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Gastrointestinal emergency room admissions and Florida red tide blooms

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ABSTRACT

Human exposure to brevetoxins during Florida red tide blooms formed by *Karenia brevis* has been documented to cause acute gastrointestinal, neurologic, and respiratory health effects. Traditionally, the routes of brevetoxin exposure have been through the consumption of contaminated bivalve shellfish and the inhalation of contaminated aerosols. However, recent studies using more sensitive methods have demonstrated the presence of brevetoxins in many components of the aquatic food web which may indicate potential alternative routes for human exposure.

This study examined whether the presence of a Florida red tide bloom affected the rates of admission for a gastrointestinal diagnosis to a hospital emergency room in Sarasota, FL. The rates of gastrointestinal diagnoses admissions were compared for a 3-month time period in 2001 when Florida red tide bloom was present onshore to the same 3-month period in 2002 when no Florida red tide bloom occurred. A significant 40% increase in the total number of gastrointestinal emergency room admissions for the Florida red tide bloom period was found compared to the non-red tide period.

These results suggest that the healthcare community may experience a significant and unrecognized impact from patients needing emergency medical care for gastrointestinal illnesses during Florida red tide blooms. Thus, additional studies characterizing the potential sources of exposure to the toxins, as well as the dose/effect relationship of brevetoxin exposure, should be undertaken.

1. Introduction

Florida red tides occur annually in the Gulf of Mexico from blooms of the marine dinoflagellate, *Karenia brevis* (*K. brevis*). These blooms (a type of harmful algal bloom or HAB) result in massive fish kills and mortalities to marine mammals and sea birds due to the production of the natural neurotoxins, the brevetoxins (Landsberg et al., 2009).

The two major routes of exposure for humans to brevetoxins produced by *K. brevis* have been oral, and more recently, respiratory (Kirkpatrick et al., 2004). It has been known for many years that human exposure to brevetoxins occurred through the consumption of contaminated shellfish, resulting in neurotoxic shellfish poisoning (NSP), an acute onset gastroenteritis with neurologic symptoms lasting several days with unknown chronic sequellae (Watkins et al., 2008). Recently, large dolphin die offs have been associated with the consumption of brevetoxin-contaminated fish even without an active Florida red tide bloom; and recent research using the new brevetoxin ELISA have detected levels of brevetoxin in planktivorous finfish, predominantly in the organs with very low levels also detected in the muscle (Flewelling et al., 2005; Naar et al., 2002, 2007). Other studies have demonstrated that human exposure to brevetoxins can also occur through the inhalation of brevetoxin-contaminated aerosols in coastal areas, resulting in acute respiratory symptoms which may persist, particularly in persons with underlying lung disease such as asthma (for review, see Kirkpatrick et al., 2004; Fleming et al., 2005, 2007, 2009). In fact, these respiratory effects may last for several days to months, including resulting in

Abbreviations: GI, gastrointestinal illness; HABs, harmful algal blooms; *K. brevis*, *Karenia brevis*; NSP, neurotoxic shellfish poisoning.

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increased emergency room admissions for respiratory illnesses (such as pneumonia and bronchitis) during active Florida red tides (Kirkpatrick et al., 2006, 2009). These data suggest that both gastrointestinal and respiratory disease may be associated with exposure to brevetoxins, and a review of emergency room data has identified under-diagnosis and under-reporting of a severe form brevetoxin-related disease, NSP (Watkins et al., 2008).

The research described above presents the possibility that low levels of gastrointestinal illness might be occurring in humans through multiple routes of exposure (including the consumption of contaminated shellfish and fish, and through seawater and aerosol exposure) during a Florida red tide event; furthermore, this gastrointestinal illness might not be severe enough to be classified as "brevetoxin poisoning," but severe enough for people to seek medical care without being recognized as illness associated with brevetoxin exposure. This study examined the demand for medical care for gastrointestinal disease in one specific health care venue, the emergency room, in months when an onshore bloom of Florida red tide was present as compared to a similar period when no red tide bloom was present.

2. Methods

This retrospective cohort study compared the rates of emergency room visits between two time periods: with an active Florida red tide bloom and without a Florida red tide bloom. Similar research methods were used in our investigation of emergency room admissions for respiratory diagnosis during a Florida red tide and during a similar non-red tide period (Kirkpatrick et al., 2006). The facility selected for the study, Sarasota Memorial Hospital (SMH), is one of four hospitals in the county; it is the largest acute care facility in Sarasota County serving 63.3% of the county's population. This healthcare facility is also closest to the coastline. Access to anonymous medical data was provided by the Decision Support Services at SMH after Institutional Review Board (IRB) approval of the study; the study was also approved by the Florida Department of Health IRB.

2.1. Exposure data

The Florida red tide bloom period was during the fall of 2001 (September 1–December 31, 2001), and the non-bloom period was during the fall of 2002 (September 1–December 31, 2002). The red tide cell count data (i.e. enumeration of numbers of cells of *K. brevis* per liter) were provided by the Phytoplankton Ecology Program at Mote Marine Laboratory, Sarasota, FL. This Program routinely monitors a minimum of 2 shore locations on its campus. Water samples are analyzed weekly during non-bloom conditions and daily during blooms. This explains the increased number of samples enumerated in 2001 (red tide period) compared to 2002 (non-red tide period).

2.2. Health endpoint data

Computerized anonymous emergency room admission data were collected for the months of October through December 2001 and for the same months in 2002 to minimize the effects of variation from gastrointestinal illness from seasonal exposures (such as influenza). In addition, since the Sarasota area has a seasonal population, using the same 3-month period adjusted for fluxes in the population as most seasonal residents have the same visitation patterns year after year.

The study data consisted of the emergency room admission diagnosis with the International Classification of Diseases (ICD) diagnosis classification for gastrointestinal disease (codes 530–579) and all other ICD diagnoses, the patient age, and the date of admission. Due to the use of anonymous data, repeated admissions by the same individual could not be identified and removed. With the assistance of 2 medical professionals, and using the ICD coding for the primary emergency room diagnosis, the following mutually exclusive gastrointestinal diagnoses were selected as being most consistent with possible exposure to brevetoxins: gastritis, duodenitis, and non-infectious enteritis and colitis (acute, chronic, unspecified, and other) (ICD 535.0–537.9 and 557.0–558.0). These four gastrointestinal diagnoses accounted for only 15% all gastrointestinal diagnosis of emergency room admissions reported during the study months. All other gastrointestinal diagnoses were grouped as "all other primary diagnoses."

2.3. Statistical analysis

The total number of emergency room admission diagnoses was evaluated for the periods October 1–December 31, 2001 and October 1–December 31, 2002. The emergency room admissions were assessed between the October and December time period, however, the 2001 September cell counts of *K. brevis* are given to document that patients reporting to the emergency room October 1, 2001 may have had a significant exposure to a Florida red tide bloom in the previous month. Using the ICD-9 codes, these diagnoses were categorized as gastritis, duodenitis, and non-infectious enteritis and colitis (acute, chronic, unspecified and other), or all other primary diagnoses. SAS, version 9.1 was used for calculations (SAS Institute, Inc., Cary, NC).

Standardized emergency room admission rates were calculated for the above diagnoses and the subgroups of age to adjust for age. The Florida population for the year 2000 was used as the standard population. The population information data were provided by the Florida Cancer Data System at the University of Miami School of Medicine (Miami, FL). Rate ratios were calculated as the standardized 2001 age rate divided by the standardized 2002 age rate, and 95% confidence intervals were calculated for these rate ratios (Clayton and Hills, 1993).

3. Results

3.1. Environmental data

Average daily cell counts of *K. brevis* by month are presented in Table 1. Significantly higher cell counts were noted in September–December 2001 compared to September–December 2002 (Kirkpatrick et al., 2006). In Fig. 1, the true cell counts are displayed on a log scale to account for the large scale changes between the two sampling periods. An arbitrary offset of 120 was added to all values to allow visualization of counts of zero. Although a slight spike in cell counts occurred in November 2002, the short duration of the increased counts meant that this was not considered a "bloom" (Kirkpatrick et al., 2006).

3.2. Emergency room admissions

The overall number of emergency room admissions during the 2001 and 2002 periods were similar (i.e. 21,308 in 2001 and 22,270 in 2002), as were the mean ages (48.93 $\pm$ 22.3 years in 2001 and

Table 1
K. brevis cell count averages by month and year (in cells/L).

	2001	2002
September	1,419,435	50,329
October	302,895	207
November	399,020	2,333
December	53,070	173

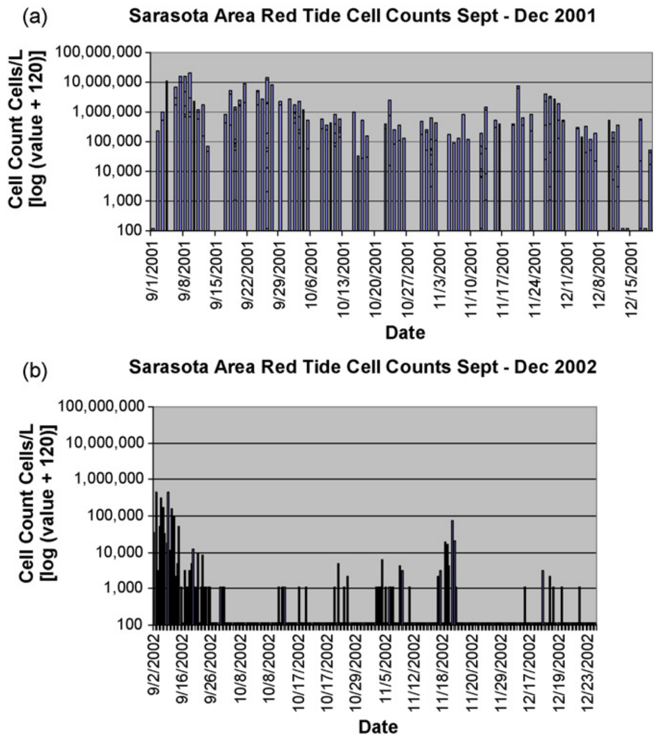

Fig. 1. (a) September–December 2001 Sarasota area red tide cell counts (shown as log[value + 120] to display counts of 'zero'). (b) September–December 2002 Sarasota area red tide cell counts (shown as log[value + 120] to display counts of 'zero').

Table 2
Demographics of the 2001 and 2002 emergency room admissions per 100,000 of Florida population.

	2001	2002	Statistical significance (*p* value)*
Number of admissions	21,308	22,270	
Mean age ± SD years	48.93 ± 22.33	48.49 ± 22.29	0.04
Age range (years)	13–106	13–103	
Gender			
Female (%)	11,407 (53.5)	12,098 (54.3)	0.10
Male (%)	9,900 (46.5)	10,172 (45.7)	
Race			
White (%)	17,593 (82.6)	18,077 (81.2)	0.0002
Other (%)	3,715 (17.4)	4,193 (18.8)	
Selected gastrointestinal diagnoses	140 (13.9)	114 (23.0)	0.04
All other GI diagnosis	864 (86.1)	833 (87.9)	

* Chi-square and *t* tests.

48.48 ± 22.3 years in 2002) and gender distribution (54% female in 2001 and 54% female in 2002) of the emergency room patients. The race distribution (82.6% white and 17.4% "other" in 2001, and 81.2% white and 18.8% "other" in 2002) was a statistically significant but not functionally different between the 2 years (see Table 2). Of the gastrointestinal diagnoses, the selected diagnoses of gastritis, duodenitis, and non-infectious enteritis and colitis (acute, chronic, unspecified and other), comprised 13.9% of emergency room admissions in 2001 and 23% in 2002.

When emergency room admissions rates were adjusted for age, the overall admission rates were not significantly different between the 2 years for all diagnoses (rate ratio = 1.01; 95% confidence interval = 0.92–1.10). However, the emergency room admission rates for the selected gastrointestinal diagnoses (1.40; 1.06–1.84) were significantly different for the Florida red tide bloom period compared to the no red tide period, with a 40% increase in gastrointestinal emergency room visits (see Table 3). There was no significant difference between the 2 time periods for the emergency room admission rates for all other gastrointestinal diagnoses (1.04; 0.94–1.16).

4. Discussion

We found a significant increase in the rate of emergency room admissions for selected gastrointestinal diseases during the 2001 red tide bloom period when compared to the 2002 non-red tide period. The increased rates of gastrointestinal disease, as well as previously documented respiratory disease increased rates (Kirkpatrick et al., 2006), may indicate that humans are being exposed to brevetoxins via more than one exposure pathway resulting in levels that can cause undiagnosed but clinically recognized health effects during active Florida red tide blooms.

The State of Florida Department of Agriculture has an exemplary program monitoring for *K. brevis* levels near regulated shellfish harvesting areas wherein high cell count levels result in the closures of affected harvesting areas. Nevertheless, there have been documented cases of persons with NSP after consuming contaminated shellfish in Florida associated with illegal recreational harvesting of shellfish (Watkins et al., 2008). Of note, many of these persons have been tourists or members of ethnic minorities without knowledge of the shellfish harvesting bans; furthermore, many of these cases were not diagnosed as being NSP at the time of the initial medical evaluation. In addition, even when shellfish harvesting bans are lifted after the shellfish are tested safe using the current regulatory method, non-acutely toxic levels of brevetoxins and brevetoxins metabolites are still present in shellfish (Plakas et al., 2008). With regards to other seafoods, the assumption has been that fish exposed to Florida red tide blooms die rapidly due to paralysis of the gills after brevetoxin exposure, leading to the huge numbers of dead fish associated with active Florida red tide blooms (Kirkpatrick et al., 2004). In fact, the public health message regarding the catch and consumption of live fish during Florida red tides has been that the filleted meat is safe to eat. Recent studies have detected brevetoxins in finfish (Flewelling et al., 2005; Naar et al., 2007). Furthermore, large dolphin die offs have been associated with consumption of brevetoxin-contaminated fish even without a documented active Florida red tide bloom (NMFS, 2004). The majority of brevetoxins detected in the finfish and in the fish found in the stomachs of the dolphins had accumulated in the entrails of the fish, with relatively

Table 3
Emergency room age adjusted admission rates per 100,000 Florida population and rate ratios (2001 vs. 2002).

	2001	2002	Rate ratios (95% confidence intervals) 2001/2002
All emergency room admissions	0.068	0.067	1.01 (0.92, 1.10)
Gastrointestinal diagnoses:			
Selected GI diagnoses	0.067 (0.055, 0.082)	0.048 (0.038, 0.061)	1.40 (1.06, 1.84)
All other GI diagnosis	0.039 (0.036, 0.042)	0.037 (0.034, 0.040)	1.04 (0.94, 1.16)

low levels in the muscle. However, if persons consumed the entire fish in a soup or stew, they would be exposed to the brevetoxins in the organs. Furthermore, since brevetoxins are rapidly absorbed into the bloodstream through inhalation exposure and from there can reach the brain (Benson et al., 1999), it is also possible that brevetoxin-contaminated aerosol exposures may also lead to gastrointestinal illnesses through the same neurologic pathway as NSP. It is even possible that people could be exposed to brevetoxins through the inadvertent consumption of contaminated seawater since studies have shown relatively high levels of brevetoxins in coastal waters during an active Florida red tide bloom (Pierce et al., 2005). Thus, there are multiple potential sources of brevetoxin exposure which could lead to gastrointestinal illness in human populations.

Although brevetoxin-related illnesses (both NSP and respiratory irrigation) and other harmful algal bloom diseases have been described in the medical literature, these diseases are significantly under-reported to public health authorities (Fleming et al., 2002; Backer et al., 2003, 2005, Watkins et al., 2008). They are under-reported because both victims and healthcare providers misdiagnose these illnesses as "food poisoning" or "asthma" without further investigation into the actual cause, and victims often do not seek formal medical care. In addition, most healthcare providers, even in endemic areas such as Sarasota (FL), are unaware of the range of exposure possibilities for brevetoxin, including the fact that whole fish (as well as shellfish), contaminated aerosols, and seawater may serve as causes of brevetoxin-associated illness in humans. This study is the first indication that the incidence of gastrointestinal illness is increased during active Florida red tide blooms; this raises questions concerning both public health recommendations and healthcare provider education in areas with active Florida red tides.

4.1. Limitations

No individual exposure information was collected for this analysis; this study only reports an association of gastrointestinal emergency room admissions with the presence or absence of Florida red tide bloom. Furthermore, since this study did not assess individual exposure, it is not possible to know if an individual was actually exposed to brevetoxins, nor to assess the latency period (i.e. the time of exposure to the time when people reported to the emergency room for medical care) associated with the observed health effects. Although the data were adjusted for age, there was no individual health assessment to explore other patterns that might have affected the increase in specific gastrointestinal admissions in 2001 compared to 2002. For example, an early influenza season in 2001 might have lead to increased gastrointestinal admissions during October through December 2001. Furthermore, individual underlying pre-disposing conditions were not examined. Finally, the amount of toxins in the water can vary within the day and over time. Environmental conditions were assessed through the water analysis of the number of red tide cells present, not the amount of brevetoxins.

5. Conclusions

This preliminary investigation explored whether there is an increased healthcare burden to the medical community when an onshore bloom occurs over a period of several months. Even with substantial under-reporting of HAB-associated diseases, the costs associated with the human health effects of marine toxins such as the brevetoxins have been estimated to account for at least 45% of the total estimated economic impact of HABs nationwide (Anderson et al., 2000). Hoagland et al. (2009) recently estimated the costs of illness for emergency room respiratory illnesses associated with *K. brevis* blooms in Sarasota County (FL) alone to range from $0.5 to $4 million/bloom, depending upon bloom severity. Since the emergency room is only one of various possible access points for people seeking medical care, the assessment of other medical venues (such as walk in clinics, private practice, and state health departments), as well as use of over-the-counter medications, is warranted in the future. The traditional public health message and healthcare provider training have not taken into account the possible extent of exposure to brevetoxins including possibly contaminated seafood (i.e. shellfish and whole fish), air, and water during an active Florida red tide bloom. Further investigation is required to assure the accuracy of this message.

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