RESEARCH COMMUNICATION

Radium-Contaminated Water: a Risk Factor for Cancer of the Upper Digestive Tract

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Abstract

There is a high incidence of oral, pharynx and esophagus cancer among males in Na Mom district in Songkhla Province in Thailand, an area where radium concentration in shallow well water is found to be higher than other areas in this province. A population-based case control study was conducted from June to November 2004 to determine the association of oral exposure to radium-contaminated water and cancer of the upper digestive tract in the district. Thirty-two confirmed cases and 128 sex and five-year birth cohort matched neighborhood controls were selected by multistage sampling from six villages in four sub-districts. All subjects were verified to have been permanent residents in the district for more than 10 years. Thirty cases were dead at the time of the study, thus their relatives were interviewed to determine their amount of water drinking, tobacco smoking, alcohol drinking, betel chewing and exposure to other potential risk factors in the past. The other two cases and all controls were directly interviewed. The concentration of radium in shallow well water at the subject's houses was estimated using a contour map of Ra-226 in the water at the location of their residence. The results showed a strong and dose-dependent association between consumption of radium-contaminated shallow well water and cancer of the upper digestive tract. In multivariate analysis controlled for important risk factors of the cancer, the odds ratios for exposure to oral radium consumption 50-100 mBq/day and >100 mBq/day compared with <50 mBq/day were 2.83 (95% CI: 0.50-16.19) and 29.76 (95% CI: 4.39-201.6) respectively. The risk also increased with consumption of fresh water fish which might have been contaminated by dissolved radium in the water. This study offers the first evidence of the association between radium and cancer of the upper digestive tract to the world literature. Further studies with other methods such as area-wide correlation of radium-uranium concentration and the incidence of the cancer and case-control studies in other populations are needed to confirm the evidence.

Key Words: Radium contamination - water - cancer - upper digestive tract

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Introduction

It was repeatedly reported in the series Cancer in Thailand from volumes I to III covering the years 1988-1997 that the incidence rates among males of cancer of the oral cavity, pharynx, and esophagus were 3 to 4 times higher in the south than other regions of Thailand (Vatanasapt et al., 1995; Derassamee et al., 1999; Sriplung et al., 2003). However, there was no good explanation for this phenomenon. Studies in southern Thailand have demonstrated risk factors of oral, pharyngeal, and esophagus cancer to be alcohol drinking, tobacco use, and betel quid chewing (Chongsuvivatwong et al., 1990; Chanvitan et al., 1990; Prateepko, 1997). These behaviours are also practiced in other parts of the country at similar rates and do not explain such a large difference in rates in different parts of the country. For example, the prevalence of cigarette smoking in Thais is reported to be highest in the northeastern region with a rate of 26% while it is average in the southern and central regions with a rate of 24% (Thaihealth, 2006).

The geology of the southeastern part of the district is predominantly late Triassic to early Jurassic granite, as shown in Figure 1 (Phungrassami, 1984). According to the radiographic contour map for uranium, the Na Mom area contains higher uranium in the granite bed rock than other nearby districts (Department of Mineral Resources, 1989). Faults in the rock cause dissolution in underground water of heavy metals, including radium, an important daughter element of uranium. A survey of shallow well waters in the area found radium concentrations in a range of 3.51-292.1 mBq/litre (Figure 2), which roughly corresponded to granite rock and faults (Wutthisasna et al., 2006), while the maximum allowed radium concentration in drinking water is 185 mBq/litre according to the United State Environmental Protection Agency (USEPA, 2001).

Shallow well water has historically been the main source of drinking water in the area until recently when pipe water has been supplied in some areas. Though it is not certain

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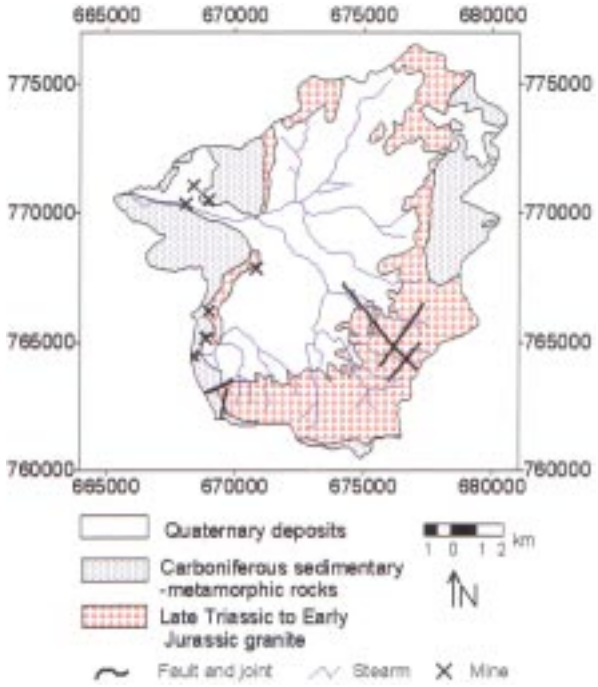

Figure 1. Geological Map of Na Mom (Redrawn from Phungrassami, 1984)

that contamination of radium in the well water is responsible for the exceptionally high incidence of cancer of the upper digestive tract in the area, the hypothesis must be tested.

Materials and Methods

A population-based case-control study was carried out using cases of oral cavity, pharynx, and esophagus cancer who were resident in Na Mom district, identified by the cancer registry of Songkhla province, the Radiotherapy Unit, Prince of Songkla University, and Na Mom Hospital from 1999 to 2004. Thirty-two cases were identified and all had pathological diagnosis. Two were living and 30 were deceased.

Four controls to one case were drawn from the general population of Na Mom within the same sex and 5-year birth cohort stratum. For convenience of visiting controls at their home, two villages were randomly selected from the two large sub-districts and one from the two small ones by population size. Then the population was pooled together and stratified by sex and 5-year birth cohort using population databases of local primary health care unit registration of residents (Health Center Information System). All 32 cases and 128 controls were verified to be permanent residents of the district for more than 10 years.

The amount of drinking water per day and exposure to other potential risk factors were assessed retrospectively by interviewing participants themselves if they were still alive or their relatives if they were dead. The residential geographic coordinates of participants were also recorded to identify the level of radium contamination in shallow well water from a GIS map previously done by Wutthisasna et al. (Wutthisasna, 2006). An estimate of the exposure to

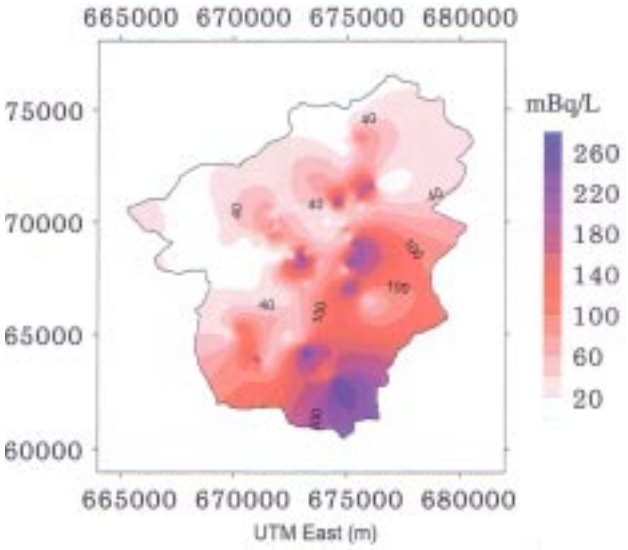

Figure 2. Contour Map of Ra-226 Concentration in Shallow Well Water in Na Mom (Reproduced from Wutthisasna et al., 2005)

radium-contaminated water was determined by multiplying the daily volume of drinking shallow well water (litres/day) by concentration of radium (mBq/litre) in shallow well water, estimated at the subject's house location.

Data analysis was performed using R program version 2.0.1. (R Development Core Team, 2004). Conditional and unconditional logistic regression models were applied to the data to test the hypothesis and adjusted for other potential risk factors.

Results

The characteristics of the 32 cases and 128 controls are shown in Table 1. Table 2 shows odds ratios of various potential risk factors in developing cancer of the upper digestive tract. In univariate analysis, drinking shallow well water and alcohol consumption had significant odds ratios

Table 1. Characteristics of the Cases and Controls

Variables	Cases		Controls		P-value*
	Number	%	Number	%	
Sex					1.00
Male	28	87.5	112	87.5	
Female	4	12.5	16	12.5	
Birth cohort					1.00
1964-1955	2	6.3	8	6.3	
1954-1945	6	18.8	24	18.8	
1944-1935	8	25.0	32	25.0	
1934-1925	13	40.6	52	40.6	
1924-1915	2	6.3	8	6.3	
<1914	1	3.1	4	3.1	
Resident (sub-district)					0.16
Na Mom	8	25.0	51	39.8	
Phichit	13	40.6	46	35.9	
Thung Khamin	4	12.5	5	3.9	
Khlong Rang	7	21.9	26	20.3	

* Chi-squared p-value.

Table 2. Association of Potential Risk Factors and Cancer of the Upper Digestive Tract

Potential risk factors	cOR	(95% CI)	aOR	(95% CI)	P-value*
Drinking shallow well water					0.98
1-4 glasses/day	1.00		1.00		
> 5 glasses/day	3.06	(1.18-7.96)	0.98	(0.21-4.53)	
Estimated daily radium intake from drinking water					<0.001
< 50 mBq/day	1.00		1.00		
50-100 mBq/day	4.42	(1.11-17.7)	2.83	(0.50-16.2)	
>100 mBq/day	16.4	(4.50-59.4)	29.8	(4.39- 201)	
Tobacco smoking					<0.001
No	1.00		1.00		
Yes	3.30	(1.09-10.0)	9.60	(1.65-56.0)	
Alcohol drinking					0.390
No to occasional	1.00		1.00		
Yes	7.52	(2.18-26.0)	2.31	(0.32-16.5)	
Betel chewing status					<0.001
No	1.00		1.00		
Yes	3.70	(1.26-10.8)	26.7	(3.55- 200)	
Sea food consumption					0.007
No to occasional	1.00		1.00		
Frequent	0.34	(0.14-0.82)	0.16	(0.04-0.68)	
Fresh water fish consumption					<0.001
No to occasional	1.00		1.00		
Frequent	8.63	(3.64-20.5)	13.5	(3.49-52.1)	
Vegetable consumption					<0.001
No to occasional	1.00		1.00		
Frequent	0.14	(0.06-0.32)	0.09	(0.02-0.34)	

cOR = crude odds ratio, aOR = adjusted odds ratio
* P-value from likelihood ratio test when removing the factor from the final model, or adding to the model if p-value is >0.05

but after adjustment for all factors by multivariate analysis they were excluded from the final unconditional logistic model. The conditional logistic model gave similar results with slightly different odds ratios and is not shown here. Consumption of radium at a level of 50-100 mBq/day increased the risk by 3 times and at a level of over 100 mBq/day increased the risk by 30 times.

Tobacco smoking and betel quid chewing were identified as significant risk factors but not alcohol consumption. Interestingly, consumption of fresh water fish was also identified as a risk factor of cancer of the upper digestive tract. Frequent consumption of sea food and vegetables were protective factors for the cancer.

Discussion

This study demonstrates that a high level of exposure to radium-contaminated water was a significant risk factor for cancer of the upper digestive tract. The risk increased with exposure levels. Studies have shown that radium ions are human carcinogens and increase the risk of cancer to varying degrees in many tissues and organs (Senior et al., 1995; Szabo et al., 1998; Kay, 1999), but not in the organs of the upper digestive tract.

Radium emits several different kinds of radiation, in particular alpha and gamma radiation. The ionizing radiation may injure the cells of the oral cavity, pharynx, and esophagus and the nearby tissues and may eventually induce cancer. It was demonstrated that radium can be absorbed from oral ingestion in either water soluble or water insoluble forms (Stehney et al., 1955; Maletskos et al., 1966; Maletskos et al., 1969). Soluble radium ions behave similarly to calcium ions (IARC, 2001), which are an important cation in saliva (Vitolo et al., 2004; Dodd et al., 2005). Thus, radium ions may circulate in the upper digestive system through the same pathways as calcium ions. In the salivary circulation, radium radiation may cause ionization of water and produce free radicals such as H, OH and electrons which are highly reactive radicals which cause damage to body tissues.

Frequent consumption of vegetables and sea food, including fish, decreased the risk of cancer of the upper digestive tract in our subjects. This finding was not surprising since it has been repeatedly illustrated in the literature that vegetables and fish are protective factors for oral, pharyngeal, and esophageal cancer (i.e. Launoy et al, 1998; Levi et al, 1998; Franceschi, 1999; Rajkumar et al, 2003; De Stefani et al, 2003; 2005).

However, an increased risk from fresh water fish consumption was not expected and requires special attention. It is possible that fresh water fish in the area might be contaminated with dissolved radium ions in the water. If this is the case, radium contamination in fresh-water food products needs further study.

One of the weaknesses of this study is the fact that most of the cases were dead and information on exposure was obtained by interviews with their relatives. This could explain the deviation of odds ratios of tobacco smoking, alcohol drinking, and betel quid chewing from that obtained from previous studies in southern Thailand (Chongsuvivatwong et al., 1990; Chanvitan et al., 1990; Prateepko, 1997). Though the magnitude of the risk of consumption of fresh-water fish and of the protection of vegetables and sea food are uncertain, the direction of the associations concerning fresh water fish as a risk factor and vegetables and sea food as protective factors seems likely since dietary behaviour was practiced at home and, thus, more easily remembered by relatives than smoking and alcohol drinking behaviours that were usually practiced outside the house at the subjects' work places.

Lack of temporal sequence of exposure and outcome is another weakness of this study, as the concentrations of radium in the wells was measured in 2003 while cancer cases were collected from 1999 to 2004, before or around the measurement of radium exposure. This was unavoidable since there was no such a study in the past. It is possible that the concentrations of radium were different in the far past from 2003, however, it is probably that the relative difference between two points was relatively constant over a few decades.

Despite the small sample size and the weaknesses

mentioned above, the highly significant association between oral radium exposure and cancer of the upper digestive system (p-value < 0.001) suggests that exposure to radiation-contaminated drinking water is likely to increase the risk of developing the cancer, especially in the southern region of Thailand where uranium and radium are significant components of the granite rock. Further investigation is needed, however, to reproduce evidences of such an association.

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