Estimating Health Risk Using a PBBK Model for the Trio Mixture of Mercury, Lead and Selenium

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Abstract: A physiologically-based biokinetic (pbbk) model for the trio mixture of lead, mercury and selenium, developed in our previous study was applied in a hypothetical environmental health risk assessment. The health risk index (HRI) to critical organs (liver, kidney, and the brain) resulting from the simultaneous exposure of individuals to the mixture of these elements were estimated. Three mining communities: Bagega, Dareta, and Abare villages of Anka L.G.A, Zamfara State, Nigeria, were used as case studies. In carrying out the hypothetical risk estimation, an exposed individual was assumed to have consumed contaminated cereals (maize, rice, and sorghum) cultivated locally in these three mining communities. Three co-exposure scenarios were simulated for each village based on selenium intake: low selenium intake (0.75µmol/kg/day), adequate selenium intake (2.5µmol/kg/day), and high selenium intake (7.5µmol/kg/day). The HRI to a given organ was calculated as the combined molar concentration of mercury and lead to the molar concentration of selenium (i.e. (Hg+Pb)/Se molar ratio). In general, the HRI to these critical organs were found to be highest when selenium intake was low, which were reduced greatly with adequate selenium intake and further reduced when selenium intake was high. At Bagega, when selenium intake was low, the simulated HRI was very high for all the three organs investigated (as high as1039, 32.7 and 5.9 for the liver, kidney, and brain, respectively). While at Dareta, with low selenium intake, only the HRI for the liver and kidney were very high (as high as 531.06 and 16.04, for liver and kidney, respectively). When selenium intake was high, only the liver had a high HRI at Bagega, while at Dareta and Abare the HRI for all three critical organs were low (< 1.0). The study showed that the health risk index to these organs were not only dependent on the concentrations of mercury and lead in these organs, but equally dependent on selenium intake.

Keywords: health, lead, mercury, model, physiologically-based, risk.

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I. Introduction

The elements Lead (Pb) and Mercury (Hg) are toxic to exposed individuals, while selenium is known to mitigate their toxic effect. Exposure to mercury is associated with a wide range of disorders and adverse health effects in humans and animals. These include, nervous system dysfunction, neurological, nephrological, immunological, cardiac, reproductive and renal disorders [1, 2, 3, 4]. Similarly, exposure to lead is implicated in a host of disease and health conditions, namely: brain damage, paralysis (lead palsy), impairment of liver structure and function, hypertension, cerebrovascular disease, cardiovascular disease, renal damage, anemia, gastrointestinal symptoms, kidney damage, damage to the reproductive and immune systems [5, 6, 7, 8]. Selenium, on the other hand, is an essential micronutrient required in trace amounts for normal growth and development in humans and animals [9].

Studies have shown that the toxicity of heavy metals such as mercury and lead results largely from the fact that they form insoluble complexes with selenium, thereby inducing selenium deficiency in target tissues [10, 11, 12, 13]. The concentration of free selenium required for its normal essential functions is therefore affected by the presence of lead or mercury in tissues. When selenium is bound to either lead or mercury, it becomes unavailable to carry out its essential functions, leading to adverse health effects and disorders.

If an individual is simultaneously or sequentially exposed to these elements, lead, mercury and selenium, the interaction between these heavy metals and selenium is expected to modify their concentration in the various tissues and consequently their toxicity. A holistic estimation of the risk posed by lead and mercury to exposed individuals should therefore take into account the interaction between these toxic elements and selenium. However, in environmental health risk assessment of the toxic elements lead and mercury, their interaction with selenium is seldom taken into consideration.

Furthermore, the use of Hg-to-Se molar ratio as the health risk index (HRI), in case of mercury toxicity, had been proposed by Ganther and cohorts as early as 1972 [14]. However, this proposal was given little or no attention because the specific underlying mechanisms of toxicity of mercury were not understood.
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until recently. It was, indeed, shown in an animal study conducted by Ralston and collaborators [15, 16], that using the Hg-to-Se molar ratio instead of the Hg concentration alone, gives a more realistic estimate of the toxicity of mercury in the brain, liver and kidney of rats. Further studies by Maza and Ojo [17] demonstrated the use of Hg-to-Se and Pb-to-Se ratios as the health risk indices of mercury and lead, respectively, in respective tissues.

In another study undertaken by us [18], a physiologically-based biokinetic (pbbk) model was developed for the mixture of the trio of mercury, lead and selenium. These models provided a platform for viewing the effect of the interaction between these elements on their respective concentrations in various human tissues. The present study is aimed at demonstrating the use of the pbbk model for the trio mixture of lead, mercury and selenium, in a hypothetical estimation of the risk that may result from simultaneous exposure to the mixture of these elements. The pbbk model for the mixture of these elements was used to estimate the possible health risk index that may result from the consumption of contaminated cereals from three communities, namely: Bagega, Dareta, and Abare villages of Anka L.G.A, Zamfara State, Nigeria. Bagega, Dareta, and Abare are three out of several villages involved in the Zamfara lead poisoning disaster of 2009 [19]. In these villages, mining activities have largely polluted the environment with heavy metals. In a study carried out by Yahaya and collaborators [19], the concentration of heavy metals in three cereals, namely: maize, rice, and sorghum, collected from these areas were determined and found to be significantly higher, particularly at Bagega and Dareta, than the WHO safe limits. Since these three cereals are widely consumed in these areas on a daily basis, their consumption was regarded as a likely source of health risk to inhabitants of these communities, hence our desire to estimate the health risk associated with their consumption.

Hypothesis: The health risk index (HRI), associated with the co-exposure to mercury, lead, and selenium is the ratio of the combined molar concentration of mercury and lead to the molar concentration of selenium (i.e. (Hg+Pb)-to-Se molar ratio). This hypothesis is predicated on the assumption that there is no significant difference between mercury and lead as far as their interaction with selenium is concerned, since both of them form insoluble complexes with selenium. As a result, selenium views mercury and lead as "identical" elements when interacting with them. Furthermore, the toxicity of mercury and lead was assumed to result largely from mercury and lead induced selenium deficiency in target tissues [10, 11, 12, 13]. Thus, for a given tissue T, the health risk index associated with mercury and lead, \( HRI_{HgPb} \), in the presence of selenium is therefore given as:

\[
HRI_{HgPb} = \frac{C_{HgT} + C_{PbT}}{C_{SeT}}
\]

(1)

Where \( C_{HgT} \), \( C_{PbT} \) and \( C_{SeT} \) are the molar concentrations of Hg, Pb and Se in tissue T, respectively.

The HRI for a given tissue gives a measure of the deficiency of free selenium in the tissue which could be available to carry out normal essential functions. The higher the HRI, the higher the health risk to the tissue in question, since there will be little or no free selenium available for its normal essential functions. A HRI of less than unity (i.e HRI < 1), suggests that there will be free selenium available for its normal essential functions, as such the risk posed to the tissue will be low. On the other hand, if the HRI is greater than unity (HRI > 1), it suggests that there will practically be no free selenium available for its normal essential functions, as a result the risk posed to the tissue will be high.

II. Methods

2.1 Materials and Data

A human physiologically-based biokinetic model for the trio mixture of mercury, lead and selenium developed in our previous study [18] was adapted and used in the hypothetical health risk assessment. Data was extracted from the published work of Yahaya and co-researchers [19]: The concentration of Pb and Hg in cereals (maize, rice and sorghum) locally cultivated in the three villages investigated (Bagega, Dareta, Abare) were extracted (Table 1). These concentrations form part of the input data that was used in the pbbk model for the mixture of mercury, lead and selenium.

<table>
<thead>
<tr>
<th>Cereal Type</th>
<th>Element</th>
<th>Bagega</th>
<th>Dareta</th>
<th>Abare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maize</td>
<td>Pb</td>
<td>0.81±0.019</td>
<td>0.050±0.003</td>
<td>0.003±0.000</td>
</tr>
<tr>
<td></td>
<td>Hg</td>
<td>0.43±0.043</td>
<td>BDL</td>
<td>0.000±0.013</td>
</tr>
<tr>
<td>Rice</td>
<td>Pb</td>
<td>0.036±0.011</td>
<td>0.042±0.031</td>
<td>0.005±0.000</td>
</tr>
<tr>
<td></td>
<td>Hg</td>
<td>0.031±0.031</td>
<td>BDL</td>
<td>BDL</td>
</tr>
</tbody>
</table>

(Extracted from [19])
2.2 Input Dose

Since maize, rice and sorghum are stable foodstuffs in these areas, it was assumed that an average person consumes approximately 0.25kg of each of these locally produced cereals daily for the period of the simulation. The daily intake of mercury and lead due to the consumption of contaminated cereals were, respectively, calculated as:

\[ \text{DIR}_Hg = \sum_i \frac{\text{D}_i \times C_{Hg}}{B_w} \]
\[ \text{DIR}_Pb = \sum_i \frac{\text{D}_i \times C_{Pb}}{B_w} \]

Where \( \text{DIR}_Hg \) and \( \text{DIR}_Pb \) are the daily intake of mercury and lead respectively, in \( \mu g/\text{kg/day} \), \( C_{Hg} \) and \( C_{Pb} \) respectively, are the concentrations (in \( \mu g/\text{kg} \)) of mercury and lead in the ith cereal, \( B_w \) is the body weight, while \( D_i \) is the daily intake (in kg/day) of the ith cereal. Input doses were in micro moles per kilogram body weight per day (\( \mu mol/\text{kg/day} \)). Thus, the input doses of mercury and lead were, respectively, calculated as:

\[ \text{Dose}_{Hg} = \frac{\text{DIR}_Hg}{M_{Hg}} \]
\[ \text{Dose}_{Pb} = \frac{\text{DIR}_Pb}{M_{Pb}} \]

Where \( M_{Hg} \) and \( M_{Pb} \) are the molar masses of mercury and lead, respectively.

2.3 Simulation

The health risk index to some critical tissues, namely; liver, kidney and brain of individuals, were simulated. The simulations were for individuals weighing 60kg, and presumed to be living in the affected communities and consume approximately 0.25kg of each of these locally produced cereals (maize, rice and sorghum) daily for the period of the simulation. For each community (village), three scenarios were modeled, based on an assumed selenium intake, namely: (a) low selenium intake (0.75\( \mu mol/\text{kg/day} \)), (b) adequate selenium intake (2.5\( \mu mol/\text{kg/day} \)), and (c) high selenium intake (7.5\( \mu mol/\text{kg/day} \)). The simulations were for a continuous exposure for 150 days.

III. Results and Discussion

The results of the simulations are presented in Fig. 1 to Fig. 7. These results show the health risk incices of three critical organs (liver, kidney and brain) of individuals presumed to be living in these communities, and consuming contaminated grains (maize, rice and sorghum) cultivated in the three villages. For each tissue, the simulation for three scenarios based on selenium intake were stacked together for ease of comparison. The simulations in Fig. 1 to Fig. 3 are for Bagega village, while Fig. 4 to Fig. 6 are for Dareta. For Abare village only the simulation for the liver was presented (Fig. 7).

3.1 Health Risk at Bagega

The results showed that at Bagega, the HRI were quite high for all the three organs investigated when selenium intake was low (Fig. 1a, Fig. 2a, and Fig. 3a). The HRI for the liver, in this scenario, was as high as 1039, while for the kidney and brain they were as high as 32.7 and 5.9, respectively. It showed that as long as selenium intake is low all the three organs will be at risk. On the other hand, with adequate selenium intake (Fig. 1b, Fig. 2b, and Fig. 3b), the HRI were reduced drastically to 12.15, 1.5 and 2.09, respectively, for the liver, kidney and brain. It showed that even with adequate selenium intake, the liver, kidney, and brain of exposed individuals could still be at high risk. However, when selenium intake was high, only the HRI for the liver was significant (Fig. 1c, Fig. 2c, and Fig. 3c), with the HRI reduced to 1.7, 0.17, and 0.23, respectively, for the liver, kidney, and brain. Thus, at Bagega, only the liver of exposed individuals could be at risk if selenium intake was high.
Figure 1. The health risk index for the liver of an individual at Bagega due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.

Figure 2. The health risk index for the kidney of an individual at Bagega due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.
Figure 3. The health risk index for the brain of an individual at Bagega due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.

3.2 Health Risk at Dareta
For Dareta, the results showed that for low selenium intake (Fig. 4a, Fig. 5a, and Fig. 6a), the HRI for the liver and kidney were very high (as high as 531.06 and 16.04, respectively), while that for the brain remained low (the highest being 0.36) throughout the period of simulation. It showed that for exposed individuals at Derata, only the liver and kidney might be at risk, if selenium intake were low. Meanwhile, with adequate selenium intake (Fig. 4b, Fig. 5b, and Fig. 6b), the HRI reduced drastically for all the three organs, with only the liver remaining high (up to 6.22). For kidney and brain the HRI were <1.0 (0.72 and 0.06, respectively, for the liver, kidney and brain). It showed that with adequate selenium intake, only the liver of exposed individuals could still be at risk. However, when selenium intake was high (Fig. 4c, Fig. 5c, and Fig. 6c), the HRI for all the three organs were <1.0 (0.88, 0.076, and 0.006, respectively, for the liver, kidney, and brain). Thus at dareta, non of the three organs could be at risk if selenium intake were high.

3.3 Health Risk at Abare
At Abare, for both high and adequate selenium intake, the HRI for all three organs were practically zero. However, with low selenium intake (Fig. 7a), the HRI for the liver was high (up to 48.46). This shows that even with low doses of lead and mercury, the HRI could still be high if selenium intake were low. It is worth noting that, while remediation exercises were conducted at Abare before the study by Yahaya and co-researchers [19], no remediation was done at Bagega and Dareta. This could be responsible for the low HRI for these tissues at Abare.
Figure 4. The health risk index for the liver of an individual at Dareta due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.

Figure 5. The health risk index for the kidney of an individual at Dareta due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.
Figure 6. The health risk index for the brain of an individual at Dareta due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.

Figure 7. The health risk index for the liver of an individual at Abare due to the consumption of 0.25kg/day of maize, rice and sorghum (a) Low selenium intake (b) Adequate selenium intake (c) High selenium intake.

IV. Conclusion

The use of a human physiologically-based biokinetic model for the mixture of lead, mercury and selenium in environmental health risk assessment was demonstrated. The model demonstrated its ability to stimulate the health risk index to the liver, kidney and brain of adult humans co-exposed to the mixture of mercury, lead and selenium. The health risk index to these organs were shown to be dependent not only on the concentrations of mercury and lead in these organs, but was equally dependent on selenium intake. The study further concluded that unless selenium intake is adequate or high, even low doses of lead and mercury could be harmful to some organs.
References


