ARSENIC EXPOSURE:
PERSPECTIVE ON
RISK ASSESSMENT

RABIYA SHABNAM
M.S.Student
ECS program
NDSU
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OVER VIEW

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INTRODUCTION

- Arsenic in the form of Arsenic(III) & Arsenic (V) causes health hazards.

- The WHO guideline for Arsenic in drinking water is 10μg/L.

- Arsenic in groundwater is an International Problem.

- Arsenic is also known to cause a variety of cancers including skin cancer (non-melanoma type), kidney, bladder, lung, prostate and liver cancer.

- Acute (short-term) arsenic poisoning may cause nausea, vomiting, diarrhea, weakness, loss of appetite, shaking, cough and headache.

- Chronic (long-term) exposure may lead to a variety of symptoms including skin pigmentation, numbness, cardiovascular disease, diabetes, and vascular disease.

- There is a dose-response relationship between the ratio of MMA/DMA in urine and the risk for skin and bladder cancer (Chen et al, 2003).
Risk Assessment

- Hazard Identification
  - Dose-response Assessment
  - Exposure Assessment

- Risk Characterization
- Risk Management
Goal of risk assessment

- Adequate Qualitative, Quantitative data concerning the exposure (Source, Amounts)
- Dose (Metabolism and disposition of active metabolites)
- Response – Good Arsenic risk assessment epidemiological data to measure risk, to understand the risk factors and disease.
Goal of risk assessment

- Two critical issues in arsenic risk assessment:
  Methylation in the dose-response relationship
- The role of internal cancers
- Exposure estimate – high / low
- Higher exposure studies has been used to measure risk.
- How arsenic can be measured using analytical methods
Human Health Exposure Assessment

- Exposure to iAs-Contaminated drinking water causes development of Cancer of Skin and internal organs.

- Exposure sources: Water, Soil, Air, Diet.

- Epidemiologic studies in highly exposed & Low levels exposure among the populations.

- Bangladesh, India, China, Taiwan, USA (Nevada)
Dose Assessment

- The dose of arsenic causing a health impact.
- The person being exposed (children are more sensitive than adults).
- The route of exposure.
- The type of health impacts being examined cancer risks.
- Lifetime cancer risk probability of $1/100,000$ or, $1 \times 10^{-5}$. 
Arsenic metabolism

- The elucidation of the metabolic pathways of inorganic arsenic and the toxicity profile of the arsenic metabolites are important.
- Epidemiological studies – geographical distributions and diseases.
- Drinking water causing different cancers and mortality rates.
- Studies on LUNG, BLADDER, KIDNEY cancer
- Case studies of Taiwan, Bangladesh, India Chile.
In vivo metabolism of inorganic arsenic.

- Arsenate (V) to Arsenate (III)
  - Arsenate reductase, Glutathione S-transferase-?, Glyceraldehyde phosphate dehydrogenase (GAPDH)-?
  - Nonenzymatic pathway

- Monomethylarsonic acid (MMA (V))
  - Glutathione S-transferase-?

- Monomethylarsonous acid (MMA (III))
  - Methyl transferase (AS3MT)
  - S-adenosymethionine (SAM)
  - S-adenosylhomocysteine (SAH)

- Dimethylarsinic acid (DMA (V))
  - Dimethylarsenous acid (DMA (III))

- Trimethyl arsine oxide (TMAO (V))
  - Trimethyl arsine (TMA (III))

ARSENIC METABOLISM

- Human beings do methylate Arsenic.
- Methylation – Cytosol.
- $\text{MMA}^\text{v}$ to $\text{DMA}^\text{v}$ – $\text{TMAO}$ – $\text{TMA}^\text{II}$
- $\text{MMA}^\text{III}$ and $\text{DMA}^\text{III}$ – More toxic.
- DMA % -indicator for metabolism.
- Metabolizing iAs – differs and effects the organ system.
Epidemiological studies - Evidences from Taiwan cancer causes

- Epidemiologic data in the areas of world with As levels in drinking water (>150 µg/L) shows risk.
- Exposure to iAs through drinking well water causes blackfoot disease (BFD) in Taiwan.
- Arsenic exposure and arsenic methylation capacity on the development of arsenic-related skin cancers and bladder cancer.
Mortality rates due to increased Arsenic in drinking water (per 100,000/year) in Taiwan

<table>
<thead>
<tr>
<th>DOSE LEVEL RISK</th>
<th>LUNG CANCER MEN</th>
<th>LUNG CANCER WOMEN</th>
<th>BLADDER CANCER MEN</th>
<th>BLADDER CANCER WOMEN</th>
<th>KIDNEY CANCER MEN</th>
<th>KIDNEY CANCER WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARSENIC μgm/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;300 μg/L</td>
<td>49.2</td>
<td>36.7</td>
<td>100.7</td>
<td>70.8</td>
<td>104.1</td>
<td>122.2</td>
</tr>
<tr>
<td>300-500 μg/L</td>
<td>22.6</td>
<td>25.6</td>
<td>61</td>
<td>57</td>
<td>92.7</td>
<td>111.3</td>
</tr>
<tr>
<td>≥600 μg/L</td>
<td>8.4</td>
<td>3.4</td>
<td>18.9</td>
<td>19.4</td>
<td>25.3</td>
<td>58</td>
</tr>
</tbody>
</table>

### Epidemiological data

- **Bangladesh and India-1950’s – arsenic 50μg/l**

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Skin</td>
<td>Symmetric hyperkeratosis of palms and soles, melanosis or depigmentation, Bowen’s disease, basal cell carcinoma and squamous cell carcinoma.</td>
</tr>
<tr>
<td>Liver</td>
<td>Enlargement, jaundice, cirrhosis, non-cirrhotic portal hypertension</td>
</tr>
<tr>
<td>Nervous System</td>
<td>Peripheral neuropathy, hearing loss</td>
</tr>
<tr>
<td>Cardiovascular System</td>
<td>Acrocyanosis and Raynaud’s Phenomenon</td>
</tr>
<tr>
<td>Hemopoietic System</td>
<td>Megalobastosis</td>
</tr>
<tr>
<td>Respiratory System</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>Endocrine System</td>
<td>Diabetes mellitus and goiter</td>
</tr>
</tbody>
</table>

- Source: *Water Engineering & Management; Mar 2002; 149, 3; ABI/INFORM Global pg35.*
Skin Lesion - Due to Arsenic
Epidemiological data

- IN USA the states affected by arsenic are Nevada, California

<table>
<thead>
<tr>
<th>Arsenic, µg/L</th>
<th>Bladder Cancer</th>
<th>Lung Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>11</td>
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<td>10</td>
<td>12</td>
<td>23</td>
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<tr>
<td>20</td>
<td>24</td>
<td>45</td>
</tr>
</tbody>
</table>

- Source - Water Engineering & Management; Mar 2002; 149, 3; ABI/INFORM Global pg35.
Analytical methods to determine arsenic

- HPLC
- Capillary zone electrophoresis
- ICP-MS (As Detection Limit (ppt) 400-500)
- Elevated As Concentration in Solid X-ray absorption technique (e.g. XANES)
- In Humans “Total Arsenic” level in the urine and Blood.
Analytical methods

- The coupling of GC and ICP-MS determine Arsenic of gaseous / volatile species.
- HPLC / ICP-MS , HPLC- Arseno sugars
- ICP-MS gives molecular information.
- ESI-MS –binding stoichiometry
- DMA\textsuperscript{v} can be identified by Electron spray-MS.
- Separation of iAs Ion-Pairing chromatography.
- As\textsuperscript{iii}, DMA\textsuperscript{v}, MMA\textsuperscript{v}, AS\textsuperscript{v}, MMA\textsuperscript{iii} and DMA\textsuperscript{iii}
ICP-MS

- IC-ICPMS Chromatogram of 10 ug/L Arsenic Species

Summary

- As- toxic and carcinogenic.
- Sort out the risk of exposure, dose response relationship.
- Risk management

- Risk of Arsenic is well known, but is used as chemotherapeutic agent – Acute promyelocytic leukemia (APL)
References

- Jurgen Mattusch and Rainer Wennrich, Microchim Acta 151, 137-139 (2005)
- X. Chris Le, Xiufen Lu, Xing-Fang Li, Arsenic Speciation, Analytical chemistry January 1, 2004, 27A-33A.
Acknowledgement

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Question?

THANK YOU