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Risk Analysis Characterization of Benzene and Demographic Factors toward Immunoglobulin A

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Abstract

BACKGROUND: Research on risk assessment at industrial sites has experienced growth during the end of this year. But in Indonesia, there is still limited research on risk assessment, especially regarding the importance of measuring non-carcinogenic risk assessment in the workplace. Benzene exposure is believed to reduce levels of immunoglobulin A (IgA) in workers.

AIM: The purpose of this study was to analyse the relationship between risk quotient (RQ) of non-carcinogenic risk assessment of benzene and demographic factors on IgA levels.

MATERIAL AND METHODS: The subjects of the study were shoe craftsmen who were at risk of benzene exposure. The study design was cross-sectional with a total population of 20 workers. Measurement of IgA levels by Immunoturbidimetric Assay with a normal standard of 2-3 mg/ml. Calculation of non-carcinogenic (RQ) risk characteristics with a comparison between risk agent non-carcinogenic intake with RfD or RfC benzene.

RESULTS: The majority of the study subjects aged over 45 years and had a working period of ≥ 25 years. There were 2 location points that had a threshold value exceeding the benzene standard (> 0.05 ppm), and 40% of the subjects had decreased IgA levels. Age and working periods had a significant relationship to IgA levels ($p = 0.027$; $p = 0.047$), while benzene and RQ levels did not have a significant relationship with IgA levels ($p = 0.179$; $p = 0.436$).

CONCLUSION: Increasing age and working period can reduce IgA levels in the body. Further research is needed on risk assessment, especially on the safe limits of benzene concentration in the workplace to find out how long benzene exposure forms a non-carcinogenic or carcinogenic risk in workers' bodies exposed to benzene.

Introduction

Research on risk assessment in industrial environments has begun to develop in recent years. The importance of knowledge about hazard risk is a very important term to avoid accidents. Risk assessment studies such as RQ of noncarcinogenic risk assessment intake, or risk characteristics of carcinogenic effects (ECR) have begun to develop, but in Indonesia, this research is still limited.

Benzene is the most important ingredient in the chemical industry. Benzene is present in solvents for waxes, resins, rubber, plastics, rubber, paint, glue [1], [2]. Benzene is non-polar and insoluble in water, but soluble in organic solvents such as diethyl ether, carbon tetrachloride or hexane [3]. Benzene evaporates into the air very quickly, dissolves little in water, and is highly flammable [1], [4]. Long-term exposure to benzene can reduce levels of Immunoglobin A (IgA).

Immunoglobulin A (IgA) is the main serum

immunoglobulin and a class of antibodies that are predominant in the external secretion that functions to coat the mucosal surface and has a key role in immune protection [5]. IgA levels in the blood serum of adults (aged 16-60 years) are 1.4-4.2 mg/ml for IgA1 and 0.2-0.5 mg/ml for IgA2. Biological half-life for IgA1 is 5-7 days, while the half-life of IgA2 is 4-6 days [6].

Several studies had shown a relationship between benzene exposure and IgA levels. Research on 13 oil tank workers with relatively low benzene exposure (0.01 ppm-0.62 ppm) showed a significant decrease in serum immunoglobulin M (IgM) and immunoglobulin A (IgA) [7]. In studies using a rat as animal subjects, there was a 50% reduction in IgA in female mice with benzene exposure of 30 and 300 ppm [8], [9]. Research on painting workers in Egypt consisted of 81 people exposed to benzene and 83 controls, showed an increase in serum IgM and a decrease in serum IgA and IgG in the exposed group compared with the control group [10]. This is due to the presence of necrosis, and liver dysfunction in the group exposed to benzene which is immune/immune suppressed [10].

However, among all previous studies, there is still no study about the correlation between the RQ of non-carcinogenic benzene and IgA levels. Research in Indonesia regarding risk assessment especially on non-carcinogenic risk characteristics of IgA levels is still limited, especially in the shoe-making industry which has a continuous risk of benzene exposure from organic glue. The previous research explains about calculated RQ at worker exposed to benzene in shoe worker industry, but not gives a correlation finding between RQ and effect of benzene exposure at worker such as decreased level of IgA serum [11], [12], [13].

Therefore, researchers are interested in analysing the relationship between the RQ of non-carcinogenic benzene and IgA levels in Oso Wilangun Tambak Fish Farmers' workers.

Material and Methods

The research subjects were all shoe craftsmen who were in Tambak Oso Wilangun Village, Surabaya with the inclusion criteria were workers in a healthy condition, workers who were not pregnant, and did not have the habit of drinking alcohol.

This study was a cross-sectional study with sampling using a total population (total sampling) of workers located in Tambak Oso Wilangun Surabaya Village, amounting to 20 people with research carried out in November-December 2017. Before data collection, this study was approved by the Faculty of Public Health's ethics committee, Airlangga University, Surabaya with ethics number 516-KEPK.

Independent variables were RQ of non-carcinogenic benzene, while the dependent variable was the IgA level of shoe craftsmen. Measurement of IgA levels was carried out by Immunoturbidimetric Assay by Parahita Laboratory with normal IgA standard values between 2-3 mg/ml. The subjects demographic data were also collected in the form of age, gender, length of work and length of service.

RQ was calculated by dividing the noncarcinogenic risk agent with its RfD or RfC with the equation [14], [15]:

$$RQ = \frac{I}{RfC \text{ or } RfD}$$

Notes:

I: non-cancer intake from the calculation of exposure (mg/kg/day);

RfC: reference concentration (mg/kg/day).

RfC value of benzene is 0.03 mg/m^3 for non-cancer effects and CSF benzene is 5.5 x 10^{-2} for the effect of cancer [16]. However, RfC value must be converted into units of mg/kg/day first by dividing it by the American default weight of 70 kg and multiplying it by the inhalation rate of 20 m^3/hour. So, we get the equation as below:

$$\text{RfC conversion} = 0.03 \frac{mg}{m3} x \frac{1}{70} kg \times 20 \frac{m^3}{day}$$

Calculation of intake was carried out in the exposure analysis by entering the variable values needed in the calculation. The data needed in the intake calculation were benzene concentration, intake rate, body weight, exposure time, the frequency of exposure, and duration of exposure. The concentration of benzene in the air was measured using Flame Ionization Detector gas chromatography (GC/FID) conducted by the Laboratory of the Occupational Health and Safety Technical Implementation Unit (UPT K3) Surabaya with a standard of 0.5 ppm [17]. All of these values were included in the intake formula as below:

$$\text{Intake} = \frac{C \times R \times t_E \times f_E \times D_t}{W_{bx} \, t_{avg}}$$

Notes:

I: Intake of the number of risk agents that individuals received per body weight per day (mg/kg/day); C: Concentration of risk agent mg/m^3; R: The intake rate, US-EPA default: 0.83 m^3/day; tE: Daily, hour/day exposure time; fE: Annual exposure frequency, day/year; Dt: Duration of exposure, real-time or 30 years (default lifespan projection) or 70 years (US-EPA life expectancy default); Wb: Weight, kg; t avg: Average time period, 30 years x 365 days/year (non-carcinogen) or 70 years x 365 days/year (carcinogens).

If the RQ value ≤ 1, then it shows the respondent exposed to benzene is still safe and has no health risk due to benzene exposure. Whereas, if the value of RQ > 1, then this indicates that respondents have health risks due to exposure to benzene.

Data analysis used analysis of Pearson Product Moment, Spearman 's Rank and Contingency Coefficient C with SPSS version 20. Correlation numbers ranged from -1 to +1. The closer to 1 the correlation is getting close to perfect. The interpretation of correlation numbers according to is if the value of r: 0-0.199: very weak; 0.20-0.399: weak; 0.40-0.599: medium; 0.60-0.79: strong and 0.80-0.10: very strong [18].

Results

The gender of men and women is equal to 10 people (50%) as shown in Table 1. Gender had an insignificant relationship with a decrease in IgA concentration (r = 0.386; p = 0.174) as shown in Table 2.

Table 1: Univariate Analysis of Research (n = 20)

Variable	n = 20 (%)	Mean	Min-Max
Demography Characteristics			
Age			
< 45 years	7 (35)	46.50	23-63 years
≥ 45 years	13 (65)		
Gender			
Man	10 (50)	-	-
Woman	10 (50)		
Working Periods			
< 25 years	9 (45)	25.575	2.5-43 years
≥ 25 years	11 (55)		
Working Time			
≤ 8 hours/day	6 (30)	10.25	6-14 hours/day
> 8 hours/day	14 (70)		
Benzene Concentration*			
> 0.5 ppm	2 (20)	-	0.0129 – 2.3330 ppm
< 0.5ppm	6 (80)		
Levels of IgA			
< 2 mg/ml	8 (40)	-	-
2-3 mg/ml	8 (40)		
> 3 mg/ml	4 (20)		
Risk of Non-Carcinogenic			
RQ < 1	7 (35)	-	-
RQ ≥ 1	13 (65)		

*except for the benzene concentration variable, benzene concentration was not measured individually but measured the location of the workplace in 8 locations.

The average age of shoeshine workers in Tambak Oso Wilangun Village was 46.6 years or 47 years. The highest number of workers were in the age range of 46-55 years (40%) as shown in Table 1. The results of the correlation analysis showed that age variables had a significant relationship with a decrease in IgA concentration (r = 0.494; p = 0.027) (Table 2).

The majority of subjects had a work period/duration of exposure ≥ 25 years (55%) (mean ± 25,575 years) as shown in Table 1. Working period variables had a significant relationship with a decrease in IgA concentration (r = 0.449; p = 0.047) as shown in Table 2.

As many as 30% of subjects had a working time of ≤ 8 hours/day, and as many as 14 people had a work duration > 8 hours/day (mean ± 10.25 hours/day; maximum = 6 hours/day; minimum = 14 hours/day) as shown in Table 1. However, the results of the correlation analysis showed that the working time variable had an insignificant relationship with a decrease in IgA concentration (r = - 0.244; p = 0.300) as shown in Table 2.

There were 2 measurement points (25%) with benzene vapour levels exceeding TLV (Threshold Limit Value) and 6 measurement points (75%) with benzene vapour levels below NAB (max-min = .01212 ± 2.3330 ppm) as shown in Table 1. Benzene levels at location 5 (measurement points 5 and 6) exceeded the threshold limit value set by Regulation of the Minister of Manpower and Transmigration No.13/MEN/X/2011. There was no significant relationship between benzene vapour levels and IgA levels (r = 0.313 and p = 0.179) as shown in Table 2.

The value of IgA concentration in blood serum workers in the footwear home industry in Tambow Osowilangun Surabaya, namely 8 workers (40%) experienced a decrease in IgA concentration, 8 workers (40%) had normal IgA concentrations and 4 workers (20%) experienced an increase in IgA concentration as shown in Table 1.

The RQ calculation for the 20 workers was obtained by RQ > 1, which was 65%, meaning that 13 people (65%) had the effect of non-cancer exposure due to benzene exposure as shown in Table 1. There was a significant relationship between the analysis of non-carcinogenic risk characteristics with a decrease in IgA levels (r = 0.567; p = 0.043) as shown in Table 2.

Table 2: Bivariate Analysis of Independent Variables with IgA Levels

Variable	*p-value*	*Pearson correlation* (r)
Age (years)	0.027*	0.494
Gender	0.174	0.386
Working periods (years)	0.047*	0.449
Working time (hours/day)	0.300	-0.244**
Benzene Concentration	0.179	0.313
RQ of Non-Carcinogenic Benzene	0.436	-0.184**

*p-value <0.05; **Correlation is negative with the intention that the independent and dependent variables are antagonistic, for example, the greater the RQ value, the lower the IgA level.

Discussion

The majority of subjects were more than 45 years of age. Age has a significant correlation with decreased IgA levels. This is consistent with other studies which state that one of the determinant factors that affect the immune system is age [19]. Older age is usually also accompanied by a decrease in resistance to toxins and viruses because it is followed by a decrease in the immune system both adaptive and innate immune response [20], [21]. Workers who

are less than 18 years of age should not work in an environment exposed to benzene, because the age of bone marrow resistance to the toxic effects of benzene is still low. The older age of labour, the higher the risk of benzene poisoning [22].

Gender does not have a significant relationship with decreased IgA levels. This is contrary to other studies stating that gender is one of the determinant factors that affect the immune system with women having a stronger immune system than men because of the presence of androgens in men that are immunosuppressive and do not fluctuate to old age [19]. However, this study is in line with other studies that show no effect of IgA values on female workers exposed to benzene in the shoe industry because there are still other variables that have a significant relationship with decreasing IgA concentrations in male workers in this study [23]. Benzene exposure in individuals is different. This is caused by several factors of each itself, including age, gender, weight, endurance, healthy life behaviour, length of exposure, the frequency of exposure, duration of exposure and work that has been done previously do [11].

Working period variables have a significant relationship with a decrease in IgA concentration. This is consistent with other studies stating that one of the factors that influence benzene exposure is the work period/duration of exposure [11]. Benzene exposure for each is influenced by the length of work/exposure time each day [11]. Conversely, the variable duration of work had an insignificant relationship with a decrease in IgA concentration. It can be assumed that there are still other variables that have a significant relationship with a decrease in IgA concentration.

The results of the study stated that the majority of benzene levels were still in the normal range (< 0.5 ppm) with only 2 location points that exceeded the standard limit. RQ calculation shows that the majority of respondents had RQ values greater than normal (RQ > 1). This is consistent with other studies that also in the shoe industry shows 60% of respondents have a normal RQ value above [24].

Toxins or benzene that enters through inhalation will get an initial immune response from lymphocytes and Antigen Presenting Cell (APC) in the lungs before finally being metabolised in the liver and bone marrow. Cells will present antigens (APC), so they can induce CD4-helper T cells which will morphofunctional as Th2-CD4 by inducing IL4. Benzene in the induction of T-CD4 cells is possible to directly cause T cell death and reduce the formation of mature B cells as a site for the formation of immunoglobulin A [19], [25], [26].

Benzene levels and non-carcinogenic risk assessment measurements did not have a significant relationship with the reduction of IgA levels. This has a difference with other studies which stated a decrease in serum IgA and IgG in workers exposed to painting or benzene [10]. The thing that makes the difference is that in this study, the majority of the location points studied is still at the safe benzene threshold. Although there are 2 places that have more benzene levels than TLV (location points 5 and 6), this is not comparable to the number of proportions in 6 locations that are still within normal limits. The limitations of this study also lie in the minimum sample in the study, which is 20 samples, which should be in the study of statistical or correlation analysis of a minimum of 30 research samples [18], [27].

These research also measured at eight locations whereas should be focusing on the riskiest locations. The volatile nature of benzene and the influence of the presence of air ventilation can also affect the absorption of benzene through inhalation [1], [28], [29], [30], [31]. The thing that affects again is the average working period for workers who are still 26 years old. The possibility of having a working period of around 26 years still has not shown the non-carcinogenic effects seen in haematological or decreased IgA levels, although the results showed that there had been a decrease of 8 workers. Therefore, further research is needed to give a new finding based on risk assessment such as calculating safe limits of workers not to be exposed to non-carcinogenic risks, calculation of Excess Cancer Risk (ECR) benzene and its association with IgA serum and other follow-up studies in the form of factors that influence the reduction of IgA in workers exposed to benzene.

In conclusion, the majority of research subjects were over 45 years of age, working ≥ 25 years, working time > 8 hours/day. There were 2 location points that had a threshold value exceeding the benzene standard (> 0.05 ppm), and 40% of subjects had decreased IgA levels. Age and tenure had a significant relationship to IgA levels, while benzene and RQ levels did not have a significant relationship with IgA levels. This research is still limited regarding small samples and benzene levels measurement is not based on per person/research subject but location. Further research is needed on risk assessment, especially the safe limits of benzene concentration in the workplace to find out how long the exposure to benzene poses non-carcinogenic and carcinogenic risks in the body of workers exposed to benzene.

Ethical Clearance

The study was approved by the institutional Ethical Board of the Public Health, Airlangga University with ethics number 516 KEK.

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