Scombroid Fish Poisoning in Israel, 2005–2007

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Abstract

Background: Scombroid fish poisoning is an acute illness caused by consumption of fish containing high concentrations of histamine. Improper handling of fish leads to bacterial contamination. Bacterial enzymes convert histidine to histamine. Symptoms develop quickly and resemble an immunoglobulin E-mediated allergic reaction. The diagnosis is often missed. Serious complications (e.g., bronchospasm, hypotension) are infrequent.

Objectives: To evaluate the prevalence and characteristics of scombroid fish poisoning in Israel as reported to the national poison information center.

Methods: We conducted a retrospective poison center chart review from January 2005 to December 2007.

Results: During the study period, 21 events of scombroid poisoning involving 46 patients were recorded. Tuna was the commonest fish consumed (84.7%). Clinical manifestations developed within 20 minutes in 65.2% of the patients. The main clinical manifestations included rash (41%), flushing (37%), gastrointestinal complaints (37%) and headache (30.4%). About 25% had abnormal vital signs; two patients developed hypotension. Treatment was supportive and included mainly H_1-antagonists (65.2%) and fluids (13%). Five patients were initially misdiagnosed as having an allergic reaction and were treated with corticosteroids (four patients) and epinephrine (one patient).

Conclusions: Scombroid fish poisoning should be suspected in patients with histamine-like manifestations that are temporally related to fish (mainly tuna) consumption, especially in outbreaks. Although scombroid poisoning is often self-limited and responds well to antihistamines, prolonged observation may be required as severe toxicity can supervene. Proper handling of fish and urgent notification of the Ministry of Health are mandatory in order to prevent this potentially serious public heath problem.

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Scombroid fish poisoning is a food-borne chemical illness associated with consumption of fish and much less frequently, cheese [1,2]. This dark-meat fish belongs to certain families, mainly Scombridae and Scomberesocidae and includes tuna, mackerel, bonito and cero [3]. The first report of scombroid poisoning was published in 1830. It involved five sailors who consumed bonito fish, a member of the Scombridae family, hence the name of the entity [4]. Other non-scombroid fish (e.g., swordfish, Australian salmon, spotted sardines) were also reported to be associated with scombroid fish poisoning [1-3]. High concentrations of histamine are found in the fish responsible for this poisoning; hence histamine is believed to be the causative agent [1,5]. Histamine is formed from histidine by a decarboxylase from bacteria found in dark-meat fish [3]. Different kinds of bacteria were identified in relation to this phenomenon, among them *Klebsiella pneumoniae*, *Proteus morganii*, *Serratia marcescens* and *Enterobacter intermedium* [6]. These bacteria constitute normal flora in fish, but their presence is usually secondary to contamination from handlers [7,8]. Improper refrigeration and handling of captured fish is the cause of massive histamine production by the above bacteria.

To the best of our knowledge, scombroid fish poisoning has never been reported in Israel. We assume that this poisoning is underdiagnosed because of its resemblance to allergic reaction and its relatively short course [1]. The objective of this study was to evaluate scombroid fish poisoning in Israel as reported to the Israel Poison Information Center, Rambam Health Care Campus.

Patients and Methods

The study was conducted using a previously reported retrospective poison center chart review methodology [9,10]. All consultations of the Israel Poison Information Center are provided by specialized physicians. Data are recorded in a comprehensive structured form that includes caller and patient demographic details, route, site and circumstances of exposure, time elapsed until consultation, clinical manifestations via a system-oriented approach, evaluation, management and follow-up recommendations. The exposure and causative agents are classified according to a previously prepared list of categories, classifications and subclassifications available at the IPIC. Subsequently, all data are entered and stored in a dedicated database using Microsoft® Access 2002 software on an SQL server. All records are subjected to routine quality control. The IPIC is the national poison information center of Israel and the only center that serves both the general public and health care facilities 24 hours a day. Reporting to the IPIC is voluntary and not mandatory. Case records in the IPIC database reflect information provided by the caller. A computerized query using the key words biological, aquatic, fish was used to retrieve all records of sombroid fish poisoning from 1 January 2005 until 31 December 2007. Data were abstracted from the records, transferred to an electronic spreadsheet (Microsoft® Excel 2002 software) and subjected to descriptive analysis. Severity of poisoning was graded according to criteria suggested by Smart [11]. Mild scombroid fish poisoning was defined as mainly dermatological mild manifestations. Patients with moderate poisoning are symptomatic, complaining mainly of

IPIC = Israel Poison Information Center

Table 1. Demographic data and characteristics of exposures of patients with scombroid fish poisoning (n=46)

No. of patients per incident	1 patient	2 patients	4 patients	15 patients
	15 (71.4%)	2 (9.6%)	3 (14.3%)	1 (4.9%)
Age range (yrs)	< 18 (10–12) 4 (8.7%)	18–50 36 (78.3%)	> 50 (50–80) 6 (13%)	
Gender	Male 30 (65.2%)	Female 16 (34.8%)		
Ingested fish	Tuna 39 (84.7%)	Other* 7 (15.3%)		
Type of fish preparation	Canned 13 (28.2%)	Steak 22 (47.8%)	Other 11 (23.9%)	
Caller origin	Public 9 (19.6%)	Clinic 7 (15.2%)	Hospital 30 (65.2%)	
Site of ingestion	Home 18 (39.1%)	Restaurant 5 (10.9%)	School 4 (8.7%)	Workplace 19 (41.1%)
Time to onset of manifestations (min)	≤ 20 30 (76%)	≤ 60 5 (10.9%)**	> 60 11 (23.9%)	

* All these patients confirmed consumption of fish other than tuna but could not identify it.

** These patients could not specify the exact time that elapsed prior to onset of toxicity.

marked gastrointestinal complaints. In severe cases at least one life-threatening sign is present (hypotension, bronchospasm, angioedema, etc.). The distribution of severity between the different age groups and by time of onset of toxicity was analyzed by chi-square analysis and Fisher exact test. The study was approved by the Institutional Review Board of Rambam Health Care Campus.

Results

Twenty-one incidents of scombroid fish poisoning involving 46 patients were recorded at the IPIC during the study period. Demographic data and characteristics of exposures are presented in Table 1.

Tuna was the most commonly consumed fish (84.7%). Time to onset of symptoms was short, up to 20 minutes in 30 patients (65.2%). The clinical manifestations of the patients are shown in Table 2. The body system most frequently involved was the skin (82.2%) followed by gastrointestinal (37%) and neurological (34.7%). The most frequent clinical manifestations were rash (41.1%), flushing (37%), headache (30.4%), erythema (23.9%), tachycardia (21.6%), diarrhea (19.6%), dyspnea (17.4%), abdominal pain (15.2%) and pruritus (15.2%).

The distribution of severity is presented in Table 3. Hypotension (systolic blood pressure < 90 mmHg) was the main feature of the two severe poisonings. No significant differences in the distribution of severity according to age groups and time to onset of clinical manifestations were found.

Thirty patients (65.2%) required observation and treatment in emergency departments, 7 were treated in ambulatory clinics, and

Table 2. Clinical manifestations of patients with scombroid fish poisoning (n=46)*

Symptoms	
Dermatological	
Rash	19 (41.1%)
Flushing	17 (37%)
Erythema	11 (23.9%)
Pruritus	7 (15.2%)
At least one dermatological manifestation	38 (82.2%)
Gastrointestinal	
Diarrhea	9 (19.6%)
Abdominal pain	7 (15.2%)
Nausea	4 (8.7%)
Vomiting	2 (4.3%)
Burning taste	4 (8.7%)
Mouth/tongue swelling	4 (8.7%)
At least one gastrointestinal manifestation	17 (37%)
Neurological	
Headache	14 (30.4%)
Dizziness	5 (10.9%)
Vision disturbance	1 (2.2%)
Tremor	1 (2.2%)
At least one neurological manifestation	16 (34.7%)
Respiratory	
Dyspnea	8 (17.4%)
General / Other	
Malaise	5 (10.9%)
Palpitation	3 (6.5%)
Warmth sensation	3 (6.5%)
Weakness	2 (4.3%)
Vital signs	
Normal	28 (75.7%)
Tachycardia** (> 100/minute)	8 (21.6%)
Hypertension** (> 140 mmHg systolic)	4 (10.8%)
Hypotension** (< 90 mmHg systolic)	2 (5.4%)
Not recorded***	9 (24.3%)

* Some patients had more than one manifestation

** Range: tachycardia 104–182/minute, hypertension 145–170 mmHg systolic, hypotension 82–90 mmHg systolic

*** These patients consulted with the IPIC but did not reach a medical facility as they recovered prior to consultation

Table 3. Distribution of the severity of scombroid fish poisoning and its association with age and time to onset of toxicity (n=46)

Severity*	Mild	Moderate	Severe
Distribution of severity	31 (67.4%)	13 (28.3%)	2 (4.3%)
Severity by age (yrs)			
< 18	0	3 (23%)	1 (50%)
18–50	27 (87%)	8 (61.5%)	0
>50	4 (13%)	2 (15.5%)	1 (50%)
Severity by time to manifestations (min)			
< 20	20 (64.6%)	9 (69.3%)	1 (50%)
>20	11 (35.4%)	4 (30.7%)	1 (50%)

* Severity was graded according to criteria suggested by Smart [11].

9 patients did not require referral to a health care facility as they recovered spontaneously before consulting the IPIC. Fourteen patients (30.4%) improved spontaneously and required no treatment. Thirty patients (65.2%) received H_1-antagonists, usually promethazine; 6 patients (13%) needed intravenous fluids. Four patients (8.7%) were treated with corticosteroids and one patient (2.2%) received epinephrine because the physician suspected allergic reaction before the diagnosis of scombroid poisoning was made. All patients recovered within several hours with no sequelae.

Discussion

During the study period 46 patients with scombroid fish poisoning were recorded. Tuna was found to be the main fish involved. Most patients developed clinical manifestations within 20 minutes. Dermatologic signs, mainly rash and flushing, gastrointestinal complaints and headache were most common. The majority of patients recovered within several hours, either spontaneously or after being treated with H_1-antagonists. Only two patients developed severe poisoning manifested as hypotension.

The time to onset of toxicity, the variety of clinical manifestations and their distribution are in accordance with data in the literature [1,2,6,11]. Severe presentation was rarely reported and included hypotension, atrial arrhythmia and respiratory disturbance [2,11,13,14]. Severe poisoning commonly develops in patients with cardiac or respiratory co-morbidities [1,2,11]. Critical observation is needed to identify severe cases since a subjective impression can be misleading.

Diagnosis of scombroid fish poisoning can be easily confused with allergic reaction, especially when only one patient presents. History of recent fish consumption, mainly tuna, should raise the suspicion of such poisoning. In the event of outbreaks, diagnosis is easier to establish [11]. Recognizing severe cases is straightforward even without specific criteria, while the distinction between mild and moderate severity by Smart criteria is rather vague and has no clinical or prognostic meaning. While severe scombroid poisoning is infrequent, referral of all such patients to an appropriate medical facility is warranted [11,12]. Rapidity of symptom onset, mild course of poisoning and the risk of vomiting preclude the use of any gastrointestinal decontamination procedure [1]. Symptoms subside within hours even without treatment; nevertheless, histamine antagonists can shorten and promptly ameliorate the symptoms and are recommended as first-line treatment [12]. In our study, treatment was based mainly on H_1-antagonists, as recommended in the literature [1-3]. H_2-antagonists, especially cimetidine, can be added to H_1-antagonists to improve outcome [15,16]. Corticosteroids are not needed, except in the case of bronchospasm since this illness is a toxic reaction and not an immune or allergic one [17]. Intravenous fluids and vasoactive medications are required for severe poisonings [13,14,17,18].

Histamine is the suspected causative agent of scombroid poisoning. It is a naturally occurring substance in the body and plays an important role in allergic and inflammatory reactions [19]. It is formed by histidine decarboxylase and either stored in the granules of mast cells and basophils or rapidly inactivated by methylation and oxidation. Metabolites are excreted in the urine. Very little histamine is excreted unchanged under normal conditions [19]. In a matter of seconds after histamine is liberated from granules and reaches systemic circulation, it interacts with several receptors and induces a variety of effects, including vasodilatation, bronchoconstiction, gastric acid secretion, smooth muscle activation and induction of pain and itching. Significant release or administration of histamine can produce profound clinical manifestations within minutes. A short duration of manifestations is anticipated due to the pharmacokinetic properties of histamine which is rapidly metabolized [19].

Consumed fish responsible for scombroid poisoning were found to contain high levels of histamine, secondary to improper handling and bacterial activity [7]. While negligible activation of histidine decarboxylase is measured in fish meat at low temperatures (close to 0°C), at temperatures higher than 26°C histamine is accumulated to toxic levels in a matter of 12 hours and even faster at higher temperatures [8]. Up to 5 mg histamine per 100 g meat is considered normal and acceptable. A histamine concentration of 20 mg/100 g is considered to be the threshold to clinical poisoning, while levels over 100 mg/100 g are related to severe poisonings [3,5,7]. Histamine is heat stable and is not destroyed by different cooking methods [3].

Assays of histamine and its metabolite in urine samples of scombroid fish poisoning patients showed levels up to 20 times higher than in the control [20]. Although it supports the diagnosis, histamine measurement in common clinical practice is not recommended. Histamine levels are poorly correlated to clinical manifestations and do not affect clinical decisions [1].

Some investigators doubt the role of histamine in causing the poisoning. Ingested histamine is extensively metabolized in the intestines and is poorly absorbed. Adding histamine to food did not induce poisoning in humans [21]. The investigators speculate that other amines may be the cause of scombroid fish poisoning, or that unknown substances in ingested food induce degranulation of mast cells and release of histamine. In contrast, Morrow et al. [20] measured high levels of histamine and its metabolite N-methyl-histamine in the urine of patients with scombroid poisoning. PDG-M, a metabolite of prostaglandin D_2, used as a marker to mast cell secretion, was not increased in the same urine [20].

The amount of fish eaten was found to be related to the development of scombroid poisoning symptoms. Feldman et al. [21] reported an outbreak of scombroid poisoning in California where 42 of 56 people who ate contaminated fish developed symptoms. These 42 patients ingested 1.5 times more fish meat on the average than those who remained asymptomatic [21]. Isoniazid and monoamine oxidase inhibitors were found to increase the risk for severe poisoning. These medications impair the metabolism of histamine by inhibiting oxidation and result in higher levels and longer duration of histamine in the body [23-25].

Reports of scombroid fish poisoning come from all over the world since the involved fish are ubiquitous and their marketing and consumption take place worldwide. It is recognized as a global food-related health problem that should be addressed

mainly by prevention and enforcement of regulations in the fish industry [1].

Our study has a few limitations: it was a retrospective study, relied on voluntary reporting, had a limited follow-up, and histamine was not determined in fish samples or biologic fluids. However, the typical histamine-like clinical manifestations together with temporal proximity to consumption of fish known to be involved in scombroid poisoning supports this diagnosis.

Conclusions

This is the first series of scombroid fish poisoning reported in Israel. Patients developed histamine-like clinical manifestations after consuming fish, mainly tuna. Most patients had mild poisoning that responded well to H_1-antagonists. Two patients were hypotensive, suggesting the need for referral to medical observation. It should be emphasized that scombroid poisoning is a toxic and not an allergic reaction, meaning that fish consumption does not have to be withheld. Proper handling of fish is of utmost importance in order to prevent poisoning. The Ministry of Health should be notified immediately in every event in order to start an investigation, identify the source and minimize or halt a possible outbreak.

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