

Correlation of Toluene Safe Concentration, Malondialdehyde and Glutathione Levels in Osowilangun Shoe Home Industry Workers

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Abstract

Introduction: Toluene is the main organic solvent found in adhesives used for shoe production in Osowilangun Shoes Home Industry. Exposure to toluene that exceeds the threshold value can cause the emergence of free radicals which eventually increase the concentration of malondialdehyde and reduce the concentration of glutathione in the body. The purpose of this research is to study the safe concentration of toluene with levels of malondialdehyde and glutathione in Osowilangun shoe home industry workers.

Methods: This is an observational study using cross sectional design and quantitative approaches. There are 25 people were taken as sample by using accidental sampling technique. Data analysis used Pearson correlation test.

Result: The average safe concentration value in this study was 1.1088 mg / m³ with an average value of malondialdehyde of 7,784 MU and glutathione of 35,655 µg / L. Pearson correlation test showed the safe concentration of toluene and malondialdehyde level was $p=0.685$ ($p> 0.05$), with relationship between safe concentrations of toluene and glutathione was $p = 0.808$ ($p <0.05$).

Conclusion: This study shows that there was no significant relationship between toluene safe concentration and levels of malondialdehyde and glutathione.

Key words: Glutation, Malondialdehyde, Safe concentration, Toluene

Introduction

Osowilangun shoe industry is an informal footwear manufacturing sector whose process include a number

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of activities of selecting raw materials, depicting patterns, cutting patterns, coloring, gluing, polishing and finishing. The production process is not related to the potential hazards for workers. Potential hazards can be physical, chemical, biological, psychological and ergonomic hazards. Glue containing organic solvents is used in the shoe production process as an adhesive is harmful to the health of workers⁴. The most widely used organic solvent in adhesives is toluene¹¹. Toluene (C₆H₅CH₃) is a colorless, odor specific with volatile properties³. Toluene is a non-polar compound that can

be carcinogenic for workers exposed in the home shoe industry. Toluene threshold value in the workplace has been regulated in Permenaker Number 5 of 2018 by 20 ppm².

Inside the human body, toluene can be a potential hazard that can cause health effects based on the dose of inhaled concentration or contact that occurs with toluene compounds. Carcinogenic intakes is used if the ECR value is $\leq 10^{-6}$ (safe) while non-carcinogenic intakes is shown by RQ if the value is ≤ 1 . This means that toxin does not have impact on the body¹⁷. Furthermore, the safe concentration of toluene can be calculated by assuming that RQ = 1. The safe limit is the limit or the lowest value that causes the level of risk to be unsafe. Safe concentration is the concentration below the safe limit while. If the value is equal to the safe limit it will cause the level of risk to become unsafe⁶.

When absorbed through inhalation, toluene enters the respiratory system, then into the veins in the alveoli and into the blood. Interaction increases the amount of toluene that can be collected by liquid blood media and facilitates the transport of toluene to all areas of the body at a greater rate than if toluene is only transported in plasma⁵. An imbalance of antioxidant enzymes with free radicals in the human body can cause damage to cell membranes. Cell membranes formed from fatty acids undergo oxidation thereby releasing malondialdehyde (MDA)⁹. Malondialdehyde (MDA) is a dialdehyde compound which is the final product of lipid peroxidation in the body through an enzymatic or nonenzymatic process⁷.

In addition, continuous and high amount of toluene exposure that exceeds the threshold value causes the formation of dangerous toluene. The role of antioxidants is very important because its function can inhibit and neutralize the occurrence of oxidation reactions involving free radicals¹³. Glutathione (GSH) is antioxidant produced to reduce harmful toluene. Antioxidants tend to react first with free radicals compared to other molecules because antioxidants are easily oxidized. In addition, the role of endogenous antioxidants is to neutralize free radicals assisted with exogenous antioxidants¹⁰. The purpose of this study was to determine the relationship between safe concentrations of toluene and malondialdehyde levels and glutathione

in Osowilangun shoe home industry workers.

Methods and Materials

This is an observational study with a quantitative approach. The design of this study is cross-sectional that is observation and measurement of variables carried out at one time. The study was conducted in the Osowilangun shoe home industry in Surabaya. Respondents from the study were 25 people taken by accidental sampling from a total population of 30 people. Data on the characteristics of respondents were taken through a questionnaire. Measurement of toluene concentrations in the air using Gas Chromatography (GC) technique which is placed at 12 predetermined points is carried out by UPTK3 of Surabaya City. Data of Toluene safe concentration is obtained

$$C_{safe} = \frac{RfC \times Wb \times T_{avg}}{R \times tE \times fE \times Dt} \text{ la}^{17}:$$

RfC = reference concentration of toluene = 5 mg/m³

$$= \frac{RfC (mg/m^3) \times R (m^3/hari)}{Wb (kg)} = RfC (mg/kg/hari)$$

Wb = weight (kg)

T_{avg} = average time period (30 years × 365 days/year)

R = respiration rate (m³/hour)

$$= \frac{(5,3 \times \ln(W_b)) - 6,9}{24} \frac{(5,3 \times \ln(W_b)) - 6,9}{24}$$

tE = daily exposure time (hours / day)

fE = annual exposure frequency (day / year)

D_t = duration of exposure (years)

Blood samples and examination of malondialdehyde (MDA) and GSH concentrations were analyzed and determined by Thiobarbuturic Acid Reactive Substance (TBARS) method at the Nutrition Laboratory of Airlangga University. Data were analyzed using Pearson correlation test.

Result

Characteristics of Respondents

Table 1. Frequency Distribution of Respondents

Respondents Characteristics	Percentage Frequency	
Age (Years)		
16-25	2	8%
26-35	1	4%
36-45	8	32%
46-55	8	32%
56-65	6	24%
Gender		
Female	13	52%
Male	12	48%
Years of Service		
< 10 years	3	12%
≥ 10 years	22	88%

Source: Primary Data

Table 1 shows that the majority of workers who became respondents were aged 36-45 years and 46-55 years (32%), respectively and only one respondent was aged 26-35 years (4%). Most respondents were female (52%) and 12 people (48%) were male. The majority of respondents have ten years of service (10 years (88%) with 3 (12%) respondents having ten years <10 years of service.

Toluene Concentration

Table 2. Distribution of Toluene Concentrations

Points of Measurement	Toluene Concentration (TLV = 20 ppm)	
	< TLV	≥ TLV
Point 1		62,7
Point 2		58,5
Point 3		137,5
Point 4		30,5
Point 5		25,5

Cont... Table 2. Distribution of Toluene Concentrations

Point 6	9,3	
Point 7		41,1
Point 8		289,3
Point 9		36,9
Point 10	11,5	
Point 11	15,8	
Point 12	9,7	

Source: UPTK3 Surabaya

Based on table 2, the highest measurement of air toluene concentration was at point 8 by 289.3 ppm. The lowest toluene concentration was at point 6 by 9.3 ppm. Measurements of toluene concentrations in the air showed that 66.7% of the measurement points with toluene concentrations exceeded TLV (20 ppm) in accordance with ACGIH (2019) and Permenaker No 5 (2018)^{1,2}. There are 4 measurement points that have a concentration of toluene in the air not exceeding TLV. The average measurement result of toluene concentration was 60.69 ppm. This shows that the average exceeds the TLV that has been set.

Toluene Safe Concentration

Table 3. Distribution of Toluene Safe Concentration to Workers

Respondent	W (kg)	C Toluene (mg/m ³)	RQ	C Aman
Respondent 1	60	1088.004	1085.02	1.00
Respondent 2	70	1088.004	992.02	1.10
Respondent 3	51	59.421	40.63	1.46
Respondent 4	100	114.705	91.51	1.25
Respondent 5	70	114.705	117.66	0.97
Respondent 6	55	235.803	134.38	1.75
Respondent 7	69	235.803	335.94	0.70
Respondent 8	41	220.008	248.24	0.89
Respondent 9	78	95.901	239.10	0.40
Respondent 10	46	59.421	59.26	1.00
Respondent 11	75	138.774	345.98	0.40
Respondent 12	84	517.112	275.04	1.88
Respondent 13	87	114.705	68.63	1.67
Respondent 14	65	114.705	152.52	0.75
Respondent 15	50	95.901	153.02	0.63

Cont.... Table 3. Distribution of Toluene Safe Concentration to Workers

Respondent 16	53	1088.004	1550.03	0.70
Respondent 17	70	220.008	112.63	1.95
Respondent 18	60	34.976	55.81	0.63
Respondent 19	55	95.901	87.44	1.10
Respondent 20	65	114.705	101.86	1.13
Respondent 21	45	235.803	125.42	1.88
Respondent 22	93	517.112	343.80	1.50
Respondent 23	55	154.570	369.95	0.42
Respondent 24	59	517.112	288.79	1.79
Respondent 25	80	36.480	48.51	0.75

Source: Primary Data

Based on table 3, the respondent’s safe concentration was determined from body weight, frequency of annual exposure, respiration rate, duration of daily exposure, toluene reference concentration, and average time period. Measurements were made by calculating the amount of toluene non carcinogenic intake with the following formula:

$$Ink = \frac{C \times R \times tE \times fE \times Dt}{Wb \times Tavg}$$

Risk characteristic value (RQ) was calculated by using the following formula:

$$RQ = \frac{Ink}{RfD \text{ atau } RfC}$$

According calculation of RQ values of 1 or less than 1 (≤ 1) indicate that the oxide has not had an impact on the body¹⁷. The safe concentration formula is as follows:

$$C_{safe} = \frac{RfC \times Wb \times Tavg}{R \times tE \times fE \times Dt}$$

The average safe concentration (C safe) of toluene is calculated based on body weight, respiration rate, daily exposure time, average non-carcinogenic time period (30 years x 365 days/year), annual frequency of exposure, and duration of exposure toluene for workers is 1.1088 mg/m³. The highest safe concentration value is 1.95 mg/m³ and the lowest is 0.40 mg/m³.

Concentration of Malondialdehyde (MDA) and Glutathione (GSH)

Table 4. Distribution of Malondialdehyde (MDA) and Glutathione (GSH) Concentrations

Respondent	Glutathione (GSH)	Malondialdehyde (MDA)
	(µmol/L)	(MU)
1	14,6	11,857
2	40,85	5,423

Cont... Table 4. Distribution of Malondialdehyde (MDA) and Glutathione (GSH) Concentrations

3	40,583	6,277
4	58,349	3,817
5	49,79	4,543
6	49,257	4,603
7	46,176	4,717
8	19,812	11,683
9	27,873	10.023
10	40,241	6,497
11	45,453	4,737
12	28,067	9,67
13	34,383	8,683
14	35,942	7,643
15	30,578	9,317
16	34,357	8,923
17	31,415	9,177
18	26,622	10,323
19	26,356	10,843
20	38,719	7,363
21	39,937	7,203
22	24,796	11,03
23	43,969	5,017
24	41,42	5,283
25	21,829	11,517

Source: Airlangga University Nutrition Laboratory Data

Glutathione concentration (GSH)

Table 4 shows that the highest glutathione concentration (GSH) was 58,349 µg / L and the lowest concentration was 14,6 µg / L. The average glutathione concentration (GSH) measurement results was 35,655 µg / L.

Malondialdehyde (MDA) concentration

Table 4 shows that the concentration of malondialdehyde (MDA) of Osowilangun shoe home industry workers ranged 3,817 MU - 11,857 MU with the highest concentration of 11,857 MU and the lowest concentration of 3,817 MU. The average measurement

result of malondialdehyde (MDA) concentration was 7.847 MU.

Relationship of Toluene Safe Concentration with Glutathione Concentration (GSH)

The results showed that there was no relationship between the safe concentration of toluene and the concentration of glutathione (GSH) in the workers studied ($p = 0.808 > 0.05$). In addition, the results of the relationship test showed that the correlation coefficient value was negative (0.051) where an increase in safe concentration decreased the concentration of glutathione.

Relationship between Toluene Safe Concentration and Malondialdehyde (MDA) Concentration

The results show that there was no relationship between the safe concentration of toluene and the concentration of malondialdehyde (MDA) in Osowilangun shoe home industry workers ($p = 0.685 > 0.05$). In addition, the results of the relationship test indicate that the correlation coefficient value was positive (0.085), when the safe concentration increased, the concentration of malondialdehyde also increased.

Discussion

In the present research the measurement of exposure to air toluene concentration was carried out at 12 points with the highest toluene concentration of 289.3 ppm, the lowest of 9.3 ppm and the average of 60.69 ppm. The highest and average concentration value of toluene exceeds the threshold value. The measurement results also indicate that most of the measurement points exceeded the TLV that have been set in Regulation of the Ministry of Manpower Number 5 of 2018 by 20 ppm². The results of the questionnaire indicate that each respondent has a different concentration of safe exposure according to the characteristics of each respondent. Based on the measurement results, the average safe concentration of 1.1088 mg/m³ with the highest safe concentration of 1.95 mg/m³ and the lowest of 0.40 mg/m³. Exposure toluene continuously and exceeding the threshold value has the potential to cause health problems for workers in the home shoe industry.

Exposure to toluene, which is one of the free radicals, can cause an increase in oxidative stress which can cause damage to cells or tissues and can be characterized by the

amount of malondialdehyde concentration in the human body¹⁵. According another research asserted that toluene exposure can increase oxidative stress parameters and cause a significant decrease in antioxidant enzyme activity²⁰. In the present study there was no significant relationship between safe concentrations of toluene and malondialdehyde (MDA) with a value of $p > 0.05$. Tambunan (2014) found that there was a significant effect of changes in MDA concentration in the body due to increased toluene exposure⁸. In this study the relationship between safe concentrations of toluene and malondialdehyde levels showed a positive direction i.e the increase in toluene concentrations also increased malondialdehyde level. According to the results of Noerhalimah's research, the level of malondialdehyde in the group exposed to car paint workshops were higher compared to those not exposed¹⁸. The results of Kim's research, showed that VOC exposure, especially toluene, could induce oxidative stress¹⁴. In addition, the study showed a significant change in the increase in malondialdehyde levels in the exposed group.

Glutathione (GSH) as an antioxidant is needed to reduce free radicals. The correlation test results showed that there was no significant relationship between the safe concentration of toluene and the concentration of glutathione (GSH) and the value ($p > 0.05$). However, the relationship test is negative, which means that when the concentration of safe (C safe) toluene increases, the concentration of glutathione (GSH) decreases. This study is in line with a study of Safyudin and Subandrate (2015) which showed a decrease in the concentration of glutathione (GSH) in workers exposed to free radicals¹². Other studies suggested that the reduction in glutathione in some tissues was caused by the effects of toluene exposure¹⁹. The results of research by Ahmadizadeh et al (2014) there was a significant difference in the reduction in glutathione level between the groups exposed to toluene and those that are not. Therefore, the observations show that toluene can reduce glutathione levels in the kidneys which supports oxidative stress depending on exposure toxicity.

Conclusion

In the present study there was no significant relationship between the safe concentration of toluene and the concentration of malondialdehyde and glutathione in

Oswilangun shoe home industry workers. There were 66,7% measurement points with toluene concentration exceeding the threshold value (TLV) of 20 ppm and there were 33,3% measurement points with toluene concentration below TLV.

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