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Research Article

The Renal Toxicity of Welding Fumes in Heavy Equipment Manufacturer Workers

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Abstract

Exposure to welding fumes in the workplace has been associated with decreasing renal function. We studied renal function parameters in men workers from heavy equipment manufacturer exposed to welding fumes. This study aimed to evaluate renal function status among worker exposed to welding fumes. A case-control design, random study, was conducted among welder (35 subjects) and non-welder (35 subjects) with more than 1 years experience in the same job task in a heavy equipment manufacturer. All subjects were completed physical examination, informed consent, questionnaire and laboratory tests. Renal function was measured as creatinine serum using enzimatic method. Urinary heavy metals level was analyzed using inductively coupled plasma mass spectrometry. Comparisson analysis between group was performed to determined median level for each variable. Linear regression model was developed to predict renal function function parameter status urinary heavy metals level as variable. This study showed there were higher creatinine serum, chromium, iron, manganese and nickel in welder than non welder($p<0.05$). After multivariate analysis, urinary nickel is a predictor for renal function status among welder. Exposure to welding fumes was significantly correlated with renal function status in welder. Nickel is the predictive variable for renal function. Although statistically significant but in clinical field needs carefully interpreting data.

Keyword: Nickel, renal function, welder, welding fumes

Toksisitas Renal Uap Las pada Pekerja Industri Alat Berat

Abstrak

Pajanan uap las di tempat kerja telah dihubungkan dengan penurunan fungsi ginjal. Dalam penelitian ini, kami menguji status fungsi ginjal pada pekerja pria yang terpajan uap las di industri alat berat. Penelitian ini mengevaluasi status fungsi ginjal pada pekerja terpajan uap las, dengan desain kontrol kasus, acak, dilakukan pada 35 subjek pengelas dan 35 bukan pengelas yang telah bekerja paling tidak 1 tahun dengan jenis pekerjaan yang sama di industri alat berat. Seluruh subjek telah melakukan pemeriksaan fisik, pengisian form kesediaan setelah penjelasan, kuesioner, dan pemeriksaan laboratorium. Pemeriksaan kadar kreatinin dilakukan dengan metode enzimatik. Pemeriksaan kadar logam berat dalam urin dengan *inductively copled plasma mass spectrometry*. Dilakukan analisis perbandingan untuk membedakan nilai median antar kelompok. Dilakukan juga analisis multivariat untuk menentukan variabel prediksi. Hasil penelitian memperlihatkan bahwa status fungsi ginjal pada pekerja las lebih rendah dibandingkan dengan bukan pengelas. Nikel urin merupakan variabel prediksi yang bermakna terhadap penurunan fungsi ginjal. Walaupun secara statistik diketahui bermakna, namun dalam penggunaan klinis harus dilakukan interpretasi dengan hati-hati.

Kata kunci: Fungsi ginjal, nikel, pengelas, uap las

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Introduction

In Indonesia, numbers of chronic kidney disease patients are rising rapidly. It has become a devastating medical, social, and economic problem for patients and their families. The causes of chronic kidney disease are variable in different part of the world, e.g. hypertension, diabetes mellitus, renal infection, autoimmune, obstruction, toxicity of some chemical substances or drugs and idiophatic causes.[1]

In the other hand, heavy metals have been used by humans for thousands of years. Although several adverse health effects of heavy metals have been known for a long time, exposure to heavy metals continues, and is even increasing in some parts of the world, in particular in less developed countries, though emissions have declined in most developed countries over the last 100 years. Although adverse health effects of heavy metals have been known for a long time, exposure to heavy metals continues and is even increasing in some areas. For example, mercury is still used in gold mining in many parts of Latin America. Arsenic is still common in wood preservatives, and tetraethyl lead remains a common additive to petrol, although this use has decreased dramatically in the developed countries.[2] Emissions of heavy metals to the environment occur via a wide range of processes and pathways, including to the air (e.g. during combustion, extraction and processing), to surface waters (via runoff and releases from storage and transport) and to the soil (and hence into groundwaters and crops).[3,4] Atmospheric emissions tend to be the greatest concern in terms of human health, both because of the quantities involved and the widespread dispersion and potential for exposure that often ensues.

In our study, we use worker who exposed to welding fumes as clinical model. Welding is a common process used to join metals by heating them to welding temperature.[5] Welding processes produce hazardous gents including fumes, gases, vapors, heat, noise and ultraviolet and infrared radiation. The fumes generated during welding are considered to be the most harmful compared with other by products of welding. Welding fumes consist of metal oxide particles and gases that are formed during welding. The particles are small enough to become and remain airborne and easily inhaled. Although it is almost impossible to consume enough iron oxide to cause a toxic effect,[6] steel contains alloying elements that, in their pure forms, could be hazardous to the worker's health. Welding fumes can induce adverse health effects, such as neurological[7], respiratory diseases[8,] and renal disease.[9]

Some heavy metals were well known as nephrotoxic substances, such as mercury[2], lead[2], and cadmium[9] with different mechanism of toxic action. In welding fumes, different metal was used with the main component as iron and manganese. Some metals were added in welding rod such as nickel, chromium, molybdenum. We observed the outcome of renal function from welder after chronic exposure.

Methods

This case-control design, random study was conducted among welder (35 subjects) and non welder (35 subject) with more than 1 years experience in the same job-task in an heavy equipment manufacturer within the industrial area at East Jakarta. The participating subjects were all welder who were willing to participate in the study which meet the inclusion criteria and non-welder from the same factory. The inclusion criteria were: (1) aged between 18–55 years; (2) agreed to undergo bio-monitoring test, and (3) agreed to fill the informed consent form. We exclude hypertension and diabetes mellitus subject.

The data collected consisted of structured interview with questionnaire to inquire several information, such as bio-data, smoking status and date of birth. Local ethic committee of Faculty of Medicine, Hasanuddin University has approved the study protocol and gave permission to perform this study.

Welding type and rod

The most common type of welding processes used in this manufacturer was manual metal arc welding (MMAW), also known as shielded metal arc welding (SMAW). In this method, an electrode rod was used to create an electric arc that produces a high temperature, which melted the base metal and the electrode to form a strong bond between the parent metal. The most rod was used in process welding was solid wire "YYY" with the composition 80–98% iron, 1.1 – 1.95% manganese and others metal (copper, chromium, nickel, molybdenum and titanium) <0.2%.

Sample collection and storage

A 50 mL polyethylene tubes (Pyridam, Indonesia) were used. The tubes were firstly decontaminated overnight with 10% HNO_3, then rinsed several times with high purity deionised water (Millipore, Germany). Samples were preserved using 16% HNO_3 trace select (Sigma, Switzerland) for 1 mL per 50 mL urine and stored at −30 ^{0}C until analysis. Human serum was collected in vaccum plastic tube (Becton Diccinson, USA).

Instrumentation

In heavy metals analysis, we used an Agilent 7700s with an integrated sample introduction system for discrete sampling (ISIS-DS) and helium collision mode. The instrument was equipped with MassHunter Workstation Revision B.01.01 for instrument control and data handling software. The ICP-MS was operated with Ni sampler and skimmer cones, MicroMist glass concentric nebulizer and quartz Scott-type spray chamber. In analysis creatininserum we modular automatic P-800 (Roche) with Jaffe Enzimatic kit (Roche).

Reagents

Plasma torch argon purity was higher than 99.99% (Linde Gas, Jakarta, Indonesia). Water was purified with Mili-Q D1 water (Merck Millipore, Darmstadt, Germany). Trace-Select® nitric acid >69% (Fluka, ST. Louis, USA), and multi-element standard solution (30 elements) (Merck, Darmstadt, Germany). The diluent solution used in this method was nitric acid 0.5%. Diluent solution was used in the preparation of all calibrators and samples during the dilution process just prior to analysis. Jaffe enzimatic kit (Roche) for creatinine in serum.

Sample preparation

Method for sample preparation according to Goullé et al., 2005, with modification. Briefly, urine samples were thawed at room temperature ±1 hour. After homogenization, 2500 μL of urine was diluted 1:2 with diluent solution up to 5000 μL, and homogenized. The limit of detection was 0.01 μg/L for iron, manganese, nickel, cadmium, chromium and 0.05 μg/L for copper, respectively. For creatinine serum, the analytical procedure was used following the kit.

Statistical analysis

Normality of data distribution was tested with Kolmogorov-Smirnov test. The differences in quantitative variables were tested with the parametric t-test or Mann-Whitney as alternative test, depending on whether the data were normality distributed or not. The non-parametric Spearman rank correlation test was used to investigate the relationship between concentrations of creatinine, iron, manganese, chromium, aluminum, nickel,

Table 1 Comparison Variables of Non-Welder and Welder

Variables	Non welder, N=35	Welder, N=35	p
Age (years)	26 (22 - 52)	34 (23–47)	0.011
Working period (years)	4 (1–27)	12 (1–24)	0.015
ALT (UI/L)	19 (5–119)	19 (7–60)	0.651
Random plasma glucose (mg%)	96 (72–144)	91 (54–163)	0.211
Serum creatinine (mg%)	0.70 (0.5–1.0)	0.90 (0.80–1.20)	0.000
Chromium in urine (µg/L)	0.17 (0.01– 3.99)	0.32 (0.04–2.06)	0.000
Manganese in urine (µg/L)	0.05 (0.01– 0.21)	0.06 (0.01–2.68)	0.016
Iron in urine (µg/L)	2.56 (0.08–6.27)	7.72 (0.20–83.61)	0.000
Nickel in urine (µg/L)	0.64 (0.01–2.09)	1.53 (0.01–4.51)	0.001
Copper in urine (µg/L)	5.58 (1.14–17.02)	6.51 (0.98–27.30)	0.503
Cadmium in urine (µg/L)	0.43 (0.05–1.10)	0.39 (0.02–1.35)	0.792
Smoking status			0.001
Non smoker (%)	29 (82.86)	16 (45.71)	
Smoker + former (%)	6 (17.14)	19 (54.29)	
Body mass index (kg/m^2)	24.58 (17.30–29.23)	22.40 (22.97–29.72)	0.177

cadmium, lead, age, working period and smoking history in welder. Correlations with a Spearman correlation coefficient (ρ) higher than 0.600 were considered strong and those with a Spearman correlation coefficient ranging from 0.300–0.599 were considered medium.[7] The non-normal variable was transformated using logarithmic model. A multivariate model was performed using linear regreesion model. Statistical analyses were performed with SPSS, version 11.5. In all statistical analyses, two-sided p-values of 0.05 were considered significant.

Results

The general characteristics of the studied population were summarized in Table 1. In total, 70 subjects were involved in this study, 35 subjects as welder and 35 subject as non-welder. All of data were non-normal. We described as median and minimum-maximum value.The median of age, working period, serum creatinine, heavy metals (except copper

Table 2 Spearman Correlation Analysis Between Creatinine Serum as Renal FunctionBiomarker and Some Risk Factors

Variables	Renal function	
	rho Spearman	p
Age	0.230	0.185
Working period	0.241	0.164
ALT	0.069	0.694
Random plasma glucose	0.163	0.349
Chromium in urine	0.108	0.537
Manganese in urine	0.217	0.210
Iron in urine	-0.030	0.864
Nickel in urine	0.489	0.003
Copper in urine	0.292	0.089
Cadmium in urine	0.351	0.039
Smoking status	-0.017	0.924
Body mass index	0.241	0.162

Table 3 Multivariate Analysis of Renal Function

Variables	ß standarized	t	Sig	CI 95%
Nickel	0.390	2.435	0.020	0.002 to 0.022
Cadmium	-0.038	-0.163	0.871	-0.054 to 0.046

and cadmium) and smoker+former were higher in welder than non-welder. Smoker and former smoker were merged because small value of former smoker and could not be tested using chi square or fisher exact test. No significant differences of ALT, glucose and body mass index between groups. We excluded diabetic and severe obesity.

The risk factors for decreasing renal function in welder

We conducted correlation analysis between creatinine as renal function biomarker and some risks for renal function disorder, only nickel and cadmium have significant correlation. Age as internal factor and working period and the others heavy metals as occupational factor were not correlated with renal function. Plasma glucose, ALT and body mass index as pathologic conditions were not correlated with renal function.

A multivariate analysis using was multiple regression between renal function biomarker and nickel and cadmium level in urine as predictive variable. In our study, we found only nickel urine level as significant predictor for renal function in welder.

Discussion

Our study is the part of biomonitoring program in worker exposed metal fumes. In the subject collection process, we exclude hypertension[12] and also diabetes mellitus[13] condition because both of these factors will affect renal function. The location of our study is near East Jakarta, Indonesia, in a heavy metal industry. Welder was collected from fabrication and foundry plan, and non-welder from administrative department not exposed with to welding fumes (finance, legal, HR, GA). In fabrication plan activity was assembling many parts, grinding, fitting, reman cylinder activity and gauging. Most worker was exposed by welding fumes from assembling and gauging, and many metals dust from grinding. The type of rod was solid wire "YYY" with the composition was 80–98% iron, 1.1 – 1.95% manganese and others metal (copper, chromium, nickel, molybdenum and titanium) <0.2%. The other plan was foundry with the main activity was smelting, molding, grinding and welding. Some variables were significantly different. There were no reference in biomonitoring level limitation for urinary iron and copper.

Age, working period, serum creatinine, chromium, manganese, iron, and nickel urin level were higher in welder than non welder. Copper and cadmium were not significant, even cadmium urine level has a tendency higher in non welder. Cadmium level will increase in smoking subject.[14] Unfortunatelly, we did not have air metals environmental data and did not correlate with urinary metals level.

None of subject in welder group has urinary chromium (reference: <10 µg/L), nickel (reference: <5 µg/L), cadmium (reference: <2.24 µg/L) higher reference from Finnish Institute in Occupational Health 2014. Iron was the most abundant metal component in welding rod and higher urinary iron level in welder group but we did not validated as reference value for biomonitoring. Only one subject from foundry plan has urinary manganese level more than the level value (reference: 0.55 µg/L).

Creatine was synthesized primarily in the liver from the methylation of glycocyamine (guanidino acetate, synthesized in the kidney from the amino acids arginine and glycine) by S-adenosyl methionine. It was then transported through blood to the other organs, muscle, and brain, where, through phosphorylation, it became the high-energy compound phosphocreatine. During all of the reaction, creatine and phosphocreatine were catalyzed by creatine kinase, and a spontaneous conversion to creatinine. Creatinine was removed from the blood chiefly by the kidneys, primarily by glomerular filtration, but also by proximal tubular secretion. Therefore, creatinine levels in serum has been used as renal function condition screening.[15] Our finding indicate creatinine serum was higher in welder than non welder.

Correlation analysis between creatinine serum and some variables affected renal function, only urinary nickel level and cadmium correlated significantly. The next statistical analysis, after logarithmic transformation for creatinine serum, only urinary nickel level has a predictive variable in welder in our study. Clinically, creatinine serum has cut off point more than 1.2 mg% indicate in decline renal function. Only one subject in welder has a borderline creatinine serum. The advantages of creatinine serum were easy test, cheaper and time validated for renal function, but less sensitive. Some renal function biomarkers was developed such as N-acetyl-glucosaminidase (NAG), cystatin C, ß2-microglobulin, Neutrophil gelatinase-associated lipocalin (NGAL) with better sensitivity and selectivity. These will detect early damage in renal organ.

Several limitation should be noted. Firstly, it was difficult to evaluate the effect of working period as the exact calculation because the complexity of jobs histories. In our study, working period have non-significant correlation. However, event in simple occupational histories, the effects of working period may be obscured by the effect of aging. The use of personal protective devices can also be quite different even the working period. At the present, all workers who are exposed to welding fumes or metal fumes wear personal protective devices. Secondly, the use of creatinine serum as renal function marker is not sensitive marker to detect early renal damage. In the interpretation data, using of control subjects very recommended as a comparator because very difficult to evaluate how much metal fumes entered to the body.

Conclusion

Exposure to welding fumes was significantly correlated with renal function status in welder. Nickel was the predictive variable for renal function. Although it was statistically significant but in clinical field need carefully interpreting data. Some chemical including heavy metal was known as nephrotoxic substances, but antidote in the case of metal toxicity was very rare and difficult to manage in our country. Hope some pharmacists can develop metal antidote with better safety and efficay in the next time.

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Conflict of interest

No conflict of interest.

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