

Treatment of a Mild Chronic Case of Ciguatera Fish Poisoning with Intravenous Mannitol, a Case Study.

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Abstract:

This article describes a recent case of ciguatera poisoning treated with intravenous mannitol. Mannitol has been used with good effect in non-controlled studies in acutely severely poisoned patients, but is not described in the treatment of chronic or milder poisoning. Our patient was a 35-year-old Niuean man who had eaten a ciguatoxic fish two weeks previously. His symptoms were not severe but were very unpleasant and restricted his ability to work. He was given a single dose of mannitol (0.66g/kg) as an intravenous infusion over two hours. His symptoms dramatically improved within 24 hours, and within a few days he felt virtually back to his former self. He experienced no side effects to the mannitol. It is suggested that intravenous mannitol may prove to be a useful treatment for mild to moderate ciguatera poisoning, and for patients who present late for treatment. (PHD, 2005 Vol 12 No 1 Pages 155 - 157)

Background

Ciguatera poisoning is a disease caused by ciguatoxin, a substance produced by the dinoflagellate *Gambierdiscus toxicus*. This dinoflagellate lives on a type of macroalgae which inhabits coral reefs. It is believed that certain conditions favour the growth of the algae and therefore predispose to the risk of ciguatera poisoning¹. These conditions include reef destruction from causes such as dynamiting and wharf construction, ocean warming and pollution e.g. sewerage outlets.

Poisoning in humans comes about as a result of ingesting fish that have fed on the affected reef. The fish itself does not become unwell, and it is impossible to distinguish healthy from toxic fish by their appearance. Fish who prey on affected reef fish, such as barracuda and moray eels, also become ciguatoxic².

Ciguatera fish poisoning has been a phenomenon in Niue for a number of years, affecting a small but significant proportion of the reef around the capital, Alofi (personal communication Brendon Pasisi, Fisheries Department, Niue). Over this time locals and the Fisheries and

Health Departments have warned of the risk of eating reef fish from this area. In 2002 there was a cluster of cases, including three hospitalisations. After that people avoided eating fish from at-risk areas. Recently some people have started eating these fish again, and another cluster of a dozen or so cases have occurred. Treatment with intravenous mannitol is standard treatment in Niue for severe cases requiring hospitalisation.

The diagnosis of ciguatera poisoning is based on the clinical picture. There is no diagnostic test, although it is possible to test reef samples for the dinoflagellate and the algae it inhabits. This was done in Niue in 2002 and both were found to be present. Symptoms of ciguatera toxicity vary in severity depending on the concentration of toxin in the offending fish, together with the quantity of fish ingested². In addition to general symptoms of malaise, weakness, muscle and joint aches, and anorexia, three categories of symptoms have been described²:

1. Gastrointestinal symptoms such as abdominal pain, nausea, vomiting and diarrhoea are prominent early on, usually within the first 12 hours.
2. Neurological symptoms such as circumoral paraesthesiae, distal paraesthesiae, hyperaesthesia, itching, hot-cold reversal, ataxia, muscle weakness, altered level of consciousness and seizures.
3. Cardiovascular problems such as arrhythmias (particularly bradycardias) also occur.

Treatment of ciguatera poisoning is supportive, with the use of intravenous fluids and analgesia. A number of other treatments have been tried, mostly with little proven benefit⁴. Many local remedies also exist, also of uncertain efficacy. A promising, but unproven, treatment for ciguatera poisoning is intravenous mannitol. Although a recent controlled study showed no benefit³, numerous uncontrolled series have shown dramatic improvement in symptoms with mannitol treatment^{4,5,6,2}.

Case study

A 35-year-old male, weight 100kg, presented two weeks after ingestion of a ciguatera fish. This fish (family Holocentridae, local name Selekihi) was cooked at a local barbecue, and at least six people became sick as a result, three of whom were seen at hospital. Symptoms amongst this group included tiredness, malaise, anorexia, vomiting, diarrhoea, perioral and distal paraesthesiae, hyperaesthesiae, cold-hot reversal, muscle and joint aches and pains, peeling skin, and itching. All experience onset of symptoms within 12 hours of ingestion of the fish.

By the time the patient presented his initial diarrhoea had settled, but he was left with a marked lingering fatigue and malaise, peeling skin of the fingers and toes, generalised paraesthesiae, insomnia and restlessness at night, loss of appetite and a chilled feeling with an intolerance to cold. Water from the shower gave him a very unpleasant sensation on his skin. He was having difficulty concentrating at work, was easily tired and irritable. He reported his urine output as normal.

Given the history of ingestion of fish from a ciguatera-affected area, together with the typical symptoms and the history of similar symptoms amongst others who ate the same fish, the possibility of alternative diagnoses such as gastroenteritis and other forms of food poisoning was thought unlikely. Other fish toxin-related illnesses have not been described in Niue in the past⁷.

After a discussion of the options, we decided to try intravenous mannitol. An infusion of Hartmann's was set up at a rate of 30ml/hr to serve as a diluent for the mannitol. Mannitol 20% was piggybacked at a rate of 150ml/hr (increasing above this rate gave him pain at the infusion site). A total of 300ml (66g of mannitol, the equivalent of 0.66mg/kg) was infused over 2 hours. This amount of mannitol was selected on the basis of previous descriptions in the literature, which recommended between 0.5 and 1.0g/kg^{2,5} given over 60 minutes.

There were no apparent side effects during the infusion, other than soreness at the drip site at the higher infusion rate, and the patient was discharged immediately afterwards.

The following day the patient phoned the hospital reporting a dramatic improvement in his symptoms, including his first good night's sleep since the onset of symptoms, a noticeable improvement in his energy levels, a marked decrease in itching and muscle pains,

and almost complete resolution of the intolerance he felt to contact with water in the shower. A follow-up at one week and two weeks later revealed a complete recovery.

Discussion

Although the symptoms of chronic ciguatera poisoning are not life threatening, and are self limiting over time, they are nevertheless unpleasant and often persistent and debilitating. Symptomatic and supportive treatment with intravenous fluids, analgesics and antihistamines give some relief, but distressing symptoms can persist for weeks or even months. Some patients present for treatment when they realise their illness is not settling after one or two weeks.

Of interest in this case is the length of time between the onset of poisoning and treatment. Past reports have suggested that mannitol treatment is most effective when commenced within 72 hours of the ingestion of the fish⁶. This case suggests that at least some patients may benefit from later treatment with mannitol. Further, the dose of mannitol used for this patient is based on

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doses used in severely poisoned patients elsewhere. It is possible that either more or less mannitol could be beneficial in this situation. The rate of mannitol infusion in chronic cases may not be critical. In our case, we slowed down the rate due to discomfort at the drip site. Much

depends on the mechanism of action of mannitol, which is unknown. Two main theories have been outlined², one suggesting a direct anti-ciguatoxin effect via a scavenger mechanism, the other an osmotic effect reducing Schwann cell oedema. If the delayed use of mannitol for ciguatera poisoning is shown to be beneficial, this would reduce the credibility of the osmotic theory. It is unclear whether patients may benefit from repeated doses.

Re-activation of symptoms with exposure to alcohol or non-ciguatoxin fish is thought to occur, particularly within weeks or months of the original poisoning. Further, ciguatoxin has a long half life, perhaps years, and subsequent poisonings are additive and cumulative i.e. it requires less toxin in subsequent ingestions to produce poisoning. It is not clear whether treatment with mannitol reduces the risk or magnitude of these effects.

Mannitol is inexpensive and readily available, and minimal side effects have been reported to date in using mannitol to treat ciguatera poisoning.

Conclusion

The author suggests that the use of mannitol for the treatment of mild to moderate cases of ciguatera poisoning may be of benefit. Furthermore, there may be

a place for the use of mannitol for ciguatera poisoning in patients who have presented later with milder but debilitating symptoms. Further work is needed to clarify the effect of mannitol in the treatment of all grades of ciguatera poisoning, and in determining effective doses and the optimum timing of administration.

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Never bear more than one kind of trouble at a time. Some people bear three - all they have had, all they have now, and all they expect to have
(Edward Everell Hale - 1822 - 1909)