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Outbreak of Puffer Fish Poisoning in Dhaka City

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Abstract:

Background: *Puffer fish poisoning is quite uncommon but not rare in Bangladesh. This is not a very common fish in Bangladesh and consumed predominantly by poor class of people as it is cheap. Puffer fishes are considered toxic because they possess a potent neurotoxin, tetrodotoxin (TTX) and its analogs.*

Methods: *In October 2014, total 11 patients from two families got admitted in Medicine unit of Dhaka Medical College on the same day with the complaints of tingling, numbness, dizziness, vertigo, postural instability and breathlessness. Both the families admitted, have ingested Puffer fish. A case control study was done where the control were taken from the vicinity with same socioeconomic background. The control group decline of any ingestion of portion of puffer fish. Hence the results and discussion are based on meticulous observation of cases. All the cases were clinically analyzed on different variables.*

Results: *Total 11 patients were from two families, lives half kilometer apart, from Dholaipar, Jatrabari, Dhaka. Mean age of cases were 25.18. Among eleven cases, 7 were male and 4 were female. Mean of lag period between Puffer fish intake and development symptom was 99.44 minute (SD 97.28). Mean of lag period between development of symptom and hospitalization in puffer fish intake group was 308.57 minute (SD 198.78).There were 4 deaths those didn't receive Neostigmine and respiratory support. Total 2 patient received Neostigmineand they recovered. Neostigmine is protective in Puffer fish poisoning (RR .889 <1) but the association is not significant (95% CI on both sides of 1).*

Conclusion: *Cluster of Puffers fish poisoning presenting as outbreaks are associated with serious consequence. The early presentation to health facility and timely neostigmine application and or respiratory support can be lifesaving.*

Key words: *Puffer fish, puffer fish poisoning, tetrodotoxin (TTX), neurotoxin, neostigmine.*

Introduction:

Puffer fish poisoning is quite uncommon but not rare in Bangladesh. It's not very popular fish in Bangladesh and consumed predominantly by poor class of people as it is cheap and also easily available especially in coastal areas. Occasionally the fish is also brought to other city markets for easy selling. Puffer fish are considered poisonous because they possess a potent neurotoxin, tetrodotoxin (TTX) and its analogs, which act on site 1 of the voltage-dependent sodium channels of excitable membranes, blocking sodium influx and consequently, action potential.[1] It has been observed that source of TTX in puffer fish is an endo symbiotic bacteria that naturally inhabits the gut of animal.[2,3] This hypothesis explains that puffer fish acquire the toxic bacteria via food chain and then remain in the fish.[4] The fish has the toxin in almost every organ but predominantly the gonads, liver etc have most of it.[5] There are special chef for preparing the delicious fish in Japan where the fish is consumed as delicatessen and expensive food item. The skill for preparing the fish is crucial as any deviation can lead to serious poisoning with neuroparalysis with potential death. The Dhaka city has not been experiencing the incidence of consumed toxic fish before this outbreak and hence the clinical and epidemiological observation was done critically.

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Methods:

In October 2014, total 11 patients got admitted in Dhaka Medical college on the same day with the complaints of tingling, numbness dizziness, vertigo, postural instability and breathlessness. Of those 11 patients, 4 patients died.

Total 11 patients were from two families, lives half kilometer apart, from Dholaipar, Jatrabari, Dhaka. On query, both the families stated that they took normal diet as every day they used to. But on further query they stated that they bought some unfamiliar fish which they consumed on that day and cooked both internal organ and fleshy part. After consumption at lunch, symptom appeared on varying severity. We couldn't examine the fish but we showed photographs of different types of Puffer fish in Bangladesh. Both the family members identified the same species of the Puffer fish and on further query they described the person from whom they bought the fish and the person was same. We searched the person in that are but the man was missing after the incident possibly due to the activity of law enforcing agency. TTX level measurement was not possible in our cases due to lack of laboratory facilities. A case control study was done as the puffer fish poisoning was not common in the city. Keeping these 11 cases, we collected 11 controls from near vicinity of two families who have similar type of socio economic status and shared similar type of food habit and water supply. Control group consumed other type of fish on that day. As the controls had no history of taking puffer fish on that day, the results and discussion was observed meticulously and outcome was also observed. The verbal autopsy was done in the death cases and in hospital daily monitoring was ensued in other admitted cases. Statistical analysis was done with SPSS 16 manufactured by Chicago Illionois. The lag period of intake, symptoms admission and outcome was recorded. Relative risk and association of treatment outcome was also measured.

Results:

Mean age of cases was 25.18 with standard of error 4.49 but in case of control mean age was 40.45 with standard of error was 5.35 (Table I). Total number patient taken Puffer fish were 11. Among them 7 were male and 4 were female.Variable symptoms developed among the patients after ingestion of puffer fish. Eighty-one percent patients developed peri oral numbness and tingling sensation in the body (Table II). Relative risk of development of symptoms with Puffer fish was much higher than control group who have taken other fish (Table III). Mean of Lag period between Puffer fish intake and development of symptom was 99.44 minute with SD 97.28 (Table IV). Mean of lag period between development of symptom and hospitalization in puffer fish intake group was 308.57 minute with SD 198.78 (Table IV). Regarding the outcome, in case of puffer fish intake group, there were four deaths who didn't receive neostigmine or any respiratory support. Total 2 patient received neostigmine and they recovered (Table V). Neostigmine is found protective in Puffer fish poisoning (RR.889 <1) but the association is not significant (95% CI on both sides of 1) (Table VI).

Table-I

Age of patients

Puffer Fish Ingested	Statistics	Std. Error
Mean (Age)	25.1818	4.49003
95% CI (Lower bound)	15.1774	
95% CI (Upper bound)	35.1862	
5% Trimmed Mean	24.8687	
Median	23.ooo	
Variance	221.764	
Std. Deviation	14.89173	
Minimum	6	
Maximum	50	

Table-II

Symptoms of puffe fish poisoning (N = 11)

Criteria	Number	%
PON	9	81
Tingling	9	81
Vomitting	7	63.6
Weakness	7	63.6
Headache	8	72.7
Blurring of Vision	6	54.5
Cramps	6	54.5
Vertigo	7	63.6
Dizziness	8	72.7
Salivation	5	45.4
Unconsciousness	5	45.4
Respiratory Failure	4	36.3

Table-III
Relative risk of development of symptoms

Symptom	RR of Puffer fish	95% CI	RR of other fish	95% CI
PON	6.5	1.8-23.26	0.413	0.11-1.55
Tingling	6.5	1.8-23.6	0.413	0.11-1.55
Nausea	3.2	1.517-6.69	0.33	0.052-1.31
Vomiting	3.2	1.7-9.36	0.33	0.052-1.31
Weakness	3.2	1.7-9.36	0.33	0.052-1.31
Headache	2.83	1.5-5.4	0.425	0.069-2.634
Blurring ofVision	3.2	1.517-6.69	0.33	0.052-1.31
Cramps	3.75	1.62- 8.68	0.612	0.168-2.25
Vertigo	3.2	1.517-6.69	0.33	0.052-1.31
Dizziness	3.2	1.517-6.69	0.33	0.052-1.31
Salivation	3.2	1.517-6.69	0.33	0.052-1.31
Unconsciousness	2.83	1.5-5.4	0.425	0.069-2.63
Respiratory failure	2.6	1.4-4.6	0.56	0.095-3.316
Death	2.6	1.4-4.6	0.56	0.095-3.316

Table-IV
Puffer fish intake and time to development of symptoms

Criteria	Number (N)	Minimum (Minutes)	Maximum (Minutes)	Mean	Std Deviation
Lag period between ingestion to development of symptoms (Minutes)	9	5.00	300.00	99.44	97.289
Lag period between symptoms to Hospitalization (Minutes)	7	180	720	308.571	198.782

Table-V
Outcome of the Patients

Puffer fish Ingestion		Develop Symptom	Hospitalization	Death	Received Neostigmine	
					Yes	No
Male	7	7	5	4	0	1
Female	4	2	2	0	2	0
Total	11	9	7	4	2	1

Table-VI

Protectivity of Neostigmine

Criteria	Value	95% confidence interval	
		Lower	Upper
For Cohort Neostigmine received	3.00	0.606	14.864

Risk estimation

RR 3 (Protective) but not significant (CI 0.6-14.864)

Discussion:

Variable symptoms developed among the patients. Maximum 81% patients developed peri oral numbness and tingling sensation in the body while 36.3% patients developed respiratory failure (Table III). Homaira N etal[6] reported tingling sensation in the body (91%), perioral numbness (68%), dizziness (64%), weakness in the limbs (60%) and nausea/vomiting (46%) which are quite similar to our findings. Relative risk of development of symptoms who took Puffer fish is much higher than those who didn't take it (Table IV).The verbal autopsy of the cases that died of the poisoning revealed that all death cases ate curry with internal organ of the Puffer fish. They also ate fleshy part of the fish. Cent percent fatal cases started with the symptom of perioral numbness, headache, vertigo, dizziness, excessive salivation, breathlessness and eventually death. Three patients were brought dead and one patient (Mr. S, 20 years of age) died 10 hours later. Unfortunately, the patient who admitted in DMCH and died after 10 hours didn't get any life support or neostigmine. Patient was managed in the medicine ward with oxygen, saline and omeprazole. Patients who died developed symptoms of peri oral numbness, tinglingling sensation nausea, excessive salivation, vomiting and breathlessness within five minutes of ingestion of puffer fish. During the TTX poisoning outbreak in Israel between 2005 and 2008, the onset of symptoms was seen within 10–60 min after ingestion.[7] CDC reported a case where a 32-year-old man while eating third bite of fugu (approximately 1 1/2 oz) within 2-3 minutes noticed tingling in his tongue and right side of his mouth.[8] Rapid onset of action possibly due to absorption of toxin through oral mucosa. Patients relative became panic and tried to make them vomit with turmeric. Three patients became unconscious two hours later and one patient became unconscious after getting admission in the medicine ward. No local physician attended the patients. Timing of the event was 3 PM local time and people were on their work. After getting the news, victim's family members came but unfortunately lack of appropriate transport facility, remoteness of the place and excessive traffic in the street delayed patients reaching hospital vey late.

In 1994, Fukuda and Tani described that there are four grades of TTX poisoning.[9] In this case series of puffer fish cohort it followed the chronology of grades that starts with peri oral numbness and ends with severe respiratory failure and hypoxia. Unfortunately emergency department of our country lacks intubation expertise which possibly could save lots of life.

Mean of lag period between intake of Puffer fish and development symptoms is 99.44 minute (Table IV) with wide of variation. This variation occurred as because 36% cases (4 in number) developed symptoms within 5 to 20 minute, 45% cases (5 in number) developed symptoms within 2 hours to 5 hours and 18% cases (2 in number) developed no symptoms at all. Those two who didn't develop any symptom took only tiny piece fleshy piece of fish. During the Bangladesh outbreak (Dhaka, Natore, Narshingdi and kishoreganj) of TTX poisoning in 2008,[10] the onset of symptoms was observed within 30 min of ingestion of puffer fish in 66% of the total number of cases. In current series, four patients who developed early symptoms ultimately died. This is possibly because of delayed hospitalization as well as lack of skill of life support management. Mean lag period of development of symptoms and hospitalization was 308.57 minutes (Table IV). But four cases who died reached to hospital between 180 to 210 minutes after development of symptoms. Delayed hospitalization was possibly lack of understanding of symptomatology with severity and poisoning scale of puffer fish by the local population and local physicians. Also the transport time due to traffic in busy Dhaka city is a big concern for late presentation.

Out of five male patients, four died but one patient who was hospitalized with only peri oral numbness (Table V). As he had no major neurological manifestation, we didn't treat him with Neostigmin. Patient recovered within 24 hours and was discharged. Two female patients developed no symptom at all.

Tetrododoxin is a heat-stable, water-soluble and a non-protein quinazoline derivative neurotoxin.[11] It competitively blocks the post-synaptic acetylcholine receptor and sodium conductance with neuronal

transmission in skeletal muscle, and thus, all the toxicity is secondary to blockage of action potential.[12.13] Neostigmine atropine combination can help in this regard. Inhibiting acetyl cholinesterase will thus increase the number of acetylcholine molecules that will find their way to a vacant receptor, and thus increase the endplate potential so that it reaches the threshold.[14] Chowdhury F R etal[15] showed that use of atropine neostigmine combination in Puffer fish poisoning causes significant improvement ($p \leq 0.5$) within 24–48 hours. In our cases we applied atropine neostigmine combination in only two cases. These two cases had features of neurotoxicity but were not in respiratory failure. Both had ataxia and one of them was restless with features of impending respiratory failure. These two patients improved quickly after giving neostigmine and atropine combination. Neostigmine was protective in Puffer poisoning (RR .889 <1) but the association is not significant (95% CI on both sides of 1) (Table VI).The effect of neostigmine for reversal of neurotoxicity was obvious in the patients who received but the effect on reversibility for respiratory failure or mortality was not obvious in this case series.

Conclusion:

Clusters of puffer fish poisoning is important as it can turns into fatality if not diagnosed quickly and intervene immediately. The lack of knowledge of symptoms and severity by physicians and poor general concept of public leads to delay of presentation in hospital. Hospital setting needs good and well equipped emergency care service including cardiorespiratory support for immediate managing the puffer fish cases. A hospital based protocol including neostigmine atropine combination is crucial and training for physicians is mandatory. Awareness build up for catching puffer fish and consumption should be prohibited by appropriate authority.

Conflict of interest: none

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