N-nitrodimethylyamine in natural and drinking water of high cancer incidence regions of Guangdong, China

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A B S T R A C T

The Guangdong province of China contains the most clearly described high-incidence of hepatocellular carcinoma (HCC) and nasopharyngeal carcinoma (NPC) areas in the world. The geographical heterogeneity of cancer incidence in the region suggests that many carcinogenic risk factors might be present in the regional geochemical environment. This paper presents the concentrations of a wide range of known carcinogens in two high cancer incidence areas in Guangdong and compared them to a low cancer incidence area in the same province. N-Nitrosamines, NO3, NO2, and ammonium were detected in groundwater, surface water, and drinking-water. The concentrations of the 7 trace metal and metalloid elements As, Cd, Ni, Cu, Pb, Zn, and Hg were determined in surface soil samples and all water samples. The results show that, compared with the guidelines or limit values for drinking-water quality in the world, the high cancer incidence areas have hazardous high levels of N-nitrodimethylamine (NDMA) in all kinds of water. Oppositely, the low cancer incidence area has a safe low level of NDMA in water bodies. The levels of NO3, NO2, and ammonium in water have the same character, although they have different expression between the two high-risk areas. The distribution of the 7 tested trace elements in surface soil has no significant correlation with cancer incidence. On the other hand, high concentrations of carcinogenic N-Nitrosamines in drinking-water and natural water bodies were identified for the first time in the high NPC and HCC incidence area.

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1. Introduction

The etiology of cancer is dominated by the interaction of genetics and environmental risk factors (including viral infection). A great majority of cancers (90–95%) are caused by environmental factors. The remaining (5–10%) are due to inherited genes (Anand et al., 2008). Some of the cancers have obviously geographical heterogeneity. As was reported by the International Agency for Research on Cancer (WHO), the south of China is a high incidence area of nasopharyngeal carcinoma (NPC) and hepatocellular carcinoma (HCC) (Boyle and Levin, 2008). NPC causes malignant tumors, which manifest in the nasopharyngeal epithelial lining, commonly known as “Guangdong Cancer”. NPC incidence is very high in southeast of Asian (10–30 cases per 100,000 capita per year), but it is rarely recorded in Europe and America (less than 3 cases reported per 100,000 capita per year). Globally, more than 80% of NCC occur in Asia and Africa (Boyle and Levin, 2008).

In the majority of high HCC incidence areas in China, the high-risk is associated with hepatitis B virus (HBV) and drinking water pollution (Yang and Zhang, 2012). Furthermore, epidemiological studies have noted that preserved foods and Epstein-Barr virus (EBV) are key exposure factors involved in NPC etiology. Food preservation, using high levels of salt (popular in the south of China) conferred a 2- to 3-fold increase in NPC risk (Boyle and Levin, 2008). The carcinogenic mechanism is that the saline preservation process produces excess of NO2 and NO3 leading to an enhanced exposure to N-Nitrosamines, in particular N-nitrosodimethylamine (NDMA), N-nitrosopyrrolidine (NPyr), and N-nitrosopiperidine (NPip). These N-Nitrosamines are postulated to be carcinogens (IARC, 1993a,b). For examples, IARC placed NDMA in Group 2A (probably carcinogenic to humans), and placed NPYP and NPIP in Group 2B (possibly carcinogenic to humans). NO2 or NO3...
ingested are reagents that under unfavorable conditions result in endogenous nitrosation and, therefore, are also classified in Group 2A (http://monographs.iarc.fr/ENG/Classification/index.php).

The Guangdong province, in the south of China, contains the most clearly described high incidence of NPC and HCC areas in the world. The incidences of NPC and HCC are unevenly distributed in the Guangdong province with some extremely high cancer incidence areas are reported. Two classic areas of high cancer incidence are studied in this paper. The Sihui region is reported as one of the highest NPC incidence area in China, and NPC incidence rates have been steadily increasing since 1979 (Huang et al., 1981; Min, 1998; Cao et al., 2011). The age-standardized incidence rate for NPC was 28.9 and 12.6 cases per 100,000 capita per year among men and women, respectively, during 1998–2002. Meanwhile, the HCC incidence was also significantly high in the Sihui region. The age-standardized incidence rate was 41.9 and 11.3 cases per 100,000 capita per year among men and woman, respectively, during 1998–2002 (Zhang et al., 2006). Another area, Shunde, was known as one of the top three highest HCC incidence areas in China (the other two areas are Qidong and Fusui). The HCC mortality rate of Shunde was 26.8 deaths per 100,000 capita per year during 1971–1979 (Lin and Lai, 2004).

Due to the geographical distribution pattern of NPC and HCC incidences, more and more attention was paid to attract to the relationship between cancer incidence and geochemical environments. In one of the first studies, Hao (1984) and Li et al. (1986) found that in Shunde the content of manganese (Mn) in soils of high HCC incidence regions is lower than in low HCC incidence regions. The Mn concentrations were even below the global average, and the content of Mn in HCC patients’ hair and blood was also lower than Mn concentrations in healthy people. They concluded that low level of the Mn might be one reason for the high cancer incidence in this area. However, Lin and Lai (2004) found that the content of Mn in soil had no significant difference between high HCC incidence region and its surrounding areas. Instead, they found that the concentrations of NH₄, NO₂, and NO₃ in surface water and groundwater were higher than the background value, and inferred that the enrichment of nitrosing agents in surface and groundwater is related to the high cancer incidence in Shunde. These results were similar to Qidong high HCC incidence area in the Jiangsu province, and Fusui in Guangxi province (Li et al., 1986; Lin, 1991; Tang and Lin, 1995). For Sihui, also a relatively higher content of nickel (Ni) was detected in aqueous environment and patients’ hair (Huang et al., 1981; Zeng and Zeng, 2000). Huang et al. (1983) also studied NO₃ and NO₂ in Sihui. A higher concentration of NO₂ was tested in NPC patients’ saliva and urine compared to healthy people, yet the concentration of NO₂ in local rice, drinking-water, and pickled food was not very different from the low NPC incidence region, only the concentrations of NO₃ was much higher in the high NPC incidence area compared to the low NPC incidence region.

So far, most of the geochemical carcinogens studies are concerned with NO₃, NO₂, and trace metal elements in the environment of Sihui and Shunde. However, none of the studies focused on drinking water resources (groundwater and surface water) as the route of N-Nitrosamines exposure, even though high levels of NO₃ and NO₂ were clearly detected in natural water. In recent years, the influence of the N-Nitrosamines in drinking water on human health has been increasingly concerned (Walse and Mitch, 2008; Plumlee et al., 2008; Asami et al., 2009). The geographical and geological environment described above indicate that plenty of NO₃ and NO₂ together with reducing environments are present in groundwater to form N-Nitrosamines. Based on that, we hypothesized that a dangerously high level of N-Nitrosamines exists in natural waters in NPC and HCC high incidence areas. The N-Nitrosamines enriched water could be of a source of increased incidence of cancer in Sihui and Shunde, because the local residents used to drink the water directly from rivers, ponds, and wells in the past. In this paper, we aimed to test this hypothesis and to assess the role of NO₃, NO₂, and also various toxic trace metal elements in water sources of NPC and HCC high incidence area of Sihui and Shunde.

2. Material and methods

2.1. Sampling

The typical high cancer incidence areas were selected to be the research areas. In Sihui, four villages in a 90 km² area were selected as a high cancer incidence research area. This area has an exceptionally high mortality due to NPC, and also a high risk of HCC. Three towns (Lecong, Longjiang, and Lelou) were selected as the survey area (120 km²) in Shunde, including a very high HCC incidence (over 80 cases per 100,000 capita per year; area H area in Fig. 2) and a low HCC incidence (less than 3 cases per 100,000 capita per year; area L area in Fig. 2).

Water samples (4 L per sample) for nitrosamines detection from Shunde and Sihui were collected in amber-glass bottles with PTFE lids. In Shunde area, water samples were collected from 12 locations, in Sihui area from 8 locations. Piped water in rural households was bottled as drinking-water samples; water from the wells was pumped out and bottled as groundwater samples; river and pond water was bottled as surface water samples. All glassware and sample bottles were washed, rinsed with reagent water, acetone rinsed, and baked at 400 °C overnight. During sample collection, sample bottles were first rinsed with a small quantity of sample. Sample bottles were then filled to zero headspace, and 1 g/L of sodium thiosulphate salt was added. Samples were kept cool and transported to the laboratory, where they were refrigerated at 4 °C until extraction, typically within two weeks. Triple blanks consisting of pure deionized reagent water and 1 g/L of sodium thiosulphate were always included in the sampling procedure. High-purity deionized water was produced from a Heal Force water purification system (Cannex Analytic Instrument, Shanghai, China). The blanks were handled like samples, transported to the field, and returned to the laboratory for analysis. Solvent blanks were analyzed for contamination by GC/MS.

For inorganics analysis in Sihui and Shunde areas, 20 untreated water samples (0.5 L per sample) and 20 filtered water samples (0.45 μm micropore membrane, 0.1 L per sample) acidified with 1 mL/L 0.5% HNO₃ were collected in PET bottles. Duplicate samples were collected from five of the locations (Tables 5 and 6, samples A and B were the same samples from one location). Basic co-factor parameters (pH, Eh, COD, etc.) were recorded on each sampling site. In addition, 495 surface soil samples (0–15 cm or 0–20 cm) were collected in Shunde area (Fig. 3), and four surface soil samples in Sihui area.

2.2. Analytical techniques

2.2.1. Detecting N-Nitrosamines in water using GC/MS-SIM

Because of the low concentrations of nitrosamines in environmental water, our team cooperated with a laboratory of China University of Geosciences (Wuhan) that developed a method to detect N-Nitrosamines in drinking-water at nanogram per liter levels using gas chromatography mass spectroscopy (GC/MS) in selected ion monitoring mode (SIM). In order to decrease the detection limits, 4 L water was needed to increase the quantities of N-Nitrosamines. The overall recoveries of the target compounds tested from 4 L of purified water were in an acceptable range (60%–107%, Table 1).
The SPE protocol closely followed that of the US EPA method 521 (USEPA, 2012). For the SPE materials, coconut charcoal EPA 521 cartridges (6 mL, 2 g) were supplied through CNW Technologies GmbH (Germany). The method developed is based on isotope dilution with labeled nitrosamines (d6-NDMA and d14-NDPA) used as internal standards. Sodium thiosulphate (reagent grade) was purchased from SCR (Sinopharm Chemical Reagent Company, Shanghai, China). Methanol and acetone were purchased from Tedia (Fairfield, USA), and dichloromethane was obtained from JT Baker (Pennsylvania, USA). A standard solution containing 2000 ng/L of nine N-nitrosamines in methanol was purchased from Supelco (Oakville, ON, Canada) containing N-nitrosodimethylamine (NDMA), N-nitrosodimethylamine (NMEA), N-nitrosodimethylamine (NDPA), N-nitrosopyrrolidine (NPIR), N-nitrosopiperidine (NPIP), N-nitrosodi-n-butylamine (NDBA), and N-
nitrosodiphenylamine (NDPhA). Isotopically labeled standards so-
luations ([6-2H]N-nitrosodimethylamine, d6-NDMA, 98.5%, and
[14-2H]N-nitroso-n-dipropylamine, d14-DPNA, 99.9%) were pur-
chased from AccuStandard Inc. (New Haven, USA). All reagents used
were of gas chromatographic (GC) grade.

The SPE eluate was concentrated under a stream of ultrahigh-
purity (UHP) N₂ using a Termovap Sample Concentrator (BF-
2000, Peta Instrument Co., China) to a final volume of 0.5 mL,
resulting in an extract concentration factor of 1000, where the in-
ternal standard (IS) DPNA-d14 (100 ng) was added. Extracts were
either analyzed immediately, or stored at 4°C prior to GC/MS
analysis.

N-Nitrosamines were chromatographically separated using an
Agilent Technologies (Avondale, USA) 6890 N gas chromatograph
coupled with a 5975 quadrupole mass selective spectrometer,
operating in electron impact (EI) mode. Samples were injected
using an Agilent 7683B (Agilent Technologies, Avondale, USA) se-
ries autosampler. Detection of compounds was carried out in
selected ion monitoring (SIM) mode. The column DB-35MS was
used (35% diphenyl/65% dimethyl polysiloxane).

For the analytical quality assurance, instrumental quantitation
parameters (IQLs), calculated by injecting 20 ng of each pure compound
and using a signal to noise ratio (S/N) of 10, varied from 1.71 (NPIP)
A-Naphthylamine Colorimetric Method 0.003
NO₂⁻N A-Naphthylamine Colorimetric Method 0.001
pH Potentiometric Method 0.1
COD Permanganate Titration 0.5
Cd, Cu, Pb, As, Hg, N Kjeldahl Method 8.0

Table 2
Method and detection limits of water sample's chemical analysis.

<table>
<thead>
<tr>
<th>Items</th>
<th>Analysis methods</th>
<th>Limits of detection (LOD) (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺, K⁺</td>
<td>Atomic Absorption Spectroscopy (AAS)</td>
<td>0.05</td>
</tr>
<tr>
<td>Ca, Mg</td>
<td>EDTA titration</td>
<td>1.0</td>
</tr>
<tr>
<td>Cl</td>
<td>AgNO₃ titration</td>
<td>1.0</td>
</tr>
<tr>
<td>F⁻</td>
<td>Ion selective electrode (ISE)</td>
<td>0.05</td>
</tr>
<tr>
<td>SO₄²⁻</td>
<td>Turbidity</td>
<td>0.2</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>Titration</td>
<td>–</td>
</tr>
<tr>
<td>NH₄⁺</td>
<td>Visual method</td>
<td>0.05</td>
</tr>
<tr>
<td>NH₃-N</td>
<td>Nessler Reagent-calorimetry</td>
<td>0.04</td>
</tr>
<tr>
<td>NO₃⁻</td>
<td>UV Spectrophotometry</td>
<td>0.2</td>
</tr>
<tr>
<td>NO₂⁻</td>
<td>UV Spectrophotometry</td>
<td>0.05</td>
</tr>
<tr>
<td>NO₂⁻</td>
<td>A-Naphthylamine Colorimetric Method</td>
<td>0.003</td>
</tr>
<tr>
<td>NO₂⁻-N</td>
<td>A-Naphthylamine Colorimetric Method</td>
<td>0.001</td>
</tr>
<tr>
<td>pH</td>
<td>Potentiometric Method</td>
<td>0.1</td>
</tr>
<tr>
<td>COD</td>
<td>Permanganate Titration</td>
<td>0.5</td>
</tr>
<tr>
<td>Cd, Cu, Pb, Zn, Ni, Cr</td>
<td>ICP-MS</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>As, Hg</td>
<td>Atomic Fluorescence Spectrometry (AFS)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 3
Analysis method and detection limits of soil sample's chemical analysis.

<table>
<thead>
<tr>
<th>Items</th>
<th>Analysis methods</th>
<th>Limits of detection (LOD) (10⁻⁶ g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cd</td>
<td>ICP-MS</td>
<td>0.02</td>
</tr>
<tr>
<td>Cu</td>
<td>ICP-OES</td>
<td>1.0</td>
</tr>
<tr>
<td>Pb</td>
<td>ICP-OES</td>
<td>1.0</td>
</tr>
<tr>
<td>Zn</td>
<td>ICP-OES</td>
<td>2.0</td>
</tr>
<tr>
<td>Ni</td>
<td>ICP-OES</td>
<td>1.0</td>
</tr>
<tr>
<td>Hg</td>
<td>AFS</td>
<td>0.0003</td>
</tr>
<tr>
<td>As</td>
<td>AFS</td>
<td>0.05</td>
</tr>
<tr>
<td>N</td>
<td>Kjeldahl Method</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Agilent Technologies (Avondale, USA) 6890 N gas chromatograph
coupled with a 5975 quadrupole mass selective spectrometer,
operating in electron impact (EI) mode. Samples were injected
using an Agilent 7683B (Agilent Technologies, Avondale, USA) se-
ries autosampler. Detection of compounds was carried out in
selected ion monitoring (SIM) mode. The column DB-35MS was
used (35% diphenyl/65% dimethyl polysiloxane).

For the analytical quality assurance, instrumental quantitation
limits (IQLs), calculated by injecting 20 ng of each pure compound
and using a signal to noise ratio (S/N) of 10, varied from 1.71 (NPIP)
to 3.98 ng (NDMA, Table 1).

2.2.2. Chemical analysis of other samples

Other chemical analyses were done by the environment laboratory
of Guangdong Province Research Center for Geoanalysis. In
total, 16 inorganic compounds (As, Cd, Hg, Pb, Ni, Cr, Cu, Zn, NH₄⁺,
NO₃⁻, NO₂⁻, pH, COD, NH₃-N, NO₃⁻-N, NO₂⁻-N) dissolved (i.e.,
<0.45 µm) in water were determined. The analysis process was
monitored by strict quality control procedures. Methods and
detection limits are compiled in Tables 2 and 3.

2.3. Statistical analysis

Statistical evaluations of the data were performed, including
mean, median and standard deviation. Combining Google Earth
satellite images and on-site records, present land-use map (2013) of
Shunde research area was drawn up (Fig. 3). In the map, the
research area was divided into eight function districts, and the
surface soil sampling sites were added in order to find out corre-
lation between land use and trace metal accumulation in surface
soil. Maps of geochemical distribution of elements in surface soils
were generated in MapGIS software (http://english.mapgis.com.cn/
3. Results

3.1. Reference values in water

In order to evaluate the content and hazard of nitrogen compounds in the water, the relative guidelines or regulated values from World Health Organization Guidelines for drinking water quality (WHO, 2012), European Union’s drinking water directive (http://ec.europa.eu/environment/water/water-drink/legislation_en.html#top-page.22/04/2015-27/04/2015), United States Environmental ProtectionAgency 2012 edition of the drinking water standards and health advisories (USEPA, 2012a,b), and China standards for drinking water quality were listed in Table 4. Since regulated value or guidelines differ between organizations or countries, and some compounds have no regulated values, this paper selects the strictest values as health reference values (RIVs, Table 4).

3.2. N-nitrosamines in water

In the high incidence area of cancer in Guangdong, carcinogenic nitrosamines in drinking water were analyzed for the first time, including NDMA and NMEA. In 15 out of 20 water samples of Shunde region, NDMA was detected with an average value of 38.9 ng/L. This seriously exceeded the reference value of 7 ng/L (at 10−5 Cancer Risk), and in 10% of the water samples (2 samples) NMEA was detected at a maximum value of 173 ng/L. In all 8 natural and drinking water samples of Sihui area, NDMA was detected at concentrations in between 40.6 and 64.7 ng/L, with an average concentration of 55.2 ng/L. On the other hand, NMEA was not detected in waters of Sihui area. The concentration of NDMA in drinking water is close to the average value.

For the samples from high HCC incidence area (excluding L area in Fig. 2b), in only five samples NDMA was detected (average 14.6 ng/L), while in two samples, both NDMA (average 48.1 ng/L) and NMEA (average 92.7 ng/L) were detected, and in only three samples no N-Nitrosamines were detected. For the samples from

Fig. 4. Distribution of As in surface soil of Shunde district.
low cancer incidence area (L area in Fig. 2b), only in sample No. 5 NDMA was detected (10.8 ng/L), but no nitrosamines were detected in sample No. 6 (Table 6).

Overall, the average concentration of NDMA in all kinds of water was higher in Sihui than in Shunde, with a smaller value range. The NDMA and NMEA concentration variation in surface water of Shunde is large. In the shallow groundwater sample (only one sample), no N-Nitrosamines were detected. The NDMA concentration of deep groundwater in Shunde is much lower than in Sihui.

3.3. Nitrate, nitrite, and ammonium in water

In water samples of Shunde, the average NH$_4^+$ concentration was 3.1 mg/L, average NO$_2^-$ concentration was 0.85 mg/L, both exceeding the reference values (RfVs). The average NO$_3^-$

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**Table 4**

Maximum contaminant levels of selected nitrogenous compounds for drinking water.

<table>
<thead>
<tr>
<th>Compound</th>
<th>WHO</th>
<th>Europe</th>
<th>U.S. EPA</th>
<th>China</th>
<th>Reference values (RfVs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium (NH$_4^+$) (mg/L)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>NO$_3^-$ (NO$_3^−$) (mg/L)</td>
<td>50</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>NO$_2^-$ (NO$_2^−$) (mg/L)</td>
<td>0.5</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>N-nitrosodimethylamine (NDMA) (ng/L)</td>
<td>100</td>
<td>–</td>
<td>7.0 (at 10$^{-5}$ Cancer Risk)</td>
<td>7.0</td>
<td></td>
</tr>
<tr>
<td>N-nitrosomethylamine (NMEA) (ng/L)</td>
<td>–</td>
<td>–</td>
<td>20 (at 10$^{-5}$ Cancer Risk)</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

*a* The compound has no regulatory maximum contaminant level (MCL) for drinking water by this organization.
concentration was 8.8 mg/L, close to the reference value (10 mg/L). In the low cancer incidence area (L area in Fig. 2b), NH$_4^+$, NO$_3^-$, and NO$_2^-$ concentration is much lower than in the high incidence area (H area in Fig. 2b), and the value is lower or close to the RIVs (Table 7). In Sihui water samples, the average NH$_4^+$ concentration was 1.1 mg/L, average NO$_3^-$ concentration was 25.6 mg/L, being 2.2 and 2.6 times greater than the reference value. The average concentration of NO$_2^-$ was less than the reference value (Table 7). Similar to N-Nitrosamines, NO$_3^-$ content in the lake water of Sihui area increased with the increasing depth. Comparing the results of Sihui and Shunde, NH$_4^+$ and NO$_2^-$ concentration in Shunde is significantly higher than in the Sihui district, but NO$_3^-$ concentration in Sihui severely exceeded those of Shunde district.

The concentration of all trace metal elements content was very low, (e.g., As average level is 6 μg/L), and didn’t exceed the guideline values of WHO (WHO, 2012).

### 3.4. Trace metal elements and nitrogen in soil

The concentrations of trace metal elements and nitrogen in soil of Shunde is shown in Table 8. Compared with the soil geochemical background value of Guangdong Province, and the value of the low incidence of cancer surrounding study area, the contents of 7 trace elements (As, Hg, Cd, Ni, Pb, Zn, and Cu) and nitrogen content in soil is significant higher in the Pearl River Delta (which accounts for about 23.2% of Guangdong province land area) than the soil geochemical background value of the Guangdong Province. But compared with the low incidence of cancer surrounding study area, these trace metals do not show obvious anomalies, and the soil nitrogen content is just 20% higher than the back ground value of Pearl River Delta soils (Table 8).

For example, average As content along the Shunde waterway is 52.1 mg/kg. The maximum is 256 mg/kg in residential area. According to the present land use map (Fig. 3) and As surface soil geochemical map (Fig. 4), As is enriched in the rivers’ S-shape bend part. Other enrichment areas are mainly distributed in the densely populated industrial and commercial area indicating anthropogenic contamination. Although the river bend is enriched in this trace element, there is a low incidence of cancer in this area (Fig. 2b, L area), while the high incidence of cancer is not identical with the As high enrichment area (Fig. 2b, H area). Other trace elements have similar distribution characteristics. Thus the high HCC incidence area do not coincide with any trace metal enrichment. Nitrogen distribution in the study area is comparatively homogeneous, and it is almost matching with the agriculture area (dike-pond agriculture area), showing that in agriculture area nitrogen compounds in soil are relatively enriched (Figs. 4 and 5).

Similarly, in Sihui district, the trace metal concentrations show no obvious anomalies in comparison to the back-ground value.

### 4. Discussion

Extremely high concentrations of N-Nitrosamine compounds (in particular, NDMA) are present in all types of water including drinking water in both Sihui and Shunde high cancer incidence areas. The low cancer incidence area of Shunde had a low and safe level of N-Nitrosamines in all water samples. The average concentration is 3–8 times higher than the quantitative estimate value of 7 ng/L at 10$^{-3}$ carcinogenic risk from oral exposure (USEPA). The concentration of NDMA in water detected certainly pose a serious health threat, and is closely related to the high incidence of cancer. Considering of the drinking water sources of the local residents, we infer from our findings that in both high HCC incidence area of Shunde and high NPC incidence area of Sihui, long-term consumption of untreated nitrogen-enriched natural water is the relevant high-risk cancer factor.

The level of N-nitrosamines in Sihui is much higher than in Shunde. Although the concentration of NO$_3^-$ in waters of Sihui is extremely large, we found higher NO$_2^-$ and NH$_4^+$ in the Shunde high cancer incidence area which is in good agreement with Lin’s results (Lin and Lai, 2004). Shunde and Sihui are located in the plain of the Pearl River Delta (112°23’–113°22’E, 22°40’–23°30’N; Fig. 1). Quaternary sediment covers this area, with a thickness of about 15–20 m. The sediment has a shallow surface layer consisting of silt and sandy silt, accompanied by large amounts of organic matter and humic matter admixed; and modern delta layer consisting of silt and sand layer. The Quaternary sediments differ in thickness and composition from different places. Parts of the sediments stores “nutritive groundwater” (NH$_4^+$ > 30 mg/L) and shallow flammable gas sources (Lin and Lai, 2004). It provides a great quantity of nitrogen (including NO$_3^-$, NO$_2^-$ and NH$_4^+$) to the natural aquifers, and as precursors of N-Nitrosamines. NO$_3^-$, NO$_2^-$ and NH$_4^+$...
could form N-Nitrosamines in a reducing aquifer environment. The high cancer incidence areas in this paper are all located in low-lying areas where frequently reducing environments may occur. Therefore, the high level of N-Nitrosamines in natural and drinking water in the area is suggested to be of natural origin. As NO3 and NO2 are carcinogens themselves, we infer that water rich of NO3 or NO2 is also significant high-risk factors for cancer in the research areas. This is because we observed that local residents were accustomed to take the natural source water directly for drinking and food preparation, although centralized supply of drinking water was installed from the year 2003 in the rural area of Shihui, distributing water from a nearby mountain water reservoir. Many families in rural areas are still using hand wells to obtain groundwater for drinking purposes. In Shunde, small waterworks were built in 1900’s, which derives surface water from large rivers nearby.

Although the average level of NDMA of Shihui waters is nearly twice as much as those of Shunde district, the concentration of NDMA in samples from Shunde varies over a large range. Moreover, two samples that detected NMEA were sampled from industrial and commercial areas, and most of samples from Shunde were surface waters. We suggest that the samples from Shunde suffered more of anthropogenic contamination than those of Shihui district.

5. Conclusion

The analytical method developed to detect N-Nitrosamines in drinking water at nanogram per liter levels using GC/MS–SIM still is under improvement. There might exist other N-Nitrosamine compounds in the environmental water system not yet detected, but the concentrations of NDMA and NMEA are huge enough to significantly increase the cancer incidence. Thus, authorities are urged to decrease the concentration of NDMA and NMEA in drinking water in order to improve health safety of drinking-water in this area. This is because the level of NDMA is far exceeding a quantitative estimate value of 7 ng/L at 10^-5 carcinogenic risk from oral exposure given by USEPA reports. In the high incidence areas, the geological environment is inducing natural and drinking water rich of NO3, NO2, and NH4. The high dissolved concentrations of the nitrogen compounds in natural water pose high-risk factors to increase formation of the N-Nitrosamines in the reducing shallow aquifers. No significant geochemical trace metal abnormalities were found which may be associated with cancer incidence. Drinking water sourced from these areas is a considerable route of exposure to N-Nitrosamines, with concomitant increase of cancer incidence.

Acknowledgment

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References


Table 8

<table>
<thead>
<tr>
<th>Element</th>
<th>Value range</th>
<th>Average Value</th>
<th>Median</th>
<th>STD</th>
<th>Background value of guangdong</th>
<th>Background Value of PRD Area</th>
<th>Values of low incidence area around</th>
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Note: * PRD=Pearl River Delta.