treatment.^[13] After treatment of 1.1 ± 0.4 mg of atropine and 1125 ± 465 ml 0.9% of saline in our patients, we observed that normal sinus rhythm and normal blood pressure values were obtained. In rare cases of mad honey poisoning, where atropine and intravenous saline treatment is not sufficient, advanced cardiac life support protocols should be implemented for the treatment of bradyarrhythmias.^[3,4,12,13] In our study, the use of a temporary cardiac pacemaker was not required.

There was no consensus in the conducted studies on how long the patients admitted with mad honey poisoning symptoms would be kept in hospital for follow-up. There are also various treatments and follow-up protocols for patients admitted to different health centers due to mad honey poisoning.^[12] Gunduz *et al.* have reported that patients with mild mad honey poisoning can be discharged safely after 2–6 h of cardiac monitoring.^[4] In another study, Gunduz *et al.* stressed that patients with mad honey poisoning should be followed-up for 6 h in emergency service units, after achieving normal heart rate and blood pressure values.^[12] Similarly, Demircan *et al.* emphasized that patients had recovered after 7 h minimum, following the ingestion of toxic substances, and fully recovered after 23.4 ± 10.5 h.^[13] Ozhan *et al.* reported in their studies that the patients were kept for 24 h in the emergency service for monitoring.^[3] It was found in our study that our patients were discharged approximately 27.7 ± 7.2 h after follow-up and monitoring. These longer periods are because of the abnormalities in cardiac arrhythmia and the severity of the observed symptoms in the patients admitted to our clinic.

Despite several complications, including asystole, during and after the mad honey poisoning, there were no mortalities reported in the literature.^[3,4,7] We also did not encounter any mortality in our study.

Although there are case reports on hepatotoxicity and hypoglycemia due to mad honey poisoning in the literature, there was no study that analyzed hematological and biochemical data.^[6,18] In our study, there were no significant pathological findings in the hematological and biochemical parameters. It is suggested that controlled clinical studies on this subject be performed.

As a result, due to the increased use of natural products in particular, patients admitted to the emergency department with mad honey poisoning can be seen in any part of Turkey. The symptoms were often related with cardiotoxic effects of the mad honey, mostly hypotension and bradycardia were observed in the patients. This study showed that it is possible to achieve normal heart rate and blood pressure values with atropine and intravenous saline in the treatment of the majority of patients but rarely invasive treatments like temporary cardiac pacing may be needed. Mad honey poisoning should be considered in the differential diagnosis, especially for middle-aged and elderly male patients, who are admitted to the emergency department with unexplained hypotension with bradycardia. There were no pathological findings in the hematological and biochemical parameters of the patients with mad honey intoxication. It should be kept in mind that mad honey poisoning may be presented with life-threatening symptoms without any hematological and biochemical disorder.

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