

# Is there a difference in mad honey poisoning between geriatric and non-geriatric patient groups?

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**Abstract. – OBJECTIVE:** This study aims to investigate the demographic, toxicological characteristics of the mad honey intoxication at ages 65 and above, to analyze the electrocardiographic parameters, and to compare with the mad honey intoxication at ages below 65 years.

**PATIENTS AND METHODS:** Eighty-two patients, who had been treated and followed-up between June 2013 and November 2014 in the Emergency Service of the Findıklı State Hospital, Turkey, due to diagnosis of mad honey intoxication, were included in our observational study. Age, gender, toxicological characteristics, laboratory parameters, heart rates, systolic and diastolic blood pressures, laboratory analyses and electrocardiographic data of the patients were recorded and analyzed. Patients with known coronary artery disease, chronic renal failure, arrhythmias, valvular heart disease, history of thyroid disease and electrolyte imbalance were not included in the study.

**RESULTS:** Eighty-two (80.5% was male and the mean age was  $53 \pm 15$  years) patients followed-up due to mad honey intoxication were included in our study. There were 64 (78%) patients aged below 65 years, and 18 (22%) patients aged 65 and above. The mean heart rate was  $45 \pm 7$  beats/min, systolic blood pressure was  $83 \pm 12$  mmHg and diastolic blood pressure was  $52 \pm 9$  mmHg on admission. The onset of symptoms of the patients was found as 0.84 hours on average after mad honey consumption, the average amount of honey consumed

was  $3.7 \pm 1.1$  tablespoons, and the mean recovery time of the symptoms was found to be 1.04 hours. The most common presenting symptoms were nausea-vomiting in 82 (100%) patients and dizziness in 73 (89%) patients. Patients were found to consume mad honey mostly for achieving a remission in gastrointestinal complaints ( $n=18$ , 22%), and for utilizing its blood pressure lowering properties ( $n=11$ , 13.4%), in addition to the dietary consumption. Looking at the heart rates of the patients on admission to the emergency service, 65 (79.3%) patients had normal sinus rhythm/sinus bradycardia, 12 (14.6%) patients had a 1st degree atrioventricular block, 3 (3.7%) patients had nodal rhythm, 1 (1.2%) patient had atrial fibrillation and 1 (1.2%) patient had preexcitation. There were no significant pathological findings in the routine laboratory examinations of patients. It was found that all patients achieved normal sinus rhythm and normal blood pressure values after medical treatment, and were discharged approximately 5.65 hours after observation and follow-up. In our study, prolonged intensive-care need, pacemaker need and mortality caused by mad honey intoxication were not found. In the comparison of data of all patients above and below 65 years of age, there was a statistically significant finding that the geriatric patients consume mad honey mostly for hypotensive purposes and gastrointestinal complaints; in addition, the symptoms were starting early and the recovery period was longer in geriatric patients.

**CONCLUSIONS:** The mad honey poisoning should be considered in previously healthy patients with unexplained symptoms of bradycardia, hypotension, and atrioventricular block. Therefore, diet history should carefully be obtained from the patients admitted with bradycardia and hypotension. And, in addition to the primary cardiac, neurological and metabolic disorders, mad honey intoxication should also be considered in the differential diagnosis. In geriatric patients admitted due to mad honey intoxication, the mad honey is usually consumed to reduce blood pressure and resolve gastrointestinal problems; and, their symptoms begin early, and last longer after mad honey consumption. In terms of other parameters, the geriatric age group has similar characteristics to non-geriatric age group.

*Key Words:*

Mad honey, Intoxication, Geriatric and non-geriatric patient

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## Introduction

In mad honey intoxications, the typical course of poisoning consists of gastrointestinal system irritation, cardiac arrhythmias, and neurological symptoms<sup>1</sup>. These symptoms include a burning sensation in the throat, itching in the mouth and nose, redness of the skin and eyes, vertigo and headaches, nausea, vomiting, salivation, cramping abdominal pain, fatigue, blurred vision, fever seizures, bradycardia, hypotension and changes in consciousness<sup>1-3</sup>. There are also reports in rare case reports on the patients with hepatotoxicity<sup>4</sup>, asystole<sup>5</sup>, myocardial infarction<sup>6</sup>, ECG ST-segment changes<sup>7</sup>, atrial fibrillation<sup>8</sup>, AV complete block<sup>9</sup>, syncope<sup>10</sup>, and transient ischemic attack<sup>11</sup> caused by mad honey intoxication. The mad honey intoxications in Turkey are caused usually by the consumption of honey containing grayanotoxin, which is produced by bees fed with “*Rhododendron ponticum*” and “*Rhododendron luteum*” flowers<sup>12</sup>.

The grayanotoxins (GT) contained in this honey leads to the toxic effects<sup>12</sup>. Grayanotoxins are nitrogen-free polyhydroxic cyclic hydrocarbons and these toxins are soluble in lipid. There are eighteen different types of grayanotoxin identified<sup>13,14</sup>. In mad honey intoxication, GT I is the main toxin responsible for the cardiac effects. Moreover, GT II has also the ability to suppress spontaneous beat rate of the sinoatrial (SA) node. Grayanotoxins act by binding to the sodium channels in cell membranes<sup>3,12-14</sup>.

In our study, 82 patients, who had been followed-up between June 2013 and November 2014 in Emergency Service in Findikli State Hospital, Turkey, due to mad honey intoxication, were included. It was aimed to analyze the demographic, toxicological characteristics of the mad honey intoxication cases, to analyze the electrocardiographic parameters, and to compare mad honey intoxication at ages above and below 65 years.

## Patients and methods

Eighty-two patients, who had been followed-up due to mad honey intoxication between June 2013 and November 2014 in Findikli State Hospital, Turkey, were included in the study. The diagnosis of mad honey intoxication was performed through the history of consumption of raw honey, prepared regionally, and the presence of typical symptoms of mad honey intoxication such as fatigue, feeling of dizziness, nausea, vertigo, bradycardia and hypotension. Physical examination was performed by emergency service physician and an internal medicine specialist. Electrocardiogram was interpreted by cardiology specialists. Patient data were recorded in the standard form created to follow the mad honey intoxication cases. In the file, patients’ age, gender, presenting blood pressure values and heart beat rates, cardiac rhythm in the ECG taken on admission, presenting symptoms, reasons for honey consumption, history of consumption of the same honey, the recovery time and the time between honey consumption and onset of symptoms, follow-up time in the emergency service, treatment administered, intensive care need and temporary pacemaker application were recorded. Patients’ hematologic, biochemical and cardiac enzyme parameters measured at the time of admission were examined. Statistical significance between the recorded parameters of patients below and above 65 years age was investigated. The patients with known coronary artery disease, chronic renal failure, arrhythmias, valvular heart disease, thyroid disease and electrolyte imbalance were not included in the study.

## Statistical Analysis

The SPSS 18.0 software program (SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis on patient data. Categorical variables were expressed by numbers or percentages, and

the continuous variables were expressed by mean  $\pm$  standard deviation. Chi-square test and Fisher's exact test were used in the comparison of the categorical variables. In the comparison of continuous variables, the Kolmogorov-Smirnov test was used first to test normal distribution of the parameters. The independent samples *t*-test was used to compare the data that fit to a normal distribution. A probability value of  $p < 0.05$  was considered statistically significant.

## Results

In our study, 82 patients (66 male patients [80.5%] and the mean age was  $53 \pm 15$  years) followed-up due to mad honey intoxication were included. There were 64 (78%) patients aged below 65 years, and 18 (22%) patients aged 65 and above.

Patients' measured mean heart rate was  $45 \pm 7$  beats/min, systolic blood pressure was  $83 \pm 12$  mmHg and diastolic blood pressure was  $52 \pm 9$  mmHg on admission to the emergency service. The onset of symptoms of the patients was found as 0.84 hours on average after mad honey consumption, the average amount of honey consumed was  $3.7 \pm 1.1$  table spoons, and the mean recovery time of the symptoms was found to be 1.04 hours.

Eighty-two patients (100%) had nausea-vomiting, 73 patients (89%) had vertigo, 13 patients (15.3%) had blurred vision, 17 patients (20.7%) had a change in consciousness, and 3 patients (3.7%) had chest pain as the presenting symptoms in the emergency service.

In addition to nutritional consumption, it was learned that mad honey was consumed for gastrointestinal complaints in 18 patients (22%), for lowering blood pressure in 11 patients (13.4%), for the treatment of diabetes in 1 patient (1.2%), and for cancer prevention in 1 patient (1.2%).

No significant pathological finding was identified in the laboratory examinations of the patients.

In the evaluation of the heart rhythms of patients on admission to emergency service, 65 (79.3%) patients had normal sinus rhythm/sinus bradycardia, 12 (14.6%) patients had a 1<sup>st</sup> degree atrioventricular block, 3 (3.7%) patients had nodal rhythm, 1 (1.2%) patient had atrial fibrillation and 1 (1.2%) patient had preexcitation.

Approximately 0.78 mg Atropine and 841  $\pm$  332 ml 9% isotonic fluid was used in the treat-

ment of patients. It was found that all patients achieved normal sinus rhythm and normal blood pressure values after treatment, and were discharged approximately 5.65 hours after observation and follow-up. In our study, prolonged intensive-care need, pacemaker need and mortality caused by mad honey intoxication were not found.

Comparison data of patients above and below 65 years of age was summarized in Table I. The parameters of 18 geriatric patients were summarized in Table II. There was a statistically significant finding that the geriatric patients consume mad honey mostly for lowering blood pressure and for gastrointestinal complaints; in addition, the symptoms were starting early, and the recovery period was longer in geriatric patients.

## Discussion

There were no studies in the literature investigating mad honey intoxication in the geriatric patients. Our study is the first research investigating the mad honey intoxication in the geriatric age group. The mad honey intoxication is seen especially in the Eastern Black Sea region of Turkey. Mad honey intoxications are mostly caused by the consumption of honey containing grayanotoxin, which is produced by the bees fed with "*Rhododendron ponticum*" and "*Rhododendron luteum*" flowers<sup>1,12</sup>. It is noteworthy that the most of the patients examined in the case series of mad honey intoxication were elderly male. In a study by Hanci et al<sup>1</sup> conducted with 72 patients, the mean age was  $49 \pm 11$ , the maximum age was 78, and 81.9% of the patients was male. In a study by Uzun et al<sup>15</sup> conducted with 46 patients, the mean age was  $52 \pm 17$ , the maximum age was 93, and 78.3% was male. In a study by Yaylaci et al<sup>16</sup> conducted with 16 patients, the mean age was  $58 \pm 10$ , the maximum age was 79, and 62.5% was male. Also, in our study, 80.5% of the 82 patients examined due to mad honey intoxication was male and the mean age was  $53 \pm 15$  years, similar to the literature. Of the patients, 18 (22%) were in the geriatric age group, and the maximum age was 86.

It has been suggested as explanatory factors for the gender and age distribution that the elderly male patients use mad honey for diabetes mellitus and chronic hypertension as a traditional treatment and also prefer it to increase sexual performance<sup>17</sup>. In addition to dietary consump-

**Table I.** Clinical characteristics all patient and statistical analyses of geriatric and non geriatric patients.

Parameters	All patient	Non geriatric patient	Geriatric patient	p
Number of patients. N (%)	82	64 (78%)	18 (22%)	>0.05
Male/Female. N (%)	66 (80.5%) / 16 (19.5%)	52 (%78.8) / 12 (%75)	14 (%21.2) / 4 (%25)	>0.05
Mean age (years)	53 ± 15	47 ± 11	73 ± 6	>0.05
Mean systolic blood pressure (mmHg)	83 ± 12	82 ± 12	87 ± 12	>0.05
Mean diastolic blood pressure (mmHg)	52 ± 9	51 ± 9	52 ± 9	>0.05
Mean pulse rate (beat/min)	45 ± 7	45 ± 6	45 ± 8	>0.05
Mean quantity of mad honey (spoons)	3.7 ± 1.1	3.5 ± 1	4.2 ± 1.2	>0.05
Symptoms. N (%)				
• Dizziness	73 (89%)	55 (85.9%)	18 (100%)	>0.05
• Nausea/vomiting	82 (100%)	64 (100%)	18 (100%)	>0.05
• Blurred vision	13 (15.9%)	8 (12.5%)	5 (27.8%)	>0.05
• Change in consciousness	11 (13.4%)	7 (8.5%)	4 (4.9%)	>0.05
• Chest pain	3 (3.7%)	1 (1.6%)	2 (11.1%)	>0.05
Reason of consumption				
• Nutrition	82 (100%)	64 (100%)	18 (100%)	>0.05
• Lower blood pressure	11 (13.4%)	4 (6.3%)	7 (38.9%)	<0.001
• Lower serum glucose level	1 (1.2%)	1 (1.6%)	0	
• Enhance sexual desire	0	0	0	
• Gastrointestinal disorders	18 (22%)	10 (15.6%)	8 (44.4%)	0.009
• Treatment of cancer	1 (1.2%)	0	1	
Previous consumption	23 (%28)	15 (23.4%)	8 (%44.4)	>0.05
Onset of symptoms (hour)	0.84	0.87	0.75	0.05
Mean duration of symptoms (hour)	1.04	1.01	1.14	0.045
Mean duration of admission (hour)	5.65	5.56	5.94	>0.05
Saline (ml)	841 ± 332	843±354	833±242	>0.05
Atropine (mg)	0.78	0.81	0.67	>0.05
Cardiac rhythm. N (%)				
• Normal sinus/Sinus bradycardia	65 (79.3%)	52 (81.3%)	13 (72.2%)	>0.05
• Nodal rhythm	3 (3.7%)	2 (3.1%)	1 (5.6%)	>0.05
• Atrial fibrillation	1 (1.2%)	0	1 (5.6%)	
• First degree atrioventricular block	12 (14.6%)	9 (14.1%)	3 (16.7%)	>0.05
• Preexcitation	1 (1.2%)	1 (1.6%)	0	

tion, it was learned in our study that mad honey was consumed for gastrointestinal complaints in 18 patients (22%), for lowering blood pressure in 11 patients (13.4%), for the treatment of diabetes in 1 patient (1.2%), and for cancer prevention in 1 patient (1.2%). In addition, the consumption of mad honey for lowering the blood pressure and for gastrointestinal problems was statistically significantly higher in the geriatric patients compared to the non-geriatric patient group. The lack of data on the use for sexual performance in our study was thought to be due to sociocultural characteristics of our region, which has a tendency to not to tell attitudes and behaviors related to sexuality.

In intoxications caused by mad honey consumption, the symptoms of toxicity may occur with the consumption of a small amount of honey. Gunduz et al<sup>18</sup> have reported in their study con-

ducted with 47 patients that the symptoms occurred with 1 tablespoon of honey consumption in most (67.4%) of the patients. On the other hand, various studies<sup>1,2,15</sup> have reported that symptoms may be seen with the consumption of different amounts of honey. In our study, the honey consumption was found as 3.7 ± 1.1 tablespoon. There was no statistically significant difference between the groups, despite the higher amount of honey consumed in the geriatric patient group compared to the non-geriatric patient group.

Gunduz et al<sup>18</sup> have reported that the symptoms began 0.5 to 9 hours after consumption of honey (approximately 2.8 ± 1.8 hours). Demircan et al<sup>17</sup> have emphasized that the symptoms began within 1 ± 0.5 hours after the honey consumption. In our study, the time of onset of the symptoms was found as 0.84 hours, consistent with the literature. The time of onset of the

**Table II.** Clinical characteristics of the geriatric patients.

No	Age years	Gender	Systol mmHg	Diastol mmHg	Pulse beat/min	Spoons	Onset of symptoms hour	Mean duration of symptoms hour	Mean duration of admission hour	Saline ml	Atropine mg	Cardiac rhythm
1	65	M	70	40	37	6	0,5	1	6	1000	1	Sinus bradycardia
2	66	M	80	40	46	5	1	1	6	500	0,5	Nodal rhythm
3	67	M	70	40	32	3	1	1	6	1000	1	Sinus bradycardia
4	68	F	80	50	45	5	1	1	6	500	1	First degree atrioventricular block
5	68	M	90	60	46	3	1	1	5	500	1	Sinus bradycardia
6	70	M	100	60	40	5	1	1	6	1000	1	Sinus bradycardia
7	70	F	110	50	46	3	1	1	4	500	0	Atrial fibrillation
8	71	M	80	50	43	3	0,5	1	7	1000	2	First degree atrioventricular block
9	71	M	100	60	47	3	0,5	1	6	1000	0	Sinus bradycardia
10	72	M	90	60	41	3	1	1	6	1000	1	First degree atrioventricular lock
11	74	M	70	40	38	6	0,5	1	6	1000	1	Sinus bradycardia
12	76	M	100	70	59	6	0,5	1	6	1000	0	Normal sinus rhythm
13	78	M	90	60	45	5	0,5	1	6	1000	0	Sinus bradycardia
14	78	F	100	60	71	5	0,5	2	6	1000	0	Normal sinus rhythm
15	80	M	90	50	53	6	0,5	2	7	1000	0	Normal sinus rhythm
16	80	M	70	40	40	3	1	1,5	6	500	1	Sinus bradycardia
17	81	F	90	60	47	3	1	1	6	1000	0,5	Sinus bradycardia
18	86	M	90	60	45	4	0,5	1	6	500	1	Sinus bradycardia

symptoms were significantly shorter in the geriatric patient group compared to non-geriatric patient group, and it was thought that this might be due to the amount consumed.

In mad honey intoxication, bradycardia and hypotension are the most common presenting symptoms of patients. Gunduz et al<sup>18</sup> have reported the mean heart rate as  $46.6 \pm 12.1$  beats/min (min 30-max 77), systolic blood pressure value as  $79.86 \pm 19.4$  mmHg (min 50-max 140) and diastolic blood pressure value as  $51.6 \pm 15.2$  mmHg (min 20-max 100), on admission to hospital. Ozhan et al<sup>2</sup> 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. Hanci et al<sup>1</sup> reported the mean heart rate as  $47.79 \pm 4.34$  beats/min, mean systolic blood pressure as  $73.33 \pm 16.41$  mmHg and the mean diastolic blood pressure as  $46.32 \pm 12.40$  mmHg. Similar to previous studies, bradycardia and hypotension were the primary symptoms on admission in our study as well, and the mean heart rate was  $45 \pm 7$  beats/min, systolic blood pressure value was  $83 \pm 12$  mmHg and diastolic blood pressure value was  $52 \pm 9$  mmHg in our patients on admission to the hospital. These findings were in line with previous reports. There was no significant difference in the geriatric patient group in these parameters.

Various cardiac arrhythmias have been reported associated with mad honey intoxication<sup>5-9,13-15,19</sup>. It has been reported in the case reports and studies that the non-specific bradyarrhythmias or sinus bradycardia have been observed in the majority of patients<sup>1,2,16,20</sup>. Heart blocks and conduction disturbances in varying degrees can also be observed, besides the sinus bradycardia in mad honey intoxication. It has been reported in a review, where 70 mad honey cases in 12 different studies had been examined, that 75% 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<sup>21</sup>. In the evaluation of the heart rhythms of patients on admission to emergency service, 65 (79.3%) patients had normal sinus rhythm/sinus bradycardia, 12 (14.6%) patients had a 1st degree atrioventricular block, 3 (3.7%) patients had nodal rhythm, 1 (1.2%) patient had atrial fibrillation and 1 (1.2%) patient had preexcitation. The rate of sinus bradycardia was 72.2% in the geri-

atric patient group in our study. Therefore, it is understood that the arrhythmias in the geriatric group seen in mad honey intoxication was not different from that of the non-geriatric group.

There was no mortal case in the case series and review of the literature related to mad honey intoxication. Despite the serious and worrying symptoms in the cases of mad honey intoxication, supportive care consisting of electrocardiographic monitoring, normal saline infusion and intravenous atropine treatment is sufficient for the improvement of symptoms in many patients<sup>1,2,16,21</sup>. Normal sinus rhythm and normal blood pressure values were found to be achieved after a 0.78 mg atropine and 841  $\pm$  332 ml 0.9% isotonic fluid treatment in our patients. In our study, intensive-care need, temporary cardiac pacemaker application, and mortality were not found.

In the studies conducted, there was no consensus on the follow-up period of the patients admitted with mad honey intoxication symptoms in hospital. There are also various treatment and follow-up protocols in different health centers applied to the patients admitted due to mad honey intoxication<sup>18</sup>. Gunduz et al<sup>3</sup> reported that the patients with mild mad honey intoxication can be discharged safely after 2-6 hours of cardiac monitoring. Gunduz et al<sup>18</sup> have stressed out in another study that the patients with mad honey intoxication should be followed up for 6 hours in emergency service units, after achieving normal heart beat rate and blood pressure values. Yaylacı et al<sup>20</sup> applied approximately  $27.7 \pm 7.2$  hours of follow-up and monitoring in their studies, and these longer periods were found to be associated with the abnormalities in cardiac rhythms and the severity of observed symptoms in the consulted patients. It was found in our study that the patients were discharged approximately 5.65 hours after follow-up and monitoring. In our study, the shorter follow-up period was associated with the rapid diagnosis and early treatment made by emergency personnel, who are experienced in this regard and know the symptoms of mad honey intoxication due to frequent mad honey intoxication cases observed in our region.

There are case reports in the literature on the syncope and transient ischemic attack-like symptoms in the geriatric patient group<sup>10,11</sup>. In our study, the most common symptoms in the geriatric patient group were dizziness and nausea-vomiting, and 4 (4.9%) patients had changes in consciousness.

## Conclusions

As a result, it's not surprising to see patients admitted to the emergency departments countrywide due to mad honey intoxication in Turkey because of the consumption of mad honey both as nutrition and as an alternative treatment method. In our study, we have identified that most of the mad honey poisoning patients were middle-aged male patients, and the symptoms were often hypotension and bradycardia. We found that, it was possible to achieve a normal heart rate and blood pressure values with atropine and intravenous crystalloid fluid treatment in all patients. For this reason, mad honey intoxication should also be considered in the differential diagnosis, especially for the middle-aged male patients, who admit to the emergency department with unexplained hypotension with bradycardia. Many parameters in the geriatric age group were found to be similar to the non-geriatric patients. There was a statistically significant finding that the geriatric patients consume mad honey mostly for lowering blood pressure and for gastrointestinal complaints; in addition, the time of onset of symptoms was shorter and the recovery period was longer in geriatric patients.

## Conflict of Interest

The Authors declare that they have no conflict of interests.

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