Original Article

Journal of Food Safety and Hygiene

Journal homepage: http://jfsh.tums.ac.ir

A clinical epidemiological onsite study of a massive outbreak of Scombroid fish poisoning after consumption of yellowtail kingfish in northern Chile

Rodrigo Zapata MD [1*], Keryma Acevedo MD[2], Martina Mella MD[3], Verena Mella[3], Keryma Zapata[3]

*[1]*Gastroenterology Unit, Department of Medicine, Faculty of Medicine, Clínica Alemana de Santiago, Universidad del Desarrollo, Santiago, Chile.*

[2]*Pediatric Neurology Unit, Division of Pediatrics, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile.*

[3]*Faculty of Medicine, Universidad del Desarrollo, Santiago, Chile*

ARTICLE INFO

Article history:
Received 07 Jul. 2020
Received in revised form 29 Aug. 2020
Accepted 11 Sep. 2020

Keywords:
Scombroid fish poisoning;
Scombrotoxism;
Histamine fish poisoning;
Scombrotoxin poisoning;
Outbreak

ABSTRACT

Scombroid fish poisoning (SFP) is an acute illness caused by the consumption of poorly preserved fish containing high levels of histamine. Symptoms develop within 1-2 h, with gastrointestinal, dermatologic, and cardiopulmonary manifestations. The diagnosis relies exclusively on the clinical picture. To describe an onsite clinical-epidemiological study of a massive outbreak of SFP occurring in Chile. Descriptive study of an outbreak occurring in a closed Convention Center after lunch with Chilean Palometa or *Seriola lalandi* (Yellowtail kingfish). An Onsite questionnaire was answered by all attendants within 24 h. Local health officials supervised the place with a second survey and sample recollection of suspected fish. Eighty-three adults attended the event, of which 81 ate fish. Mean age: 58.5 years old, 82.7% women. The symptomatic attack rate of people eating suspected poisoned fish was 79% (64 out of 81 participants). Most common symptoms included: diarrhea (68%); headache (64%); flushing (64%) and diffuse redness (56%). Mean incubation period: 77 min (30-240 min). 98.4% of patients recovered within 10 h. Ten patients were referred to the emergency room, but none were admitted. There was a presumption of loss of refrigeration in the handling of fish, and confirmation of SFP by clinical basis, incubation period and attack rate. Fish was the only food item associated with illness (Odds ratio: 19, p = 0.014; Fisher two tails). This is one of the 5 largest outbreaks of SFP with fresh fish, ever reported in the literature. The clinical picture and rapid onset of symptoms made it possible to suspect SFP allowing timely management of patients. It is relevant to spread the knowledge about this underdiagnosed and underreported syndrome.

Citation: Zapata R, Acevedo K, Mella M, Mella V, Zapata K. **A clinical epidemiological onsite study of a massive outbreak of Scombroid fish poisoning after consumption of yellowtail kingfish in northern Chile.** J food safe & hyg 2020; 6(3):145-159.

1. Introduction

Scombroid fish poisoning (SFP), also known as "histamine fish poisoning" or "scombrotoxin poisoning", is an under recognized acute toxic illness caused by the consumption of poorly preserved fish containing high concentrations of histamine and other histamine-like substances (1-3). This is the result of decomposition of the fish improperly refrigerated after capture, where their flesh (rich in histidine) is decarboxylated by the fish's enteric bacteria

*Corresponding author. Tel.: +56993465228
E-mail address: rzapata@alemana.cl

(*Morganella*, *Klebsiella*, *Pseudomonas*, *Carnobacterium*, *Clostridium*), forming variable amounts of Histamine (4,5).

The disease was initially described back in 1799 in Great Britain and re-emerged in the medical literature in the 1950s, together with a rise in fish consumption, determining many outbreaks in different countries including Japan, USA, Australia, China, and Canada (5). Case reports have been described in different settings, including restaurants, cafeterias, schools, army barracks, and medical conferences, usually as sporadic cases or in small clusters of 2-5 patients (6).

Scombroid fish poisoning is an acute histaminergic intoxication, secondary to a massive intestinal absorption of histamine, beginning within 1-2 h of ingestion of the contaminated fish, resembling an allergic reaction with an erythematous urticarial rash affecting both the face and upper trunk with flushing (1,3). Some patients may refer a burning sensation of the mouth and throat, or a peppery and metallic taste during ingestion of the contaminated fish (2). Systemic symptomatology (mainly gastrointestinal, dermatologic and cardiopulmonary) develops rapidly, but usually resolves rapidly within few h. The clinical picture is usually mild to moderate, but it can be severe and even life-threatening in some cases (1). Treatment has been directed to control the symptoms with anti-H1-blockers. The diagnosis of SFP relies exclusively on the clinical picture and setting, but requires a high index of suspicion (1-3), and may be confirmed by laboratory measurements of His in the suspected fish (1).

The name scombroid (from Greek: scombros, mackerel or tunny), is derived from the family of dark meat saltwater bony fish known as Scombridae (e.g., tuna, bonito, mackerel, skipjack), which is the most commonly associated with this kind of intoxication (4). They contain freer histidine in their muscles as compared with lighter meat fish from freshwater. This explains, in part, the higher incidence and regional variations of SFP seen with these fish (7). Other non-scombroid species (bluefish, Mahi-Mahi, herring, marlin, Yellowtail kingfish, Amberjack, anchovies and sardines), with relatively high levels of naturally-occurring histidine in their flesh, have also been associated with histamine fish poisoning (3). Histamine is heat stable organic nitrogenous compound, hence cooking of the fish does not reduce the risk of SFP (8). Based on histamine concentrations that can cause intoxication, regulations around the world have stablished its maximum levels between 50 and 200 mg/kg for raw fish (9).

SFP is considered the most common reported seafood poisoning in the United States, accounting for about 38-40% of fish poisoning, and about 5-7% of all reported foodborne disease outbreaks (FDO) (10-12). Overall, reported incidences of SFP are most likely underestimated. As the illness is usually mild, self-limited, recovers rapidly, and has no long-term sequelae, individuals may not seek medical attention; and many of those being evaluated are often misdiagnosed as seafood allergy (1,2). Predictions point to a progressive increase in SFP cases during the next decades due to an increase of trips to coastal destinations, consumption of fish and growth of coastal towns and cities with poor implementation of fish extraction policies (13).

In this study, we report a massive outbreak of SFP in a coastal city in northern Chile. To the best of our knowledge, this is one of the largest reported outbreaks of SFP after intake of fresh fish. It includes a detailed onsite-epidemiological description and a thorough review of the literature.

2.Materials and Methods

This is a report of an outbreak of SFP occurring on April 16th 2016, in a closed convention center in La Serena, a coastal city in northern Chile (Fig. 1). After having lunch with Chilean Palometa or *Seriola lalandi sp* (Yellowtail kingfish), 64 participants presented an erythematous skin rash and flushing, headache, palpitations and diarrhea. Signs and symptoms developed within min to few h after eating lunch. Several patients were treated with antihistamines and showed immediate improvement. An onsite detailed epidemiologic investigation was undertaken to characterize the outbreak and determine its cause. A secondary objective of this report is to increase awareness of this disease and educate on measures to prevent and manage SFP in the acute setting.

2.1. Epidemiological investigation

This is a descriptive onsite epidemiological study (cross-sectional) of a massive outbreak of SFP occurring on April 16th 2016, in a closed Convention Center of volunteers and personnel of a health organization, held in the coastal city of La Serena, in Northern Chile. This case-control study included all participants of this convention who ate lunch. This outbreak also describes how healthy and sick participants were organized by few physicians, to optimize the management of an emergency situation.

After morning work sessions, lunch was served around 1 pm, and included a first course of salad (tomato and lettuce), and a second course of Chilean Palometa fish or *Seriola lalandi* sp, sided with roasted potatoes. Full portions of fish were approximately 150-200 g per person. Dessert consisted of a mix of fresh fruits.

During lunch, some participants described a peppery or metallic taste of the fish. Few min to 4 h after lunch, most people started complaining of symptoms consistent with SFP. As they felt sicker, they gathered in the lobby of the convention center, where they were assisted and triaged by 4 medical doctors and 2 nurses participating in the meeting.

A case was defined as having flushing accompanied by other manifestations, such as headache, rash, chills, and gastrointestinal symptoms (nausea, abdominal pain, diarrhea, and vomiting). Controls were people not reporting any of these symptoms after lunch. All cases and controls completed questionnaires exploring demographic characteristics, food items and amounts consumed at lunch, and (for cases), symptoms and onset times.After managing the emergency, a clinical and epidemiological 2-page questionnaire in relation to this outbreak, was prepared by two of the authors (RZ and KA); and the day after, given to all participants, who completed the survey. The results of this survey are presented here in detail. Data were transferred to an electronic excel database for subsequent descriptive statistical analyses.

The local state health public officials (SEREMI: Secretaría Regional Ministerial de Salud of Coquimbo) were immediately notified. Onsite supervision by local authorities was performed the following day, including a survey of affected and non-affected patients and interviews

with the Convention Center's manager and chef. Samples of food and suspected fish were collected for bacteriological studies. Histamine levels of fish's samples were measured via HPLC (high-performance liquid chromatography, using a fluorescence detection method). Part of the study was the result of a simultaneous and parallel epidemiological investigation conducted by the local state health public officials SEREMI, in accordance with the Act on the Prevention and Control of Infectious Diseases. Their conclusions were liberated as part of public transparence information (ORD. 971, 19th August 2016).

2.2. Statistical analysis

Descriptive statistical analyses of all biodemographic and clinical data available were performed. The relationship between consumption of certain food items and illness was assessed by calculating odds ratio (ORs) with 95% confident intervals (CIs) (Fisher 2 tails) with the aid of SPSS software (version 20.0; IBM Corp., Armonk, NY, USA). The attack rate proportions between different groups of people were compared through Chi-square. A P-value of < 0.05 was considered statistically significant.

2.3. Ethical statement

This is an observational descriptive (non-interventional) study that maintained the information confidential, with anonymous data and following the principles outlined in the Declaration of Helsinki. All the convention participants (whether or not affected) received information about the disease and the nature of the study, and gave their voluntary written informed consent at the moment of filling-up the survey and for the use of photographs. According to regulations, as this was a severe food-borne outbreak with immediate public health threat, no previous ethical committee approval was required.

3.Results

A total of 83 attendees participated in this closed convention. All of them completed the questionnaire the day after the outbreak. The results are based on those who ate any amount of fish (n=81/83; 97.5%). The mean age of participants was 58.5 $\pm$ 14.1 years-old (range: 26-82 years), 82.7% (67/81) female, with 58 of them (58/81: 71.6%) being older than 50 years of age.

The symptomatic attack rate of people eating suspected poisoned fish was 79% (64 out of 81 participants). The main characteristics of symptomatic patients are shown in Table 1 and figures 2 and 3. SFP was rapidly suspected after the first few symptomatic cases, due to symptoms and form of presentation. The lobby of the hotel served as a triage post, where patients were evaluated by 4 physicians and a nurse. Severe symptomatic patients were transferred to the nursing area.

All asymptomatic or oligosymptomatic participants helped in the management of those who were sicker. Once SFP was suspected, and after seeing the first few symptomatic patients, all participants (whether symptomatic or not) received immediately oral anti-H1-blockers (chlorpheniramine 4 mg *PO*).

Depending on the severity of illness, some cases were managed with a step-up therapy including iv steroids (chlorpheniramine 10 mg IV and betamethasone 4 mg IV) (photograph 1).

Finally, the 10 sickest patients (10/81:15.6%), including one pregnant patient, who were not responding to initial treatment or looked very sick, were referred to the nearest emergency room.

Patients managed in the ER received iv hydration, anti H1-blockers and some of them repeated doses of iv steroids, and oxygen by mask. All were discharged after a mean of 28 h, with the diagnosis of SFP. No significant differences were found in patients requiring ER in relation to age and gender vs those with less severe disease (Table 1).

Clinical manifestations included varying degrees of flushing, short term diarrhea, abdominal cramps, headache, feverishness, nausea, rapid pulse, pruritus, dizziness, vomiting, facial and torso swelling and rash, transient numbness around the mouth, and abdominal pain (Table 1 and Photograph 1).

The time lapse between fish ingestion and onset of systemic symptoms ranged between 30 to 240 min, with an average time of 1.3 + 0.9 h (figure 3).

Fifty-nine percent of participants (48/81) ate more than 50% of the portion of the fish (> 100 grams) and out of this group, 85.4% of them had systemic symptoms. In comparison, of those eating less than 20% of the fish portion (< 40 grams; n=17/81; 21%), only 41.7% had systemic symptoms (p=0.0005). No correlation was found between patient`s weight and SFP incidence rate.

Most of the participants (53/ 81; 65.4%) eating any portion of fish noted a strange burning or tingling sensation on the tongue, and varying degrees of peppery and/or metallic taste of the fish. This observation did not correlate with the severity of systemic symptoms.

In relation to the course of the disease, 98.4 % of symptomatic patients (63/64) had a favorable clinical course, with complete resolution of symptoms within 10 h.

Only, one patient, with a known liver cirrhosis (primary biliary cholangitis, Child-Pugh A on ursodeoxicholic acid 1.000 mg/day for more than a year) had persistent systemic symptoms for more than 24 h, which required ER management the following day.

The SEREMI local health agency final report concluded few weeks later that "there was a presumption of loss of refrigeration in the handling of the fish, and a clear confirmation of this outbreak of SFP by clinical basis, incubation period and attack rate with the suspicious fish, with a significant odds ratio of 19 (p = 0.014, Fisher two tails) (SEREMI Ord 971). Measurements from a sample of fish taken the following day after the massive intoxication showed low levels of histamine (<15 mg/kg). Furthermore, bacteriological studies were negative for *Enterobacteriaceae*, including *Salmonella*, *Shigella*, *Staphylococcus aureus*, *Vibrio* species, *Listeria monocytogenes*, *Yersinia enterocolitica*, *Bacillus cereus*, pathological *Escherichia coli*, *Clostridium perfringens*, and *Campylobacter jejuni*.

Table 1. Clinical characteristics of symptomatic patients with SFP (n= 64) (ER: emergency room)

Group	Characteristics	Patients	%	Comments
Gender	Male	14	19%	2 sent to ER (14.2%)
	Female	40	81%	8 sent to ER (20%)
Age group	<50 years	19	30%	4 sent to ER (21%)
	50-60 years	12	19%	1 sent to ER (8.3%)
	>60 years	33	51%	5 sent to ER (9.8%)
Signs or symptoms	Diarrhea	44	68%	16 cases with severe diarrhea (≥ 3 stools)
	Headache	41	64%	
	Redness	36	59%	25 cases with generalized redness
	Flushing	38	59%	
	Palpitations	27	42%	
	Abdominal pain	20	31%	
	Red eye or tearing	17	26%	
	Fainting sensation	12	19%	
	Nausea	12	19%	
	Generalized pruritus	11	17%	
	Thoracic pain or dyspnea	9	14%	
	Vomiting	3	5%	

Table 2. Summary of the largest outbreaks of SFP (with more than 40 patients involved) after intake of fresh fish, published in the medical .literature, with descriptive information

Reference	Year outbreak	Number affected cases	City, Country	Source SFP	Attack rate	Gap time to symptoms (min)	Symptoms in affected patients
Chen KT, et al (23)	1987	115 adults	Employee cafeteria, Store, Southern Taiwan	White-tipped mackerel	56%	10-240	Dz (78%); Fl (62%); H (51%); N (37%); perioral numbness (35%); Palpitations (30%); Pr (28%); F (24%), D (13%).
Wu SF, et al (24)	2003	94 kindergarten children	Kindergarten, Taichung, Taiwan	Spoiled fish (not specified)	NS	40-50	Hyperemia face & neck (94%) N & V (17%); AP (17%), P (4%); H and Dz (4%); D (3%).
Demoncheaux JP, et al (25)	2012	71 Adults (armed forces)	Military catering facility, Dakar, Senegal.	Yellowfin Tuna	30%	min-240	Fl (85%); weakness (70%); H (59%); T (42%); D (34%).
Zapata R, et al (current study)	2016	64 adults	Convention Center, Coquimbo, Northern Chile	Yellowtail kingfish (Chilean Palometa)	76%	min-240	D (68%); H (64%); Fl (58%); Burning sensation tongue (65%); SR (58%); T (42%); AP (34%); N (16%) V (6%).
Kang CR, et al (26)	2016	55 Primary school students	Elementary School, Seoul, Korea	Yellowtail fish	5.4%	10-520	Fl (100%); H (72,7%); warmth sensation (21%); N (18%); Chills (16%); SR (13%); AP (9%); D (4%); V (2%).
Feldman KA, et al (27)	2003	42 adults	Retreat Center, Marin County California, USA	Escolar fish	75%	min-120	H (67%); facial Fl (62%); Palpitations (57%); N (48%); Dz (48%); D (41%); sweating (33%); AP (31%); V (19%).
Velut G, et al. (28)	2017	40 adults	French military Unit, Near Paris, France	Yellowfin tuna filet	16.6%	min - 135	H (77%); facial Fl (55%); SR (48%); N (39%); Palpitations (35%); D (35%); weakness (32%); AP (32%); Pr (23%); Burning sensation tongue (19%); V (10%)

Abbreviations: SFP: scombroid fish poisoning; Dz: Dizziness; Fl: Flushing; H: Headache; N: Nausea; F. Fever; D: Diarrhea; V: Vomiting; .AP: Abdominal pain; Pr: Pruritus; W: Weakness; T: Tachycardia; S: Sweating; SR: Skin rash

Figure 1. Convention Center in the City of Coquimbo, Northern Chile.

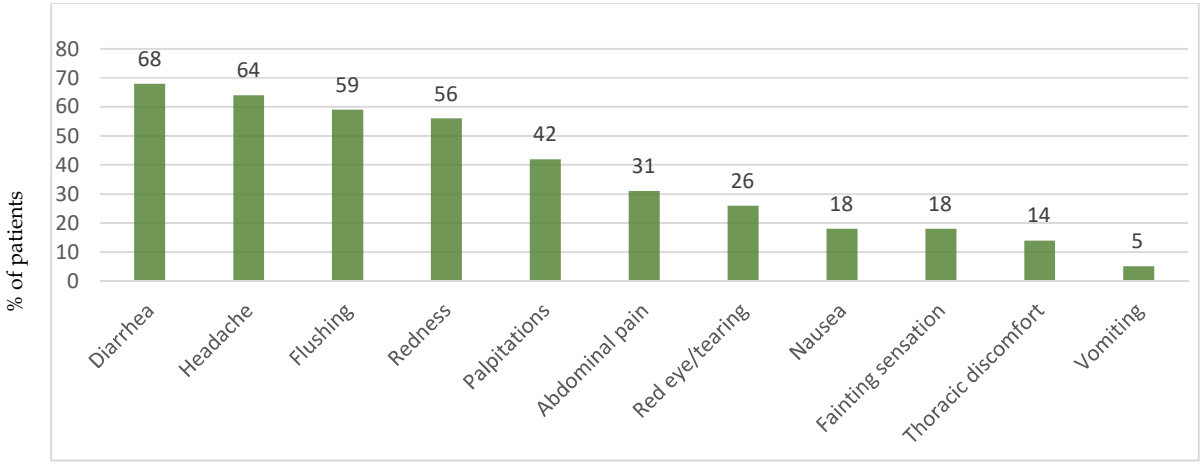


Figure 2. Clinical manifestations of patients with scombroid fish poisoning (n=64)

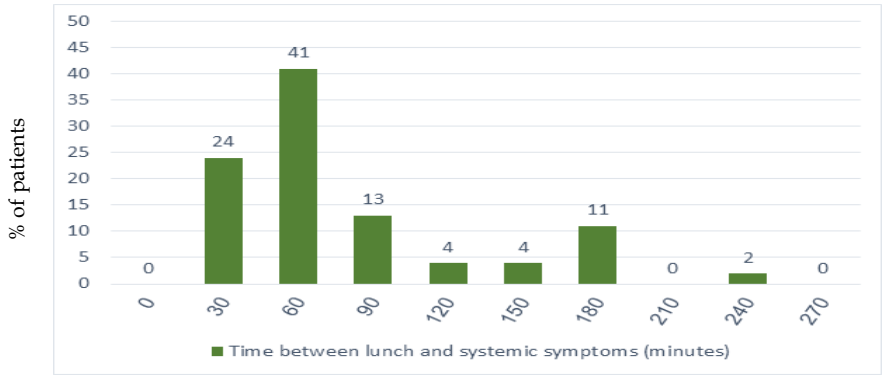
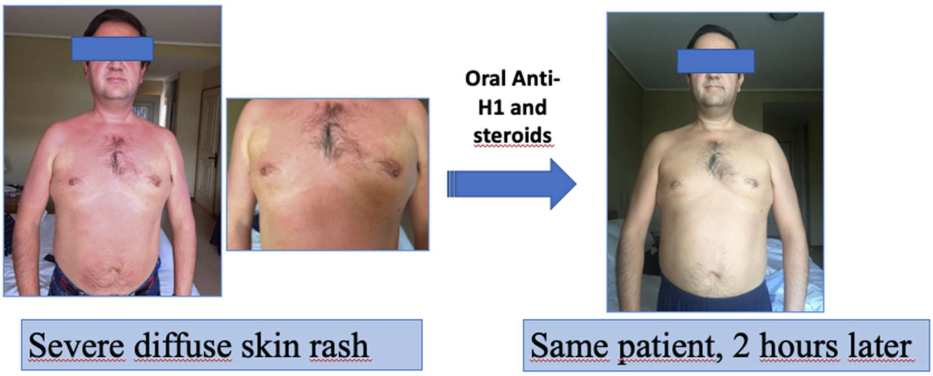


Figure 3. Time of onset of clinical manifestations of SFP, by 30-min intervals after lunch. Ordinate, percentages of patients affected.



Photograph 1. Patient with severe diffuse skin rash due to SFP, treated with anti-H1-blockers and oral steroids.

4.Discussion

Despite considerable advances in food safety during recent decades in the world, foodborne disease outbreaks (FDO) remain a serious world public health problem (12). The World Health Organization (WHO) defines a foodborne illness as one resulting from the consumption of food containing "microbial agents such as bacteria, viruses, parasites or food contaminated by poisonous chemicals or biotoxins" (12). FDO has been defined as the occurrence of two or more cases of a similar illness resulting from the ingestion of a common food. More than 250 different agents have been associated with foodborne diseases in humans (14).

Seafood consumption is currently the leading cause of foodborne illness with known etiology in the US. Nearly 10% of the infectious FDO reported to the Communicable Disease Surveillance Centre were associated with fish, and about half of them to SFP, which is hence, the most common cause of seafood poisoning (15-16). The annual acute care costs of seafood-borne diseases in the US, have been estimated to be up to two-thirds of a billion dollars (13).

During the period 2009-2015 in the US, the CDC reported that out of 2,953 outbreaks of confirmed etiology, SFP caused 95 outbreaks (3%) (12). In 2017 there were 17 confirmed or suspected outbreaks of SFP in the US (affecting 58 people with 1 hospitalization and no deaths,

with a mean of 3.4 affected people per outbreak), of a total of 841 foodborne disease outbreaks reported by the Foodborne disease outbreak surveillance system (17).

These data have major limitations, including underreporting of outbreaks, since the majority of foodborne illnesses occur outside the context of a recognized outbreak and they are only visible if related to public health or economic issues.

Many countries have not established adequate surveillance or reporting systems to identify and track foodborne illnesses. Therefore, information is scarce and not reliable. Nevertheless, we know from countries having these mechanisms of surveillance, that seafood poisoning is a major health problem and the most commonly occurring causes are scombroid (SFP) followed by Ciguatera poisoning (10).

Chile is a narrow and long country located in the southwest area of South America, between the Andes Mountains and the Pacific Ocean, with a large coastal area (approximately 4,200 km), and a population of nearly 18 million inhabitants. Fisheries and aquaculture are considered amongst the most important economic and socially productive activities in Chile. The coastal line of northern Chile (18º-23ºS) where this outbreak occurred, is inhabited by numerous coastal or neritic fish species (18), including Chilean Palometa fish or *Seriola lalandi* sp (also called Hiramasa in Japan). Young Palometa fish grow up to 7 kg, and are known to form shoals of several hundred fish and can be extracted along all year, close to the coast from shallow water down to depths of around 50 m in tropical and subtropical waters of the Atlantic, Indian and Pacific oceans (19,20).

During the last few decades, FDO have also become an important source of morbidity in our country. By law regulations (decree law No 158; 2004) of the Ministry of Health, every FDO should be notified immediately to the SEREMI of health (Secretaría Regional Ministerial), which has full responsibility to perform a local detailed investigation of any outbreak and keep a public record of FDO through daily notification. They perform "in situ" surveys and send samples of suspected food for bacteriological/toxin studies to the ISP (Instituto de Salud Pública). Nevertheless, there are still many barriers and difficulties to study these outbreaks, including scarce and isolated laboratory centers, poor la. tools and significant delays due to work overload. In 2016, there were a total of 1,096 suspected FDO in Chile, affecting 6,513 people, with 28.9% of them attributed to sea products, and no deaths reported (21). Of 256 FDO with confirmed etiology: 72 outbreaks (28%) were caused by SFP, being the second etiology after Salmonella spp intoxication (35%) (21,22).

This report of a massive outbreak of SFP in Chile illustrates very well the form of presentation and characteristics of this disease. The diagnosis of SFP is a clinical one, and based on the typical signs and symptoms and their evolution over time. In our opinion, in this outbreak, there was no other differential diagnosis other than SFP. The epidemic curve in this outbreak showed that the onset time of symptoms was between 30-90 min after ingestion of the presumably contaminated fish, very similar to what has been published in previous reports (Figure 3). The attack rate in our study was 79%, significantly higher than in other international series (Table 2) (23-28), possibly secondary to the fixed meal served to participants.

Table 2 summarizes the main epidemiological and clinical characteristics of the largest outbreaks of SFP published in the medical literature in the last 40 years involving more than 40 patients, including this report.

We were able to suspect very early the possibility of SFP in this outbreak since many attendees presented the typical manifestations of scombroid intoxication, including cutaneous, respiratory and gastrointestinal symptoms after eating fish, therefore ruling out an allergic reaction, which should only affect 1-2 patients, since it is an idiosyncratic reaction. The most common symptoms and signs seen in more than 50% of patients included: diarrhea, headache, flushing and an erythematous skin rash (Table 1, photograph 1, and Figure 2). The early and timely diagnosis of SFP made it possible to administer rapidly oral or iv anti-H1-blockers to all patients, even in those without the full clinical presentation. This measure probably contributed to reduce the severity of symptoms of some patients.

The illness resolved completely within 10 h in 63 out of 64 patients. The only patient with persistent and severe symptoms had cirrhosis, a condition that has been associated with prolonged and severe manifestations, due to accumulation of histamine that is metabolized by the liver (30). In the literature, more severe presentations have been reported including life-threatening conditions as: pulmonary edema, angina, arrhythmias, myocardial dysfunction and even death (30-34).

We found a significant correlation between the size of the portion of eaten fish and the attack rate. Those attendees that ate more than 50% of the portion of the fish (> 100 grams) had an attack rate of 85.4%; and those eating less than 20% of the fish portion (< 40 grams) had an attack rate of 41% (p=0.0005).

We found no relation of gender nor age of the attendees, and the attack rate of SFP. The most significant contributing factor to SFP is not cooling the harvested fish properly and timely, which allows bacterial proliferation. Strict control of the cold chain is essential to prevent the formation of His, so fish should be chilled as soon as possible after catching, and be brought preferably below 10°C within 4 h with lengthier storage of fish at 0°C (32°F) or below, using ice, brine and/or mechanical refrigeration, as this is the critical period for bacterial growth and histamine production (35,36).

In general, the fish with high levels of histamine, does not appear spoiled, but might have a peppery taste. It has to be emphasized that once histamine is produced, as a heat-stable substance, it is not destroyed neither by cooking nor by freezing (35). The illness can thus occur after ingestion of either fresh or canned fish. The toxic dose threshold for histamine in food is unknown, though factors such as histamine concentration in the eaten fish and individual susceptibility may increase the toxic effect. A threshold dose is considered to be 90 mg/kg, although levels as low as 5-10 mg/kg could possibly be harmful; particularly in susceptible individuals (1). The standard method for detection of histamine and other biogenic amines is high-performance liquid chromatography (HPLC), but other methods (including radioimmunoassay and ELISA kits) are commercially available (37). Histamine can be rapidly produced in fish stored at ≥ 20°C, and elevated levels of histamine (> 200 mg/kg of flesh or 200 ppm) have been reported after storing food for a few h at 20–35°C (19). Most outbreaks of SFP, have been associated with fish histamine levels ≥ 200 ppm, although some outbreaks were associated with levels as low as 50 ,ppm.

Australia and New Zealand established histamine values above 200 ppm as a maximum limit in raw fish, whereas the FDA considers 50 ppm for United States and Canada (9, 36). The lower level of 50 ppm, has been derived from the different distribution of amines in large fish (i.e., if in one section of a fish the histamine concentration is 50 ppm, in other parts of the same fish 500 ppm can be found (9,37).

The integrity of the cold chain and sanitary conditions must be protected throughout all the processing stages (catching/transport/delivery/sale). Records of cold chain integrity should be kept at all stages of the food chain. In the current descriptive study, histamine, levels were low (<15 ppm), but there was a clear presumption of loss of refrigeration in the handling of the fish. Sanitary authorities confirmed SFP by clinical basis, incubation period and attack rate associated to the consumption of Yellowtail kingfish as the only food item positively responsible of FDO. In other experiences, like in Australia (2001-2013) in 7 out of the 57 outbreaks of SFP, the analysis showed negative or low levels of histamine in the samples of evaluated fish, which raises the question on toxic dose threshold and in the veracity of the analyzed samples (38). In this outbreak we presumed that the examined fish samples were taken from a different batch the following day after the outbreak, as the Convention Center`s manager was alerted about the inspection and considering the possibility of sanitary sanctions that are associated with proved SFP. Other seafood poisoning diseases that may be considered in different settings may include: Ciguatera fish poisoning (considered the second cause for seafood poisoning worldwide, but it has not been described in Chile); diarrhetic; paralytic; neurotoxic; amnestic; and pfiesteria fish poisonings, which are all caused by dinoflagellates ingested by fish or shellfish and also the Puffer fish poisoning caused by tetrodotoxin produced by certain infecting or symbiotic bacteria in puffer fish (10,39,40). As opposed to SFP, where the symptoms are due to a massive intake of histamine (chemical reaction) produced by bacterial spoilage of improperly refrigerated fish, in these other illnesses the manifestations are the consequence of ingesting preformed toxins and neurotoxins produced by marine unicellular algae or phytoplankton (1).

A recent systematic-review and meta-analysis of histamine food poisoning including 52 reports of 103 incidents affecting 1,171 people (6), concluded that the most common species of fish reported as cause for SFP were tuna (32%); *Scombridae* other than tuna (7,8%); mahi mahi (3,8%); Istiophosridae (10%) and other species (15,2%), which included mainly *Seriola Ialandi* (like our report), and *Arripis trutta*. The main sources reported for Histamine food poisoning were: fish and seafood (98%; 101 incidents) and cheese (2%; 2 incidents) and the intoxications occurred at: Restaurants (40%); Institutional foodservices; Company or Community; and Private homes (18%). In this metanalysis and after analyzing in detail all data, there were no clues of association between other conditions (gender, alcohol consumption, previous medication, and consumption of histamine releasing food) and histamine poisoning. Among the 101 incidents related to fish and seafood, 22 consisted of canned products (21.7%), mainly canned tuna, all but 2 of them (90.1%) occurring before 1985 (6). At present, canned histamine intoxications are rare, due to the widespread worldwide application of Hazard analysis critical control point (HACCP) principles focused on the identification, assessment and control of hazards for food safety and prevention (41,42).

5.Conclusion

This is the first published report on SFP occurring in Chile, including an onsite epidemiological analysis. Patients developed histamine-like clinical manifestations after consuming Yellowtail kingfish. Most patients had mild poisoning that responded to H_1-antagonists and recovered completely in less than 10 h. About 15% of patients were referred to emergency room due to severe symptoms, but none was admitted. It should be emphasized that SFP is a toxic histamine mediated syndrome and not an allergic reaction. Proper handling, storage and cooling of fish is of utmost importance in order to prevent poisoning. This study illustrates the importance of SFP reporting, since it increases the awareness of this under-recognized disease and enables public health authorities to launch timely control and preventive measures.

Acknowledgements

We thank Dr Patricio Zapata and Mrs. Carolina Larrain, for .the English revision of the final manuscript

References

1. Feng C, Teuber S, Gershwin ME. Histamine (Scombroid) Fish Poisoning: A Comprehensive Review. Clin Rev Allergy Immunol 2016; 50: 64-69.
2. Lehane L, Olley J. Histamine fish poisoning revisited. Int J Food Microbiol 2000; 58: 1-37.
3. Hungerford JM. Scombroid poisoning: a review. Toxicon 2010; 56: 231-43.
4. McInerney J, Sahgal P, Vogel M, et al. Scombroid poisoning. Ann Emerg Med 1996; 28: 235-38.
5. Taylor SL, Stratton JE, Nordlee JA. Histamine poisoning (scombroid fish poisoning): an allergy-like intoxication. J Toxicol Clin Toxicol 1989; 27: 225–40.
6. Colombo FM, Cattaneo P, Confalonieri E, et al. Histamine food poisonings: A systematic review and meta-analysis, Crit Rev Food Sci Nutr 2018; 58: 1131-51.
7. Ruiz-Capillas C, Moral A. Free amino acids and biogenic amines in red and white muscle of tuna stored in controlled atmospheres. Amino Acids 2004; 26: 125–32.
8. Smolinska S, Jutel M, Crameri R, et al. Histamine and gut mucosal immune regulation. Allergy 2014; 69: 273–81.
9. Visciano P, Schirone M, Paparella A. An Overview of Histamine and Other Biogenic Amines in Fish and Fish Products. Foods 2020; 9: 1795-1809.
10. Pennotti R, Scallan E, Backer L, et al. Ciguatera and Scombroid fish poisoning in the United States. Foodborne Pathog Dis 2013; 10:105 9-66.
11. Gould LH, Walsh KA, Vieira AR, et al. Surveillance for foodborne disease outbreaks—United States, 1998–2008. Morbidity and Mortality Weekly Report: MMWR Surveill 2013; 62: 1-34.
12. Dewey-Mattia D, Manikonda K, Hall AJ, et al. Surveillance for foodborne disease outbreaks- United States, 2009-2015. MMWR Surveill 2018; 67: 1-11.
13. Ralston EP, Kite-Powell H, Beet A. An estimate of the cost of acute health effects from food- and water-borne marine pathogens and toxins in the USA. J Water Health 2011; 9: 680–694.
14. Bari L, Ukulu DO. Foodborne illness and microbial agents: General overview. In: Bari L, Ukuku DO, Eds: Foodborne pathogens and food safety. Food biology Series. 1st ed. CRC Press, Taylor and Francis Group. Boca Raton, USA. 2016; p.16-34.
15. Lipp EK*, Rose JB. The role of seafood in foodborne diseases in the United States of America.* Rev Sci Tech 1997*;* 16*:*620*–40.*

16. Huss HH, Ababouch L, Gram L. Assessment and management of seafood safety and quality: FAO fisheries technical paper. Report no. 444. Rome, Italy: Food and Agriculture Organization of the United Nations; 2004.
17. CDC Annual summaries of foodborne outbreaks. Atlanta, GA: US Department of Health and Human Services; Surveillance for foodborne disease outbreaks-United States, 2017: Annual report P 1-10. https://www.cdc.gov/fdoss/pdf/2017_FoodBorneOutbreaks_508.pdf , accessed on June 20th, 2021.
18. Navarrete AH, Lagos NA, Ojeda P. Latitudinal diversity patterns of Chilean coastal fishes: Searching for causal processes. Rev Chile His Nat 2014; 87: 1-11.
19. Seriola lalandi Valenciennes, 1833, Yellowtail amberjack http://www.fishbase.org/Summary/SpeciesSummary.php?id=382&lang=Spanish, accessed on June 20th, 2021.
20. Final Report: Caracterización pesquerías de palometa, reineta, cojinoba y dorado en la III y IV regiones de Chile. Universidad Católica del Norte. In. https://www.subpesca.cl/fipa/613/articles-89547_informe_final.pdf , accessed on June 20th, 2021.
21. Ministry of Health, Chile. Web site epidemiology MINSAL.http://epi.minsal.cl/wp-content/uploads/2017/09/Informe_ETA_2016_anual_preliminar.pdf , accessed on June 20th, 2021.
22. Torres J, Voisier A, Berrios I, et al. Knowledge and application in hygienic practices in food preparation and self-report of food poisoning in Chilean homes. Rev Chil Infectol 2016; 35: 483-89.
23. Chen KT, Malison MD. Outbreak of Scombroid fish poisoning, Taiwan. Americ J Public Health 1987; 77: 1335-36.
24. Wu SF, Chen W. An outbreak of scombroid fish poisoning in a kindergarten. Acta Paediatr Taiwan 2003; 44: 297-99.
25. Demoncheaux JP, Michel R, Mazenot C, et al. A large outbreak of scombroid fish poisoning associated with eating yellowfin tuna (Thunnus albacares) at a military mass catering in Dakar, Senegal. Epidemiol Infect 2012; 140: 1008-12.
26. Kang CR, Kim YY, Lee JI, et al. An outbreak of Scombroid fish poisoning associated with consumption of Yellowtail fish in Seoul, Korea. J Korean Med Sci 2018; 33: e235.
27. Feldman KA, Werner SB, Cronan S, et al. A large outbreak of Scombroid fish poisoning associated with eating escolar fish (Lepidocybium flavobrunneum). Epidemiol Infect 2005; 133: 29-33,
28. Velut G, Delon F, Mérigaud JP, et al. Histamine food poisoning: a sudden, large outbreak linked to fresh yellowfin tuna from Reunion Island, France, April 2017. Euro Surveill. 2019; 24: pii=1800405.
29. Maintz L, Novak N. Histamine and histamine intolerance. Am J Clinic Nutr 2007; 85; 1185-96.
30. D'Aloia A, Vizzardi E, Pina PD, et al. A Scombroid poisoning causing a life-threatening acute pulmonary edema and coronary syndrome in a young healthy patient. Cardiovas Toxicol 2011; 11:280–83.
31. Grinda JM, Bellenfant F, Brivet FG, et al. Biventricular assist device for Scombroid poisoning with refractory myocardial dysfunction: a bridge to recovery. Critic Care Med 2004; 32: 1957–59.
32. Coppola G, Caccamo G, Bacarella D, et al. Vasospastic angina and Scombroid syndrome: a case report. Acta Clinica Belgica 2012; 67: 222–25.

33. Borade PS, Ballary CC, Lee DK, et al. A fishy cause of sudden near fatal hypotension. Resuscitation 2007; 72: 158–60.
34. Iannuzzi M, D'Ignazio N, Bressy L, et al. Severe Scombroid fish poisoning syndrome requiring aggressive fluid resuscitation in the emergency department: two case reports. Minerva Anestesiol 2007; 73: 481–83.
35. Johnson EA, Schantz EJ. Miscellaneous natural intoxicants. Chapter 17. In: H.P Riedeman and D.O.Cliver (Eds), Foodborne infections and intoxications, 3rd Ed, pp 663-709. 2006. Elsevier Inc. Academic Press, San Diego, CA, USA. ISBN–13: 978-0-12-588365-8
36. Lazaro CA, Conte-Junior CA. Detection of biogenic amines: Quality and toxicity indicators in food of animal origin. In Food Control and Biosecurity; Holban, A.M., Grumezescu, A.M., Eds.; Elsevier: Amsterdam, The Netherlands, 2018; 16, pp. 225–257.
37. Food and Drug Administration. Fish and Fishery Products Hazards and Controls Guidance, 4th ed.; Chapter 7. Scombrotoxin (Histamine) Formation; FDA: Silver Spring, MD, USA, 2020; pp. 113–152.
38. Histamine fish poisoning in Australia, 2001 to 2013. In https://www.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi3804c.htm, accessed on June 20th, 2021.
39. Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. Emerg Infect Dis 2011; 17: 7–15.
40. Jong EC. Fish and Shellfish poisoning: Toxic syndromes. In Travel and tropical medicine manual. Edited by Sanford CA, Pottinger PS, Jong EC. Fifth Ed. Section 4. Chapter 34. Elsevier Inc. ICBM 978-0-323-37506-1. 2017: p 451-456.
41. Ropkins K, Beck AJ. Evaluation of worldwide approaches to the use of HACCP to control food safety. Trends Food Sci and Tech 2000; 11; 10-21.
42. The HACCP system by the FAO (Food and Agriculture Organization) http://www.fao.org/3/y4743e/y4743e0i.htm, accessed on June 20th, 2021.