Ciguatera poisoning and confirmation of ciguatoxins in fish imported into New Zealand

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ABSTRACT

Ciguatera poisoning has caused illnesses in New Zealand through the consumption of contaminated reef fish imported from Pacific Islands. In May 2020 five people became ill and one was hospitalised following the consumption of Fiji Kawakawa (camouflage grouper; *Epinephelus polyphekadion*). The fish was purchased in New Zealand but imported from Fiji. The meal remnants were analysed for ciguatoxins, the causative compounds of ciguatera poisoning, and showed the presence of the three main toxic fish metabolites. Other fish tested from the same shipment did not contain detectable levels of ciguatoxins, indicating they were likely not toxic.

Ciguatera poisoning (CP) is the most common non-microbial food-borne illness in the world. It is prevalent in the circumtropical regions of the world and is caused by the consumption of fish, invertebrates, gastropods and bivalve molluscs contaminated with ciguatoxins (CTXs) and possibly maitotoxins (MTXs).[1,2]

Although fatalities are uncommon, there is no reliable treatment or antidote, and therefore cases of chronic illness provide most of the data for epidemiological assessments.[3] Folk remedies based on the local flora are used in many Pacific Islands, and intravenous mannitol has been suggested as a possible treatment,[4] although the efficacy of mannitol has been disputed.[5] Due to the lack of a proven antidote, treatment is largely supportive and symptom-driven, which complicates the diagnostic process.

All CP cases reported in New Zealand to date have resulted from the consumption of contaminated reef fish by Pacific Island tourists who have returned to New Zealand from the Pacific Islands and become ill, or from the consumption of reef fish imported into New Zealand. Several cases of CP, linked to moray eel (Muraenidae sp.) brought back from Samoa, were reported in Wellington, New Zealand, in 2016.[6] Several more CP cases were diagnosed in 2019 on the basis of symptoms following the consumption of moray eel brought back from the Kingdom of Tonga and home-smoked.[7] No cases of CP from locally caught and consumed fish have been reported in New Zealand.

Case report

From 10 March until 21 May 2020, Fiji Kawakawa (camouflage grouper; *Epinephelus polyphekadion*) imported from Fiji was sold by Krazy Mart in Christchurch, New Zealand. At the beginning of May 2020, five adults from two families became ill after consuming some of the imported fish. Two were females aged in their forties and fifties and three were males aged between 19 and 58 years old. The eldest male, who had consumed four times the amount of the other diners, was hospitalised within 48 hours of consuming the fish meal. The symptoms were typical of CP (inversion of hot and cold, paraesthesia and dysaesthesia) and the patients were clinically diagnosed as suffering from CP.

Methods

Meal remnants from the intoxication event (fried fish and fried fish curry; Figure 1) were received at Cawthron Institute on 2 June

2020. The samples had the skin and bones removed prior to being homogenised in their entirety. Analysis was performed using an in-house liquid chromatography-tandem mass spectrometry (LC-MS/MS) quantitative method for accurate and specific detection of selected CTXs and MTXs.[8] The most commonly implicated CTX fish metabolite in the Pacific region, P-CTX-1B, had a limit of quantitation (LoQ) of 0.1 µg/kg.

Fish imported in the same batch as those that caused the intoxication event were recalled and tested using the LC-MS/MS method above. They were all labelled 'Fiji Kawakawa' but were in fact a mix of camouflage grouper (*Epinephelus polyphekadion*) and another, somewhat-morphologically-similar species, squaretail grouper (*Plectropomus areolatus*).

Results

Results of the analyses, as reported to the Canterbury District Health Board, had quantifiable levels of P-CTX-1B. The fried fish sample contained 0.29 µg/kg and the curried fish sample contained 0.21 µg/kg P-CTX-1B. The curried fish sample contained less fish, although it had a coconut base. As CTXs are lipophilic, the whole sample was tested. Two additional CTX fish metabolites, 52-*epi*-54-deoxyCTX-1B (P-CTX-2) and 54-deoxyCTX-1B (P-CTX-3), were also easily detected in both samples. However, as calibrated reference material was not available, they were not able to be quantified.

Associated fish from the same shipment as the recalled product were also tested but were negative for the fish metabolite CTXs.

Discussion

Pharmacological assessments have shown that CTXs bind to site five of the voltage-gated sodium channel found in muscles. This binding causes the activation of the sodium/potassium ion pump by modifying the voltage-dependence across the membrane and thereby creating an influx of sodium ions into the cell.[9,10] Intoxication manifests as a wide array of symptoms, including gastrointestinal discomfort (eg, vomiting, diarrhoea, nausea), neurological impairment (eg, inversion of hot and cold, dysaesthesia, paraethesia) and/or cardiovascular complications (eg, hypotension, bradycardia).[11,12] Interestingly, differences in symptoms and intrinsic potencies can be geographically assigned (eg, the Caribbean and the Pacific), which helps with clinical diagnosis.[10,11] This is most likely due to structure-activity and pharmacokinetic differences between the different CTX analogues. The onset of clinical symptoms can appear from 2–30 hours after consumption of ciguatoxic fish, and three key neurological symptoms are characteristic of CP from the Pacific region: inversion of hot and cold, dysaesthesia and paraesthesia.[12,13]

The toxins found in fish that cause the poisoning syndrome have their origins in a single-celled microalgae from the genus *Gambierdiscus* (Dinophyceae). *Gambierdiscus* is epiphytic on macroalgae, eel grasses and coralline turfs and is consumed with the host substrate by herbivorous and coral-grazing reef fish. Omnivorous and carnivorous fish prey on these species and the toxins are biotransformed and biomag-

Figure 1: Remnants of fish meals linked to ciguatera poisoning cases in Christchurch, New Zealand.

nified up the marine food web.[14] The only known CTX producer in New Zealand waters is *Gambierdiscus polynesiensis*, which has been isolated from Rangitāhua (the Kermadec Islands), a New Zealand territory approximately 1,000 km northeast of the mainland.[15] The species has also been isolated throughout the tropical South West Pacific. A related genus, *Fukuyoa* (previously classified as *Gambierdiscus*), has been isolated from the Bay of Islands, but does not produce CTXs or MTXs.[15]

In the Pacific region, P-CTX-1B has been well documented in many fish species[16] and is typically the dominant CTX analogue in ciguatoxic fish. No regulatory limits have been officially set for CTXs, although the United States Food and Drug Administration has established a guidance level of 0.01 µg/kg P-CTX-1B equivalents for Pacific CTXs and 0.1 µg/kg C-CTX-1 equivalents for Caribbean CTXs.[17] The difference between the two levels is due to the differences observed in the potency between these CTX analogues. The meal remnants linked to this poisoning had 0.29 and 0.21 µg/kg P-CTX-1B for the fried fish and fish curry, respectively, which is well above the guidance level. Although analytical methods are essential for regulatory monitoring, globally there is currently no method that can accurately and specifically quantify the different CTX analogues down to this level.

The intoxication event presented here is from fish imported from Fiji and sold in New Zealand. It is important to also focus on the increasing sea surface temperatures and changes in the prevailing currents due to climate change. This is causing an expansion of the sub-tropical/temperate latitudes, which in turn means the habitable range of *Gambierdiscus* is also expanding. This is evident as CP in Australia has historically been along the coast of Queensland, however in recent years fish caught in New South Wales waters have caused CP events.[18] The coastal waters around New Zealand are also warming up and therefore the risk of locally contracted cases of CP is increasing.[15,19]

Conclusions

The illnesses reported in Christchurch in May 2020 and diagnosed as CP were caused by fish that had been imported from Fiji and which were shown to be contaminated with CTXs. The risk of suffering from CP after eating reef fish from the Pacific region is real and should be considered in any instance where there is illness following consumption of such a meal. Testing of meal remnants will help confirm a CP diagnosis, but only the fish eaten is of interest, as CTX concentrations differ widely between individual fish, even from the same catch.

Competing interests:
Nil.
Acknowledgements:
The research into this event was conducted with funding from the MBIE-funded Seafood Safety research programme (contract CAWX1801) and a doctoral scholarship from the New Zealand Food Safety Science and Research Centre, awarded to J. Sam Murray.
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