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TOXICOLOGY INVESTIGATION

Nutmeg Poisonings: A Retrospective Review of 10 Years Experience from the Illinois Poison Center, 2001–2011

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Abstract Nutmeg is a commonly consumed spice. The toxic effects of nutmeg have been purported to be due mainly to myristicin oil. Prior poison center series of nutmeg exposures show very few unintentional exposures of nutmeg to children younger than 13. Case series from these centers did not record drug exposures combined with nutmeg. This study is a review of Illinois Poison Center (IPC) data regarding nutmeg exposures from January of 2001 to December 2011. The goal of this study was to compare the Illinois data to the literature as well as look for current trends in nutmeg poisonings. The data were extracted using the code for hallucinogenic plants in the IPC database, and poisonings unrelated to nutmeg exposure were eliminated. Medical outcomes were noted as recorded. Thirty-two cases of nutmeg ingestion were reported. Of the 17 (53.1 %) unintentional exposures, 10 subjects (58.8 %) were under the age of 13. Four of the exposures in children under the age of 13 were ocular exposures. Fifteen exposures (46.9 %) were intentional exposures. Of these intentional exposures, five (33.3 %) were recorded to have combined drug intoxication. All of these were between the ages of 15 and 20. One patient with polypharmaceutical exposure required ventilatory support in the hospital. Our study shows an unexpected percentage of unintentional exposures in juveniles under the age of 13, out of the total exposures to nutmeg. Mixing of nutmeg with other drugs was seen and required more intervention in adolescents. More education about these two factors, i.e., nutmeg exposures as intentional polypharmacy in adolescents and unintentional exposures in young children, is advised.

Keywords Nutmeg · Myristicin oil · Polypharmacy · Overdose · Hallucinogen

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Introduction

Nutmeg is a commonly used spice derived from the seed of the *Myristica fragrans* tree. The spice is normally used in small amounts to flavor seasonal beverages and baked goods. When large amounts are taken, several toxic effects, including tachycardia, nausea, vomiting, agitation, and hallucinations, have been noted [1–3]. These effects have been attributed to myristicin, the ingredient contributing to the largest portion of

the volatile oil of nutmeg. Myristicin is metabolized to 3-methoxy-4,5 methylenedioxyamphetamine also known as MMDA. MMDA is a sympathomimetic with hallucinogenic properties and believed to be the compound associated with nutmeg's hallucinogenic effects [1]. Myristicin is also implicated in monoamine oxidase inhibition [2]. Another important chemical component is elemincin, which has been shown to decrease muscle coordination and activity [4]. Many of the toxic cases reported to poison centers across the country are the result of abuse of the spice as a means of inducing this purported hallucinatory effect [2, 3]. Recent review articles have found that nutmeg exposures reported to poison centers were mostly intentional and seen primarily in adolescents [2, 3]. There are two cases in the literature of fatalities from nutmeg overdose [5, 6]. Importantly, the most recent case of fatality from nutmeg overdose involved the simultaneous abuse of a fatal dose of flunitrazepam [2, 5].

The current study is a retrospective review of calls received by the Illinois Poison Center (IPC), from January, 2001 to December, 2011, regarding nutmeg exposures. We performed our analysis to see if the patterns in Illinois resembled those of data centers in Texas and California and to examine current trends in Illinois nutmeg intoxications.

Methods

The IPC services the state of Illinois and allows telephone access to a trained staff that provides information and advice about toxic exposures. Data from all calls received are noted and kept on a data entry form stored on the IPC database using Visual Dotlab. For this inquiry, all data for nutmeg exposures received by the IPC from January 1st, 2001 to December 31st, 2011 were reviewed. IRB approval was not required as all the data was de-identified. These data were queried using the American Association of Poison Control Centers (AAPCC) generic code for hallucinogenic plants (AAPCC code 093000). Next, resulting cases were searched for the terms "nutmeg" and "*Myristica fragrans*," both by searching for the coding number of these items as well as searching free text descriptions of patient exposures. Prior to analysis, identifiers of patients and their providers were removed. Subsequently, data were extracted using Microsoft Excel software (Microsoft Corp, Redmond, WA). To ensure accuracy in counting, the data were also extracted by programming methods using regular expression mining tools. Data were sorted by age, gender, route of exposure, classification as intentional or unintentional, amount ingested, outcome, treatment, and site of treatment. Medical outcomes were classified by trained health care professionals at the IPC based on those used in the National Poison Data System)database and appear as None, Minor, Moderate, Major, Death, or Unable to follow up (potentially toxic exposure) [7]. Adult patients whose ages were unknown (but who were classified as over the age of 20 years) were not included in age calculations. Two-tailed probability Fisher's exact tests was used to compare categorical data. Statistical significance was defined as $p<0.05$. Calculations were performed using R, version 2.14.0, (Institute for Statistics and Mathematics, Vienna Austria).

Results

A total of 32 cases of nutmeg ingestion were reported to the IPC between 2001 and 2011 (see Tables 1 and 2). The patients' ages ranged from 2 to 30 years old with a mean of 13.3 (standard deviation of 8.35) and a median of 16. Of the total, 22 patients (68.8 %) were male and 10 patients (31.3 %) were female. Fifteen exposures (46.9 %) were classified as intentional exposures. Of the intentional exposures, 13 (86.7 %) were males and 10 (66.7 %) were patients between the ages of 13 and 19. Of the 17 (53.1 %) unintentional exposures, 10 (58.8 %) were under the age of 13, 2 (11.8 %) were between ages 13 and 19, 3 (17.6 %) were over the age of 19, and 3 (17.6 %) were adults whose age was unknown. Those younger than 13 were significantly less likely to have intentionally been exposed to nutmeg than older patients ($p<0.05$).

In total, ten (31.3 %) patients were treated in a hospital, seven (70.0 %) of which were patients that had intentionally

Table 1 Patient demographics

	Intentional (%) n=15	Unintentional (%) n=17	Total (%) n=32
Patient gender			
Male	13 (59.0)	9 (40.9)	22 (68.8)
Female	2 (20.0)	8 (80.0)	10 (31.2)
Patient age (years)			
<13	0	10 (100)	10 (31.2)
13–19	10 (83.3)	2 (16.7)	12 (37.5)
>19	2 (40.0)	3 (60.0)	5 (15.6)
Unknown (above age 20)	3 (60.0)	2 (40.0)	5 (15.6)
Management site			
Own residence	7 (35.0)	13 (65.0)	20 (62.5)
Hospital	7 (70.0)	3 (30.0)	10 (31.2)
Unknown acute care facility in Illinois	1 (50.0)	1 (50.0)	2 (6.25)
Outcome			
No effect	0	5 (100)	5 (15.6)
Minor	5 (35.7)	9 (64.3)	14 (43.8)
Moderate	4 (100)	0	4 (12.5)
Major	0	0	0
Death	0	0	0
Follow up unknown	6 (66.7)	3 (33.3)	9 (28.1)

Table 2 Clinical effects

	Intentional (%) n=15	Unintentional (%) n=17	Total (%) n=32
Cardiovascular			
Hypertension	0	1 (7.14)	1 (2.27)
Tachycardia	3 (10.0)	0	3 (6.82)
Gastrointestinal			
Nausea	1 (3.33)	2 (14.3)	3 (6.82)
Vomiting	2 (6.67)	1 (7.14)	3 (6.82)
Upset	2 (6.67)	1 (7.14)	3 (6.82)
Central nervous system			
Hallucination/paranoia	4 (13.3)	0	4 (9.08)
Agitation/irritability	3 (10.0)	1 (7.14)	4 (9.08)
Drowsiness	3 (10.0)	1 (7.14)	4 (9.08)
Dry mouth	2 (6.67)	1 (7.14)	3 (6.82)
Confusion	1 (3.33)	0	1 (2.27)
Seizure	1 (3.33)	0	1 (2.27)
Dizziness/vertigo/syncope	4 (13.3)	1 (7.14)	5 (11.4)
Respiratory			
Depression	1 (3.33)	0	0
Ocular			
Ocular dysfunction	0	4 (28.6)	4 (9.08)
Mydriasis	3 (10.0)	0	3 (6.82)
Blurred vision	1 (3.33)	1 (7.14)	2 (4.55)
Total	30	14	44

ingested the spice. In this data, intent was not significantly associated with presentation to a healthcare facility (p=0.12). Four (57.1 %) of the seven intentional use patients were admitted and received medical treatment. All patients that were hospitalized were between 15 and 17 years of age.

Those with intentional nutmeg ingestion were significantly more likely to have ingested other substances than those with unintentional exposure (p=0.015). Of the 15 intentional exposures, 5 (33.3 %) were recorded to have combined drug intoxication. These patients ranged in age from 15 to 20 (see Tables 3 and 4). Two of the incidents of mixed drug use were classified as possible suicide attempts. All four of the hospitalized patients had taken more than one substance.

Table 3 Hospital treatments

Age	Sex	Treatments
17	Male	Intravenous fluid, benzodiazepines, activated charcoal
17	Female	Intravenous fluid
15	Male	Intravenous fluid, benzodiazepines
16	Female	Intravenous fluid, antihistamine, ventilator/oxygen

Table 4 Secondary drugs taken

Age	Sex	Drugs taken
17	Male	Cannabis
17	Female	Amphetamines, lisdexamfetamine
15	Male	Benzodiazepines, diphenhydramine
16	Female	Duloxetine, clonazepam, benzodiazepines, acetaminophen, K2
20	Male	Cough syrup, acetaminophen, antihistamine

Discussion

This study analyzes the reports of nutmeg exposures called to the IPC during the 10-year period from 2001 to 2011. Like other inquiries of a similar nature, the data show cases of toxicity from both intentional and unintentional exposures to nutmeg. Though retrospective data regarding these exposures has been previously reported [2, 3], our data differs. One difference involves the percentage of exposures of children under the age of 13 years old. In a recent study of reports of nutmeg toxicity calls to the California Poison Control System, only 3 out of 119 cases (2.5 %) involved children under the age of 13 [2]. An examination of the Texas Poison Centers also revealed low numbers with just 2 patients out of 17 juvenile cases being under 13 (11.8 %) [3]. In the present report from the IPC, we found 10 out of the total of 32 exposures (31.3 %) occurred in individuals under the age of 13. The unexpected percentage of juvenile cases in our series observed could be due to the small sample size or due to differences in the population studied. This finding in our study suggests that there is a need to educate parents regarding child safety and the risk of exposure to toxic household items. Additional studies will be required to determine the clinical relevance of these findings and the appropriate methods of prevention.

The data received from the IPC presents obstacles due to its retrospective nature and potential for sampling error. In addition, many reports documented distress calls to the IPC but were unable to follow up with information from any hospital or urgent care facility. This discrepancy is further exaggerated by the small sample size of the data. It is anticipated that most cases of toxicity arising from nutmeg exposure are underreported. Underreporting of toxic exposures to hallucinogenic and other substances used to induce intoxication has been described frequently in the toxicology literature [8–10]. Therefore, these kinds of retrospective studies likely represent a small sample of the exposed population, but are nonetheless useful in clarifying the effects of clinical exposure.

An important note to make about classification of reports of toxic exposures can be illustrated from this data. There were several cases in which classifying the exposure was difficult because the intent of the patient was unclear. One example of

this situation was a male patient who said that he drank a cup of Starbucks coffee containing ten tablespoons of nutmeg. This case was classified by the call recipient as unintentional, though the circumstances strongly suggest that the exposure was intentional. Interestingly, another call involved a 16-year-old girl who reported taking 25 g of nutmeg after reading that nutmeg was a "colon cleanser" in a popular teen magazine. This was reported by the call recipient as an intentional use exposure. Though these classifications do not affect the outcome of the patient, they do exhibit a potential for inaccuracy or inconsistency in reporting that may be important in retrospective studies of toxic exposures.

Three serious side effects of nutmeg—urinary retention, tremor, and seizure—were deemed by recorders in separate instances to be unrelated to the exposures. The literature shows tremor in animals receiving toxic nutmeg doses to be related to the anticholinergic effects of nutmeg attributed to myristicin and elemicin [4]. Urinary retention has also been noted as a potential side effect from the anticholinergic properties of nutmeg [11]. In a published case report of an extreme psychosis related to nutmeg intoxication, the patient experienced seizures, although this was speculated to be from excessive water intake [12]. In the data presented here, a patient with a past history of seizure also experienced a seizure after the exposure. This appears to be the first report of a seizure occurring in a patient with nutmeg overdose and a past history of seizure disorder. These published reports along with the effects seen in this study provide a possible association between nutmeg and neurologic toxicity.

Treatments administered to hospitalized patients are listed in Table 3. The most drastic medical intervention in our series was required for a 16-year-old female who received intubation and ventilatory support for approximately 24 h due to respiratory depression. This patient also presented with tremor. It is important to note that this patient was reported to have taken duloxetine, clonazepam, K2 (a synthetic cannabinoid), and acetaminophen, as well as nutmeg as part of a suicide attempt. Duloxetine can be associated with tremor and seizure, as well as EKG changes, and the synthetic cannabinoids have been reported to cause tremor, agitation, and respiratory depression. This patient exhibited symptoms that have been attributed to nutmeg toxicity including respiratory depression, hallucination, drowsiness, tremor, and tachycardia [2, 13–15]. This case is similar to a reported case in the literature that received criticism for claiming a patient's death was related to nutmeg when the patient had also taken a toxic dose of flunitrazepam [5].

The finding of multiple cases of combining nutmeg with other drugs (33 % of intentional exposures) is unique to this paper. Although the literature notes a fatal case of nutmeg intoxication with flunitrazepam, retrospective studies from other poison centers do not reveal information about cases of nutmeg being taken with other drugs [2, 3, 5]. Our data suggest that nutmeg abuse can be a marker for polypharmacy overdoses. These patients presented with more serious symptoms and toxicity than nutmeg exposures without other substances.

In summary, our data show a number of calls to the IPC regarding pediatric and adolescent exposures to nutmeg. Furthermore, we have demonstrated a significant percentage of intentional exposures where nutmeg was consumed in combination with other psychoactive agents. In addition, our study shows cases of unintentional exposures in juveniles under the age of 13, out of the total exposures to nutmeg. Healthcare professionals should be aware of these two factors, i.e., nutmeg exposures as intentional polypharmacy in adolescents and unintentional exposures in young children is advised.

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