Histamine Poisoning Associated With Eating Tuna Burgers

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Persons with histamine (or scombroid) poisoning often seek emergency medical care because of its toxic clinical manifestations. During the period 1998 through 1999, more cases of histamine poisoning were reported to the North Carolina Department of Health and Human Services than usual. No evidence existed that reporting practices had changed during the period 1997 through 1998, suggesting an actual increase in reported morbidity. With an increasingly health-conscious public eating less red meat and more seafood, we wondered if this increase was from more consumption of fish or from changes in food-handling practices. We evaluated a case series to describe the increase in histamine poisoning, identify characteristics associated with case patients, and develop recommendations for prevention.

Methods
For this study, histamine poisoning was defined as an illness occurring within 2 hours of eating fish in North Carolina for the period from July 1998 through February 1999, with at least 2 of the following symptoms: rash, facial flushing, vomiting, diarrhea, dyspnea, a tight feeling in the throat, headache, or a metallic or peppery taste in the mouth. We searched computerized phone log records from the North Carolina Department of Health and Human Services for the period 1994 through 1999, including all communications between the county and state health departments, then reviewed all local health department records of these cases of histamine poisoning. Records of histamine poisoning cases at the North Carolina Department of Agriculture were also reviewed.

Once the case series was assembled, we traced shipments of the implicated fish by interviewing seafood distributors and reviewing restaurant inspection logs and seafood supply orders. Restaurant chefs or managers were interviewed for information on where their fish came from, how it was prepared, and when it was served.

Histamine, putrescine, and cadaverine levels in the implicated fish samples were tested by the Southeast Regional Laboratory of the US Food and Drug Administration (FDA) using Association of Official Analytical Chemists methods. A histamine level greater than 50 ppm is considered evidence of decomposition by the FDA for regulatory purposes. For industry quality-control purposes, a histamine level of 20 ppm or greater indicates that some

Context Histamine poisoning occurs when persons ingest fish in which bacteria have converted histidine to histamine, a process that usually can be controlled by storage at low temperatures. From 1994 to 1997, North Carolina averaged 2 cases annually; however, from July 1998 to February 1999, a total of 22 cases of histamine fish poisoning were reported.

Objectives To examine the increase in histamine case reports, identify risk factors for poisoning, and develop recommendations for prevention.


Subjects Reported case-patients with 2 of the following symptoms within 2 hours of eating tuna: rash, facial flushing, vomiting, diarrhea, dyspnea, a tight feeling in the throat, headache, or a metallic or peppery taste in the mouth.

Results Twenty cases occurred during 5 outbreaks, and there were 2 single occurrences. Of the 22 persons affected, 19 (86%) sought emergency medical care. All case-patients ate tuna: 18 ate tuna burgers, 2 ate salad containing tuna, and 2 ate filets. Tuna samples (available from 3 outbreaks) had histamine levels above the Food and Drug Administration regulatory level of 50 ppm (levels were between 213 and 3245 ppm). In 19 cases, the tuna used to prepare burgers or salads was frozen and thawed more than once before serving. Violations of recommended temperature controls were identified in 2 of the 5 restaurants, accounting for 14 (64%) cases.

Conclusions Tuna burgers, a relatively new menu item in restaurants, were associated with an increase in histamine poisoning cases in North Carolina. Tuna ground for burgers can be susceptible to both temperature fluctuations and bacterial contamination.
violation of temperature controls has occurred. While there are no established regulatory action levels for putrescine and cadaverine, they are considered markers of decomposition and their presence indicates product abuse.

RESULTS

From 1994 through 1997, no more than 4 cases of histamine poisoning had been reported annually (Figure). During the 8-month period of July 1998 through February 1999, a total of 22 cases of histamine poisoning from fish were reported in North Carolina. Twenty-one cases were restaurant-associated and involved 4 different establishments, whereas 1 case-patient cooked and ate the fish at home. The fish prepared and eaten in the home was transported unfrozen in the trunk of a car for several hours before consumption. All cases occurred in persons aged 18 years or older. Four counties were involved; 3 of the outbreaks, involving 15 (68%) cases, occurred in 1 eastern North Carolina county, whereas the 2 remaining outbreaks and 2 individual cases occurred in 3 counties in central North Carolina. All case-patients ate tuna; 18 (82%) ate tuna burgers, and 2 ate salad containing tuna. The 2 single-event case-patients ate tuna filets. Of the 22 persons affected, 86% sought medical care. There were no hospitalizations, serious complications, or deaths.

The tuna shipments containing the implicated fish were all brought into Miami, Fla, from both local and international waters. Seafood distributors delivered shipments to North Carolina in refrigerated trucks within 7 to 14 days of arrival in Florida. The tuna for burgers and salads was from the belly meat of the fish. This meat was saved in freezer bags and stored in both freezers and coolers for 2 to 4 days until served as salads or burgers. Once the tuna was ground, patties were formed and stored in the cooler until cooked and served. Inspection of this process showed several freezing and thawing cycles. These food-handling practices were common to all restaurants that served the implicated tuna burgers. Restaurant inspections identified inadequate refrigeration in 2 of the 5 restaurants, accounting for 14 (64%) cases. In 1 restaurant that showed violations of storage temperature controls, the grinder used to make the tuna burgers was not sanitized between uses.

Fourteen representative tuna samples from 3 outbreaks of tuna-associated illness were available for laboratory testing (Table). The highest levels of histamine were measured in samples collected from tuna burgers left over from the first outbreak (July 1998; n = 11). For this outbreak, levels of histamine, putrescine, and cadaverine indicative of decomposition were also detected in samples of tuna that had not been ground. However, levels were much lower when compared with the ground tuna patties. For the second outbreak (September 1998; n = 2), all tuna burgers were consumed before the cases were reported, preventing testing of the implicated product. Samples collected for analysis from the third outbreak (February 1999; n = 2) included pieces of tuna from the same shipment as the tuna salad eaten by the 2 case-patients. Detectable levels of histamine and putrescine were also found in tuna samples taken from that shipment at the market that provided the fish eaten at the restaurant where the third outbreak occurred.

COMMENT

Histamine poisoning is a chemical intoxication with a short incubation pe-
HISTAMINE POISONING FROM TUNA

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riod, usually ranging from minutes to a few hours after ingestion. Symptoms include tingling and burning sensations around the mouth, headache, facial flushing and sweating, rash and itching on the upper body, abdominal cramps, nausea, vomiting, diarrhea, and heart palpitations. In most persons, symptoms are self-limiting, although histamine poisoning can be life-threatening in persons with conditions such as asthma and heart disease. Some drugs, such as monoamine oxidase inhibitors, can worsen or prolong an attack by inhibiting the breakdown of histamine. Antihistamine medication such as diphenhydramine and cimetidine often relieve symptoms; however, severe cases of toxicity can require the same aggressive management as acute anaphylaxis. Symptoms related to histamine poisoning can also be similar to those of coronary heart disease, increasing the possibility of an invasive medical intervention if misdiagnosed.

Histamine poisoning from fish is probably the principal cause of morbidity from toxic fish consumption worldwide, and it is the only form of fish poisoning caused by bacterial contamination. Spoiled fish of the family Scombridae (eg, tuna, mackerel, and bonito) are commonly implicated, hence the term scombroid fish poisoning. However, other types of fish are often implicated in histamine poisoning from fish, including mahimahi, bluefish, salmon, amberjack, herrings, sardines, and anchovies. Forty-two percent of all histamine outbreaks reported to the Centers for Disease Control and Prevention during the period 1978 through 1982 occurred in non-scombroid fish. Because this condition is not specific to scombroid fish, histamine poisoning is a more appropriate descriptive term for this food-related illness.

High histamine levels are formed by bacterial proliferation on the surface of fish that have been improperly refrigerated. These histamine-forming bacteria usually belong to the Enterobacteriaceae family, which have the enzyme necessary to decarboxylate histidine to histamine. Because histamine poisoning has been reported after consumption of fish containing low levels of histamine, other vasoactive amines present in the fish (eg, putrescine and cadaverine) might act synergistically with histamine to lower the toxic dose threshold. Putrescine and cadaverine have been shown to potentiate histamine toxicity through inhibition of metabolizing enzymes that detoxify histamine.

Histamine development is more likely to occur in raw, unfrozen fish. Because the fish might appear and smell normal, the consumer is unlikely to identify a problem before eating the fish. Once the bacteria have formed the enzyme histidine decarboxylase, histamine production can continue even if the bacteria are killed. Although cooking can inactivate both the enzyme and the bacteria, the toxic factors produced are heat stable and, once formed, are not destroyed by cooking, smoking, or freezing.

In this investigation, tuna burgers were associated with an increase in histamine poisoning cases in North Carolina. For histamine to form in the fish, the tuna had to be mishandled at some point between capture and consumption. Tuna can be especially vulnerable to temperature fluctuations because their average body temperature when caught tends to be several degrees warmer than that of other types of fish. Belly meat might have an increased susceptibility to bacterial contamination during the evisceration process because of its proximity to the fish gut cavity, where histamine-forming bacteria reside. Furthermore, thin pieces of fish, such as the belly meat used for ground tuna and salads, might be more vulnerable to temperature fluctuations than thicker tuna files. Violation of storage and temperature controls are also more likely with tuna used for salads and burgers, because pieces are stored over a longer period than files and exposed to multiple thawing and refreezing cycles. The grinding process used to make tuna burgers also might contaminate the fish by either mixing histamine-forming bacteria into previously uncontaminated material or by increasing the temperature of the tuna through mechanical friction. This hypothesis is supported by evidence that the prepared tuna burgers contained higher toxic amine levels than unground fish from the same shipment.

Underreporting was 1 of the limitations of this investigation. Documentation of histamine poisoning has been inconsistent because of a vague case definition and insufficient knowledge about it in the medical community. Many mild, self-limiting histamine-like reactions might not have been linked to an actual episode of eating fish. When medical attention is sought, physicians might misdiagnose histamine poisoning cases as a "seafood allergy" or confuse symptoms with those of other types of seafood toxins. Allergic symptoms and those related to fish poisoning can be similar, and both are responsive to antihistamine treatment. Tracing to the origin of contamination was another limitation because inspection records were only available for the restaurants involved. If problems were not found at the restaurant, we could not be sure where violations of temperature controls or mishandling might have occurred. The critical hazard point could have occurred anywhere from the tuna boat to the restaurant.

Based on the findings of this investigation, we can make several recommendations. Scientific evidence has shown that rapid chilling of fish on the fishing vessel and keeping the temperature of the fish lower than 0°C throughout storage and distribution is the best way to prevent histamine formation. This is lower than the current FDA recommendation of 5°C. Prospective studies are needed to determine where the highest risk for violations of temperature controls occurs in the path from sea to table.

In December 1997, the FDA launched a new program that requires seafood processors to follow a modern safety system known as Hazard Analysis Critical Control Point (HACCP). This system requires hazard analysis at all stages of processing, establishment of critical control points within the food chain continuum, establishment and monitoring...
of histamine and temperature limits, and verification that the program is being followed. To monitor histamine, implicated fish products must be sent to the regional FDA seafood laboratory for testing.

Although the FDA has regulated seafood for decades, its jurisdiction is limited to imported (international and interstate) products. Local wholesale seafood businesses are subject to state government inspection, which includes enforcement of the new HACCP rules. The feasibility of applying principles similar to those of HACCP to recreational and commercial fishing vessels, retail seafood facilities, and restaurants to improve seafood safety should be tested and evaluated. Following recent reported outbreaks, investigators recommended that regulations be developed and enforced concerning how long a fish can remain on a fishing line; however, further evaluation is needed before policies like this can be considered for implementation.

Better recognition of and surveillance for histamine poisoning from fish are needed, particularly given the increased consumption of fish. Although all food-borne illnesses are reportable in North Carolina, a specific line item for histamine poisoning on the reporting card is needed to accurately document the magnitude of this problem, and identify where food-safety interventions are needed. Furthermore, the sensitivity of testing for histamine poisoning would improve if acceptable levels for nonhistamine amines (e.g., putrescine and cadaverine) were standardized. Currently, histamine activity cannot be readily determined in the commercial environment, and after-the-fact laboratory testing only confirms that an unsafe product has already been consumed. A simple and cost-effective test that is sensitive enough to detect contamination before a health problem occurs is needed. For example, cultures are used to enforce the zero tolerance policy for *Listeria monocytogenes* in ready-to-eat processed meats.

**REFERENCES**


