Prediction of The Needs for Benzene Detox with Foods Intake Containing CYP2E1 Enzyme, Sulfation, and Glutathione at Gas Stations Pancoranmas Depok, Indonesia

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Abstract

Background: Benzene was a dangerous chemical compound which was one of the products of gas stations and one of the chemicals contained in gasoline and it was carcinogenic. TTo reduce and eliminate toxin of benzene from human body, could be used the detoxification process. One of the detoxification process approach was using foods. The aim of this research was to calculate the foods intake containing CYP2E1 enzyme, sulfation, and glutathione to improve benzene detox.

Method: The type ofr esearch was descriptive study. The subjects was 15 workers. Location of this research was in gas station Pancoranmas Depok. Variables were body weight, duration of work, working time perweek, working time perday, and benzene concentration. After getting all variables above, breathing rate and intake non-carcinogen per respondent can be calculated. Then, effective doses of foods containing CYP2E1 enzyme, sulfation, and glutathione would be obtained.

Results: All respondents were at workplace shows benzene concentration below the TLV. The highest effective dose of foods containing CYP2E1 enzyme was cow brain, sulfation was tuna, and glutathione was carrot.

Conclusion: The level of adequacy of enzyme of each respondent was different. Effective dose of each respondent depending on body weight, duration of work, and benzene concentration at workplace. Every respondent could choose foods depending on their needs and taste.

Keyword: *Benzene, CYP2E1, Detoxification, Glutathione, Sulfation*

Introduction

According to the Central Bureau of Statistics, the number of vehicle users such as private cars has reached almost 15 million, for private motorbike users reaching 105 million in 2016. The use of the vehicle certainly requires fuel. One of the efforts to obtain fuel is through a Gas Station (SPBU). Every day, gas stations will refuel. The odor can cause a smell that is quite stinging so that it can be inhaled into the workers' body. The smell of this fuel contains organic compounds, namely benzene.

Benzene is a colorless and sweet-smelling liquid, evaporates very quickly in the air but difficult to dissolve in water. Based on the results of the NCI (National Cancer Institute) and CAPM (Chinese Academy of

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Preventive Medicine) studies, it was stated that fopoietic malignancies lymphohema and hematological disorders in 74,828 benzene-exposed workers in 672 factories in 12 cities in China, increased the risk of all types of ANLL leukemia (Acute Nonlymhocytic Leukemia) and a combination of ANLL and precursor MDS (Myelodisplastic Syndrome) [1] (Travis et.al, 1994). If workers are exposed to benzene it will cause a variety of negative things such as dizziness, nausea, kidney and liver problems, even if in long-term exposure and in a long duration it will cause cancer to cause death. Body receptors that will interact with toxins namely cells, enzymes, DNA / RNA, oxygen transport. The interaction between benzene and the receptors above causes work-related diseases.

Regulation of Indonesian Ministry of Manpower and Transmigration Number PER13/MEN/X/2011 and American Conference of Government Industrial Hygienists (ACGIH) in 2007, set the threshold limit value (TLV) for benzene exposure at workplace is 0.5 ppm (1.6 mg/m^3) [2-3]. Benzene included as a carcinogenic group in humans. National Institute for Occupational Health and Safety (NIOSH) in 2005, set the recommended exposure limit for 8 hours of work at 0.1 ppm (0.32 mg/m^3) [4] . While according to Agency for Toxic Substance and Disease Registry (ATSDR) in 2007, set the minimal risk levels (MRLs) for benzene exposure is 0.009 ppm (0.02 mg/m^3) per day which for acute effect and 0.003 ppm (0.009 mg/m^3) per day for chronic effect [5] . The most vulnerable population to the accumulation of benzene exposure is gas stations workers. This is because SPBU workers work every day at the place so that continuous exposure can occur which over time accumulates the concentration of benzene can become quite high in the workers' body.

Previous research, states that the benzene concentration at gas station Pancoranmas Depok is 0.02 ppm (0.06 mg/m^3) at both administration and operational units[6]. That means it is still below the threshold limit value (TLV) according to Regulation of Ministry of Manpower and Transmigration Number PER13/MEN/X/2011 and American Conference of Government Industrial Hygienists (ACGIH) in 2007. This concentration value also below the TLV based on manual calculation of safe concentration at gas station Pancoranmas Depok is 0.03 ppm (0.09 mg/m^3). But this concentration value is above the TLV of minimum risk level (MRL) according to ATSDR [5].

Although the benzene concentration in the gas station Pancoranmas Depok is below TLV, solution is needed to reduce negative impact of benzene exposure for gas station workers. One way is detoxify toxin from the body. One detoxification method that can be used is detoxification using food. Before toxins can be detoxified from the body, a biotransformation process is needed in the body. The purpose ofbiotransformation is to convert non-polar to polar, then to become hydrophilic so that it can be excreted out of the body. Biotransformation occurs in two phases. The first phase is the functional phase where the functional group matches the oxidation, reduction and hydrolosis reactions. Then the second phase is the conjugate reaction phase involving several types of endogenous metabolites in the body in the endoplasmic reticulum [7] (Tualeka, 2013).

Research using foods approach as benzene detoxification is still very limited. Foods containing CYP2E1 enzyme such as cow liver, cow brains, and salmon [8-9]. Foods containing sulfation such as egg, chicken, and tuna, and foods containing glutathione such as broccoli (Forman et al, 2010), carrot, and tomato [10-11] (Dhivya, 2012). But there has never been a research that explains how much intake of these foods is needed to improve benzene detoxification, especially in populations that exposed to benzene in the long time. Based on the background above, the aim of this research is to calculate the intake of foods (effective doses) containing CYP2E1 enzyme, sulfation, and glutathione to detoxify benzene at gas station workers in Pancoranmas Depok.

Method and Materials

The type of research was descriptive study. Subjects were workers in gas station Pancoranmas Depok. The inclusion criteria were workers who had worked in this industry for 10 years or more and willing to be used as research respondents. The sample of was 15 respondents.

Variables calculated were body weight, duration of working (years), working time per week (days), average of working everyday (hours) of respondents, bennzene concentration at 2 locations in this gas station. Measurement of respodents weight using manual measurement method with body scales. Measurement of duration of work, working time per week, and average of working everyday were obtained with indepth interview with respondents. Then, measurement of benzene concentration at environment using

measurement method of NIOSH 1501 (2003) with aromatic hydrocarbon sampling method [4]. Air samples were taken using a calibrated personal sampler pump. The filter used to absorb toluene vapour was a charcoal tube SKC 226-01. Air samples were analyzed using Gas Chromatography-Flame Ionization Detector (GC-FID). Willingness to participate in research was made in writing through informed consent and this study had received prior ethical approval by the Ethics Committee of the Faculty of Public Health, Airlangga University with ethical number 516 KEP-K.

After getting all variables above, can be found breathing rate and intake non-carcinogen of benzene per respondent. Then, effective dose of foods containing CYP2E1 enzyme, sulfation, and glutathione would be obtained by manual calculating, use the formula below :

Explanantion:

Intake nc (non-carcinogen) =

C : Benzene concentration (mg/m^3)

R : Breathing rate (m^3/hour)

Dt : Duration of working (years)

fE : Working time per week (days)

tE : Average of working time per day (hours)

Wb : Weight (kg)

C enzyme [12]

CYP2E1 enzyme = 0.0000088 mmol/ml

Sulfation = 0.0001 mmol/ml

Glutathione = 0.00000099 mmol/ml

A = Content of enzyme in 100 grams of food

CYP2E1 enzyme

- Cow liver : 5.6 mg
- Cow brain : 1.8 mg
- Salmon : 6.6 mg

Sulfation

- Egg : 1.477 g
- Chicken : 0.801 g
- Tuna : 0.755 g

Glutathione

- Broccoli : 7.8 mg
- Carrot : 5.9 mg
- Tomato : 10.9 mg

Results

Distribution of Benzene Concentration at Workplace

Figure 1. Distribution of Benzene Concentration at Workplace

In Figure 1 shows that all respondents are at workplace with benzene concentration below the threshold limit value (TLV). The TLV of benzene concentration in the air is 0.5 ppm (1.6 mg/m^3). While, there is no respondent who is at workplace with benzene concentration above TLV. Measurements of benzene concentrations are carried out at administration and operational units. The benzene concentration in both units are 0.02 ppm (0.06 mg/m^3).

Effective Dose of Foods Containing CYP2E1 Enzyme to Benzene Detox

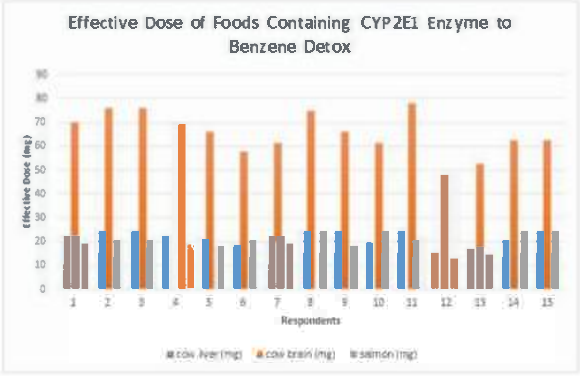

Figure 2. Effective Dose of Foods Containing CYP2E1 Enzyme to Benzene Detox

In Figure 2 shows that the effective dose of cow brain has the highest dose, while salmon has the lowest dose from foods containing CYP2E1 enzyme. The highest effective dose of cow liver, cow brain, and salmon are 25.08 mg, 78.05 mg, and 21.28 mg (respondent 11). While the lowest effective dose of cow liver, cow brain, and salmon are 15.36 mg, 47.8 mg, and 13.03 mg (respondent 12).

Effective Dose of Foods Containing Sulfation to Benzene Detox

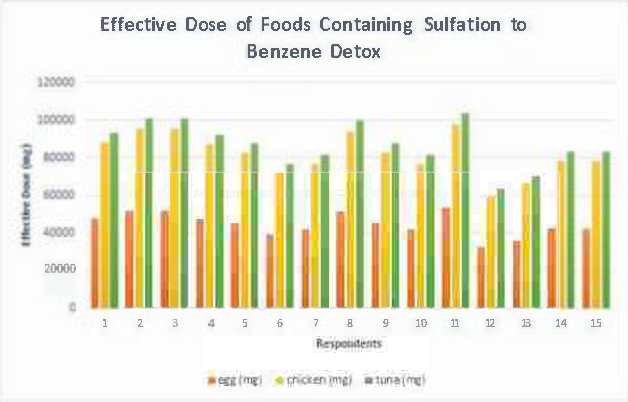

Figure 3. Effective Dose of Foods Containing Sulfation to Benzene Detox

In Figure 3 shows that the effective dose of tuna has the highest dose, while egg has the lowest dose from foods containing sulfation. The highest effective dose of egg, chicken, and tuna are 53,093 mg, 97,901 mg, and 103,866 mg (respondent 11). While the lowest effective dose of egg, chicken, and tuna are mg.32,346 mg, 59,644 mg, and 63,278 mg (respondent 12).

Effective Dose of Foods Containing Glutathione to Benzene Detox

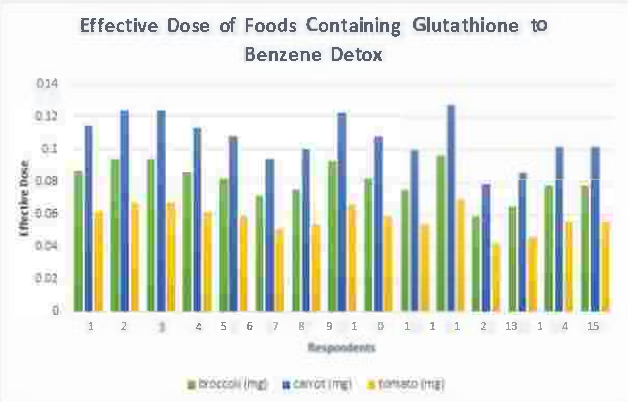

Figure 4. Effective Dose of Foods Containing Glutathione to Benzene Detox

In Figure 4 shows that the effective dose of carrot has the highest dose, while tomato has the lowest dose from foods containing glutathione. The highest effective dose of broccoli, carrot, and tomato are 0.09 mg, 0.12 mg, and 0.06 mg (respondent 11). While the lowest effective dose of broccoli, carrot, and tomato are 0.05 mg, 0.07 mg, and 0.04 mg (respondent 12).

Discussion

Distribution diagram analysis between benzene concentration and the threshold limit value (TLV) shows that all respondents are at workplace with benzene concentration below TLV according to Regulation of Ministry of Manpower and Transmigration Number PER13/MEN/X/2011 about The Threshold Limit Value of Physical and Chemical Factors at Workplace [2]. Detoxification is very important to be done in order to remove harmful chemicals in the body. Many toxins are spread on this earth such as in the sea, rivers, food, drinks, and objects around us. Detoxification can be done uses foods approach. Food-based nutrition be involved in the detoxification process. Several publications that had used cells, animals and clinical studies show that food-based components and nutrients could modulate the process of conversion and excretion of toxins from the body [13].

CYP2E1 enzyme catalyzes the oxidation reaction of benzene to benzene oxide which is in balance with benzene oxepin. Then metabolized to phenol (the main metabolite product of benzene). Phenol is then oxidized with CYP2E1 catalyst to catechol or hydroquinone, which is then oxidized by the enzyme myeloperoxidase (MPO) to be a reactive metabolite 1,2- and 1,4-benzuinon. Catechol and hydroquinone can be converted to metabolites 1,2,4-benzenatriol with CYP2E1 catalysts [14-15]. Food sources of CYP2E1 enzyme like cow liver, cow brain, and salmon [8-9]. Specific foods and nutrients can induce metabolic enzymes, such as sulfation. Sulfation can be catalyzed by enzyme sulfotransferase. This enzyme can be found in the liver, intestines, adrenal glands, brain, and skin. The sulfating process is a detoxification process that can reduce the toxicology of a chemical. The decline in the function of this enzyme can be caused by genetic or certain chemicals. The activity of the sulfotransferase enzyme depends on inorganic sulfate reserves. Food sources of sulfation-containing compounds such as egg, chicken, and tuna [9]. Enzyme that responsible for metabolizing glutathione is the glutathione s-transferase enzyme. Involving antioxidant responsive elements and xenobiotic responsive elements. Many foods to be

upregulation of this enzyme, including garlic, fish oil, black soybean, broccoli, carrot, tomato, curcumin, etc. Genetic variances, gender, and maybe body weight can play a role in the effects of dietary factors on GST enzymes [9].

Based on the results of data analysis, the effective dose of cow liver, cow brain, and salmon that the body needs to remove benzene out of the body as shown in Figure 2-4. The effective dose of each food is different depending on the physical of individu. The higher concentration of benzene in the body, the higher detox mass of cow liver, cow brain, and salmon needed. Also with detox mass of egg, chicken, tuna, broccoli, carrot, and tomato. This is consistent with the formulation that has been made in previous studies which states that it has a synergistic relationship with substance concentration [16]. Maximum consumption mass of foods containing CYP2E1 enzyme like cow liver is 26.08 mg, cow brain is 78.05 mg, and salmon is 21.28 mg. Maximum consumption of foods containing sulfation and glutathione like egg is 53.09 g, chicken is 97.9 g, tuna is 103.86 g, and broccoli is 0.09 mg, carrot is 0.12 mg, and tomato is 0.06 mg. Foods in the diagram can be chosen by each respondent needs and tastes. If the respondent does not like the cow liver and cow brain, he/she can consume salmon according to the effective dose of salmon needed, and vice verca. Also with foods containing sulfation and glutathione. The consumption of each food can be regulated by each respondent, can be divided into several days.

Conclusion

All of respondents were at workplace with benzene concentrations below the threshold limit value (TLV). Intake of foods that contain CYP2E1 enzyme (cow liver, cow brain, and salmon), sulfation (egg, chicken, and tuna) and glutathione (broccoli, carrot, and tomato) were expected to increase detoxification of benzene. The effective dose was required by the respondents depending on body weight, duration of work, and benzene concentration at workplace. The higher the benzene concentration, the higher the needs for foods containing CYP2E1 enzyme, sulfation, and glutathione that the body needs. Body weight and duration of work could also be another factors in differences of individual intake. Every respondent could choose foods depending on their needs and tastes.

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