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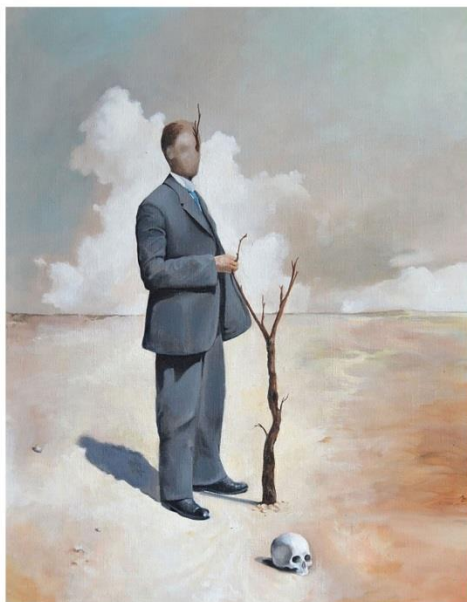
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Determination of Reference Dose (RfD) of Mercury Exposure Based on NOAEL Mercury

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Abstract

This study aimed to determine the RfD from mercury exposure in Bulawa Subdistrict in Bone Bolango District using NOAEL mercury in white mice and body weight and height of Indonesians who were exposed to mercury. This was an observational study with a cross-sectional design using manual quantitative data analysis methods. As a result, the average mercury concentration in respondents' drinking water and fish consumed was 0.000478 mg/L and 0.0298 mg/kg. In conclusion, the average mercury concentration in respondents' drinking water and fish consumed is still below the threshold limit value set by the national standard for mercury concentrations.

Keywords: Mercury, Gold Mining, Safe Concentration, Community.

Determinación de la dosis de referencia (RfD) de la exposición al mercurio basada en NOAEL Mercury

Resumen

Este estudio tuvo como objetivo determinar la RfD de la exposición al mercurio en el subdistrito de Bulawa en el distrito Bone Bolango utilizando NOAEL mercurio en ratones blancos y el peso corporal y la altura de los indonesios que estuvieron expuestos al mercurio. Este fue un estudio observacional con un diseño transversal que utiliza métodos manuales de análisis cuantitativo de datos. Como resultado, la concentración promedio de mercurio en el consumo de agua y pescado de los encuestados fue de 0.000478 mg / L y 0.0298 mg / kg. En conclusión, la concentración promedio de mercurio en el agua potable y el pescado consumidos de los encuestados todavía está por debajo del valor límite establecido por el estándar nacional para las concentraciones de mercurio.

Palabras clave: mercurio, minería de oro, concentración segura, comunidad.

1. INTRODUCTION

Mercury (Hg) is a heavy metal. It is liquid, silver-white color, and easily evaporates at room temperature. In everyday life, mercury has been widely used. Mercury is used in a variety of industries, such as electrical equipment, measuring instruments, agriculture, cosmetics and other necessities. As the mercury is widely used, more organisms experience mercury poisoning.

The use of mercury in the industry often results in environmental pollution, both through wastewater and through air ventilation systems. The mercury waste which is disposed of rivers, beaches or water bodies around these industries can contaminate fish and other aquatic creatures, including algae and aquatic plants. The fish and those aquatic animals are then consumed by humans. This will contribute to human exposure to mercury in their bodies. The FDA (Food and Drug Administration) sets a limit on the maximum mercury content of 0.005 ppm for food, while the WHO (World Health Organization) sets the maximum limit for water, which is 0.001 ppm.

Damage caused by metal mercury in the body is generally permanent. Up to now, an effective way to repair the damage to these functions remains unknown. The effects of mercury on health are mainly related to the nervous system, which is very sensitive to all

forms of mercury. Mercury exposure can cause severe effects on humans, including weak immune system, delay in neuronal development on children, and heart health in adults (TUALEKA, WIBRATA, AHSAN, RAHMAWATI, RUSSENG, WAHYU, 2019).

Early clinical manifestations of mercury intoxication are sleep disturbances, mood changes known as erethism, tingling starting from the area around the mouth to the fingers and hands, decreasing hearing, vision and memory. In severe intoxication, the patient might show clinical symptoms such as tremor, coordination disorders, balance disorders, staggering pathways (ataxia), which cause people to be afraid to walk. This is due to the damage to the cerebellum tissue.

Being poisoned is also very dangerous for pregnant women. It can cause mental retardation for infants, ignorance, and stiffness (spastic). The methyl mercury substance that enters the body of a pregnant woman not only pollutes the woman but also the baby through the umbilical cord. Therefore, mercury is very hazardous to pregnant women, nursing mothers and those who suffer from organic or functional neurological and mental disorders (SUDARMAJI & SUWARNI, 2004).

Theoretically, humans can be exposed to mercury from the environment through three ways of the entrance, namely skin, digestive and respiratory tract. Exposure through the skin and inhalation are the most important occupational pathways, especially for inorganic mercury. Organic mercury exposure is more common through the digestive tract because the organic mercury comes in along with the food people consumed.

Epidemiological studies show that methyl and ethyl mercury poisoning is mostly caused by the consumption of fish obtained from polluted areas or foods made from plants that are sprayed with alkyl mercury fungicides (MERGLER, ANDERSON, CHAN, MAHAFFEY, MURRAY & SAKAMOTO, 2007). The results of research conducted by the Center for Environmental Studies of Gadjah Mada University (UGM) on the Kenjeran beach in Surabaya showed that respondents who consumed contaminated fish with an average Hg level of 99.11 grams/day had Hg level of 0.511 ppb in their hair.

In 1995, there was an increasing mercury level in the hair of people in the Kuopio region of Finland. The sample in this study had relatively high mercury levels, most of which came from contaminated local freshwater fish. Fish intake is the main source of mercury exposure, especially in the form of methylmercury. Another research on fish consumption indicates that there is a statistically significant relationship between fish consumption with mercury levels in the blood with occupation as a confounding factor. This means that respondents who consume fish 5-7 times a week have 17 times more risk of mercury contamination in their blood with a concentration of > 1.5 µg/dl, compared to people who only consume fish as much as 1-2 times a week (MALAKA, 1996).

A study by Siprianus SINGGA (2015) conducted on Bulawa Subdistrict, Bone Bolango District, which was exposed to mercury both through drinking water and through fish, found that the average of mercury concentration in respondents' blood was 125.4939 µg/L, it also found that average of mercury concentrations in respondents' hair

was 5,0480 $\mu\text{g/g}$. There is no previous research that calculated the Reference Dose (RfD) of mercury in the community of Bulawa District, Bone Bolango Regency using Indonesian anthropometric data. These previous studies used mercury RfD issued by research from America and Europe so that it cannot be used as a reference in determining risk for Indonesian as it is not that accurate (BUDIONO, 2003).

This study calculated RfD of mercury derived from the experimental dose of NOAEL (No Observed Adverse Effect Level) using the characteristics of the experimental animals of white mice (*Rattus Novergicus*) from Indonesia and anthropometric factors (Wb, tE, fE, and Dt of people in Bulawa Subdistrict of Bone Bolango District). The purpose of this study was to determine the RfD of mercury exposure in the Bulawa Subdistrict of Bone Bolango District. Thus, the results could be used to estimate the safe amount of mercury exposure for the community without causing harmful effects for their life (ALMATSIER, 2010).

2. MATERIAL AND METHODS

This research was conducted in Bulawa Subdistrict of Bone Bolango District, Gorontalo Province. This is an observational study with a cross-sectional design. The population in this study was all people in Bulawa Subdistrict of Bone Bolango District who were exposed to mercury both through drinking water and through fish. The

sample was drawn using a purposive sampling technique. The sample was 100 people. Data were collected using laboratory examination for mercury concentrations in human blood and hair and in fish and drinking water. The data also covered respondent weight and other data obtained from questionnaire interviews such as respondents' characteristics, frequency of exposure, duration of exposure and consumption rate.

The variables were mercury concentration in human blood and hair, mercury concentrations in fish and drinking water, human body weight, height, respiratory rate, body surface area, weight of white mice, body surface of white mice, the highest dose of toxin without effect on experimental animals (NOAEL), Km factor in animals (Animal Km), Factor Km in society (Human Km), and RfD. Data were analyzed using manual quantitative data analysis to determine RfD.

3. FINDINGS

3.1 Characteristics and Body Surface Area of Experimental Animal

In general, human response to toxicity is qualitatively similar to animal response, so that the facts in this study can be used as a basis for extrapolation from animal data to humans. The experimental animals used in this study were white mice (*rattus norvegicus*).

Table 1: Distribution of Experimental Animal Characteristic (White Mice)

| Research Object (White Mice) | W (kg) | BSA (m ²) |
|------------------------------|-------------|-----------------------|
| 1 | 0.1405 | 0.024165 |
| 2 | 0.1405 | 0.024165 |
| 3 | 0.141 | 0.024223 |
| 4 | 0.141 | 0.024223 |
| 5 | 0.1395 | 0.02405 |
| 6 | 0.1415 | 0.024165 |
| Total | 0.844 | 0.144991 |
| Average | 0,140666667 | 0.024165167 |

To calculate the body surface area of the experimental animal, the following formula is used:

$$BSA = 0,09 w^{0,67}$$

Annotation:

BSA : Body Surface Area (m²)

W : Weight (kg)

3.2 Characteristic, Body Surface Area and Respiration Rate of Community

The characteristics of the community included the bodyweight of 100 people in Bulawa Subdistrict. The average body weight was 55 kg. For community height data, researchers used the average value of Indonesian adult height of 159 cm. Knowing data mentioned above,

the body surface and respiratory rate of the people can be calculated using the following formula:

1. Community Body Surface Area

$$BSA = \sqrt{W \cdot h / 3600}$$

Annotation:

BSA: Body Surface Area (m²)

W: Weight (kg)

H: Height (cm)

$$\begin{aligned} BSA &= \sqrt{W \cdot h / 3600} \\ &= \sqrt{55.159 / 3600} \\ &= 1.55 \text{ m}^2 \end{aligned}$$

2. Fish and drinking Water consumption Rate

Rate of fish consumption = 0.2 kg/ day

Rate of drinking water consumption = 2 L/day

Table 2: Characteristic and Body Surface Area of Community

| Sample | W Avg | h Avg | BSA Avg (m ²) |
|--------|----------|----------|------------------------------|
| 100 | 55 | 159 | 1.55 |

The calculation showed that the average body surface area of the respondents was 1.55 m².

A. Mercury Concentration

Mercury concentration on the drinking water

The average mercury concentration in respondents' drinking water was 0.000478 mg/L. The highest average was found in West Kaidundu, which is 0.00065 mg/L and the lowest is in Mamungaa Village, which is 0.000285 mg/L.

Mercury concentration in fish

The average mercury concentration in the fish that is always consumed by residents of Bulawa Subdistrict was 0.0298 mg/kg. The highest distribution of mercury concentration was found in Laligo Pealii fish, which was 0.04103 mg/kg and the lowest was found in Decapterus muroadsi fish, which was 0.01880 mg/kg.

1. Mercury concentration in respondents' blood

The average concentration of mercury in the respondents' blood was 125.4939 $\mu\text{g/L}$ with a median value of 101.665 $\mu\text{g/L}$. The minimum mercury concentration in the blood was 2.92 $\mu\text{g/L}$ and the maximum was 378.90 $\mu\text{g/L}$.

2. Mercury concentration in respondents' hair

The average concentration of mercury in the respondents' hair was 5.0480 $\mu\text{g/g}$ with a median value of 4.0750 $\mu\text{g/g}$. The minimum concentration of mercury found in their hair was 0.48 $\mu\text{g/g}$ and the maximum concentration was 260.20 $\mu\text{g/g}$.

B. Animal Km and Human Km

To determine the safe limits of toxic doses for the community, first, Animal Km and Human Km need to be carefully calculated.

1. Animal Km

$$\text{Animal Km} = \frac{W_{\text{animal}}}{\text{BSA}_{\text{animal}}}$$

Annotation

Animal km: Km factor of the animal

W: animal weight

BSA: Body Surface Area of the animal

Table 3: Results of Animal Km Calculation on the experimental animal

| Research Object (White Mice) | W (kg) | BSA (m ²) | Animal km (W/BSA) |
|------------------------------|--------|-----------------------|-------------------|
| 1 | 0.1405 | 0.024165 | 5.8141941 |
| 2 | 0.1405 | 0.024165 | 5.8141941 |
| 3 | 0.141 | 0.024223 | 5.820914 |
| 4 | 0.141 | 0.024223 | 5.820914 |
| 5 | 0.1395 | 0.02405 | 5.8004158 |
| 6 | 0.1415 | 0.024165 | 5.8555762 |
| Average | 0.1406 | 0.024165 | 5.82 |

Table 3 shows the result of the calculation process. It is clear that the average score for Animal Km of the experimental animal was 5.82.

2. Human Km

$$\text{Human Km} = \frac{W_{\text{human}}}{\text{BSA}_{\text{human}}}$$

Annotation

Human Km: Km factor of human

W : body weight

BSA: Body Surface Area

Table 4: Results of Human Km Calculation on the community of
Bulawa Subdistrict

| Number of respondents | W avg | BSA avg | Human km Avg |
|-----------------------|-------|---------|--------------|
| 100 | 55 | 1.55 | 35.48 |

Table 4 shows that the Hasil perhitungan Human Km of the community in Bulawa Subdistrict was 35.48.

C. No Observed Adverse Effect Level (NOAEL)

To find out the safe dosage without causing any effects, a toxicity test was carried out by determining the highest dose without causing effects on experimental animals or called No Observed Adverse Effect Level (NOAEL). According to WHO, the NOAEL value of mercury is 0.23 mg/kg per human body weight per day.

D. Reference Dose (RfD)

SARIDEWI & TUALEKA (2019) stated that the RfD calculation is done using a formula from Shaw et al. (2007):

$$RfD = NOAEL \frac{\text{Animal Km}}{\text{Human Km}}$$

Annotation

RfD : Reference Dose (mg/kg)

Animal Km: Km factor of the experimental animal

Human Km: Km factor of human

The Reference Dose (RfD) was obtained from NOAEL, the average of Animal Km and Human Km as below:

$$\text{RfD} = \text{NOAEL} \frac{\text{Animal Km}}{\text{Human Km}}$$

$$= 0.23 \frac{5.82}{35.48}$$

$$= 0.0377 \text{ mg/kg}$$

Form the calculation above, it is clearly seen that the Reference of Dose (RfD) of mercury in the community of Bulawa Subdistrict of Bone Bolango District is 0.0377 mg/kg.

4. CONCLUSIONS

The results showed that the average mercury concentration in fish consumed by respondents and the community in Bulawa District was 0.0298 mg/kg. This is still below the threshold limit value set by the national standard for mercury concentrations in fish which was 0.3 mg/kg. The average mercury concentration in their drinking water is 0.000478 mg/L. This is also below the threshold limit value set by the national standard for mercury concentration in drinking water of 0.001 mg/L.

The average mercury concentration in the respondents' blood was 125.4939 $\mu\text{g/L}$. This indicates that the mercury concentration in the respondents' blood has passed threshold limit value set by the national standard of 8.0 $\mu\text{g/L}$. This also happened for the hair. The average mercury concentrations in the respondents' hair were 5.0480 $\mu\text{g/g}$, exceeding the threshold limit values set by the national standard for mercury concentration in the hair of 2.0 $\mu\text{g/g}$.

This study calculated the average of mercury RfD to be 0.0377 mg/kg. It is greater than the RfD value set by USEPA (1997), which has been used in PAHRUDDIN's research in (2017) of 0.0003 mg/kg. It is also greater than the one set by the Agency for Toxic Substances and Disease Register of 0.0004 mg/kg. Therefore, the RfD value in this research is not safe.

Among the efforts to control the mercury exposure is, for the community of Bulawa Subdistrict, to limit their consumption rate and frequency of marine fish, so that the risk of mercury exposure, which is hazardous to their health, can be reduced. For the government and related institutions, it is suggested carrying out strict monitoring of activities in the gold mining sites which can pollute the environment.

The government and related institution are also suggested to routinely monitoring mercury concentrations in drinking water and fish consumed by the community as well as carrying out regular health promotion program, called Information and Education Communication (KIE) about the dangers of mercury and its effects on health, so that people know and are aware of the dangers they face. In addition, technical control can be carried out by the government and related

institutions in the form of handling mercury pollution using the role of microorganisms or bioaccumulation, bioremediation and bio-removal processes.

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