AJAB

Asian J Agri & Biol. 2018;Special Issue:1-5.

Original Research Article

A pragmatic approach of genotoxic monitoring: the exposure-effect continuum of metalworking fluid with chromium and nickel among machinists at bearing manufacturing industry

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Received:
November 09, 2017

Accepted:
February 28, 2018

Published:
May 30, 2018

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Abstract

A pragmatic approach of human biological monitoring was used to measure the exposure level, and examining the blood and urine metabolites (=exposure biomonitoring) which is complemented by estimating the biological effects (=effect biomonitoring). In this cross-sectional study, a total of 53 exposed machinists who were exposed to chromium and nickel in working metal fluids were recruited. The study aimed to determine the different genotoxic endpoints of the metalworking fluid with chromium and nickel by considering the exposure-effect continuum approach. Result showed that the mean values for both the personal air, blood and urine of chromium and nickel concentrations exceeded the reference value. Linear regression analysis showed that both blood and urine chromium is the significant factors for micronuclei and comet tail length formation among machinists.

Keywords: Exposure-Effect Continuum; Genotoxic Effects; Chromium; Nickel

Introduction

Metalworking fluids (MWF) are widely used during the machining of metals to provide lubrication and cooling, and to help carry away debris and final metal particles. Machinists in metalworking processes are inevitably exposed to chromium (Cr) and nickel (Ni) fumes. Inhalation of particulate Ni and Cr compounds result in lung injury with marked inflammatory response in the lung. Therefore, the major concern in this study is to highlight the accidental inhalation of the mists, aerosol or vapor generated during machining operations through inhalation. Past studies highlighted that industrial use of Cr and Ni have direct relationship between DNA-reactive oxygen species (ROS) and Ni- or Cr- induced DNA damage (Valko *et al.*, 2006). The structural genetic lesions produced by Ni- or Cr- induced ROS may lead to DNA adducts, DNA strand breaks, DNA-protein crosslinks and etc. (Nickens *et al*., 2010; McCarroll *et al*., 2010)

Although toxicology studies have widely been performed to determine the toxicological characteristics of industrial-based heavy metals towards human health, there is still dearth of research associate the exposure pathway and biological markers to the genotoxicity end points. The objective of this study is to use the pragmatic approach to determine the different genotoxic endpoints of the MWF with Cr and Ni by considering the exposure effect continuum approach among machinists at bearing manufacturing industry.

Materials and Method

Study Design

This is a cross-sectional study applied the principle of human biological monitoring to identify and quantify the level of exposure and the potential health effects to the MWF.

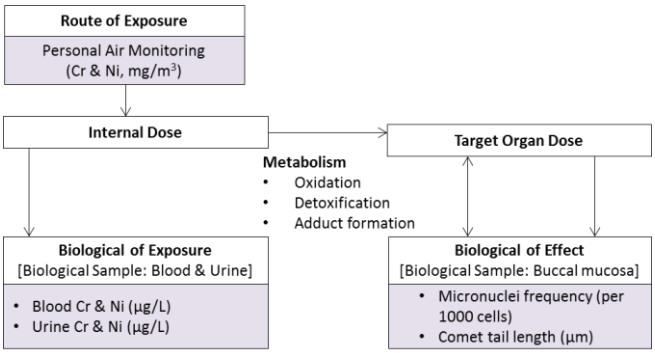

Figure 1: Pathways for biological measurements of MWF (Adapted from Kapka-Skrzypczak et al., 2011)

A total of 53 exposed machinists were recruited, excluded those who (i) had history of exposure to cytotoxic therapeutic drugs and radiation, (ii) medical condition, such as diabetes and kidney problem. In order to characterize the risk of genotoxic effects, a pragmatic approach of measuring the blood and urine metabolites (=exposure biomonitoring) is complemented by estimating the genotoxic effects (=effect biomonitoring). The principle of exposure-effect continuum is adapted as shown in Figure 1.

Study Location

This study was approved by the Ethics Committee of the University Research Involving Human of Universiti Putra Malaysia. Data collection was carried out from January – April, 2014. Study was carried out at a bearing manufacturing industry in which the MWF is widely used in the workplace.

Personal Air Sampling and Analyses

An 8-hours-time weighted average for personal air sampling was measured by using the personal air sampling pump with cellulose ester membrane filter. The pump was attached to the machinists' collar neck to collect the breathed air within his breathing zone. The procedures of sampling air referred to the National Institute of Occupational Safety and Health (NIOSH) Method 7300.

Biological Sampling (Urine, Blood)

Urine samples were collected using disposable polyethylene urine containers at the end of the subjects' work shift; whereas the venous blood was sampled between 08.00a.m and 10.00a.m. All subjects were required to fast in the preceding 10 hour and they were also required to abstain from alcohol in the preceding 24 hour before the samples were taken (Zailina et al., 2015).

Biological Sampling (Buccal Mucosa Cells)

In order to ensure minimal invasive manner is applied, the exfoliated buccal mucosa cells were sampled for genotoxicity assessment purposes. Participants were instructed to rinse their mouth with water before the sampling began (Vivien et al., 2015)

Genotoxicity Test (Comet Assay)

The Comet Assay is a fast and effective way to measure DNA damage by estimating the comet tail length (µm). This assay was based on the standard procedure from Comet Assay Kit (Trevigen, USA). The tail length was measured (µm) to indicate the distance of DNA migration from the body of nuclear core and it was used to evaluate the extent of DNA damage.

Genotoxicity Test (Micronuclei (MN) Assay)

MN assay is used to estimate the possibility of early cancer risk experienced by the study population. The presence of MN in the cells is round or oval in shape and their diameter ranged between 1/3 - 1/10 of the main nucleus' diameter

Results

All the machinists recruited in this study are male and Muslims, who do not consume alcohol. Around 50.9% are 40 years old and above, 39.5% reported with normal BMI, 64.2% claimed that they live at least 10km distance from the industrial area, 64.2% have less than 10 years of working experience at the current workplace, and only 39.6% of the machinists are smokers.

Table 1 highlights the measured personal air sample, biomarker of exposure (urine and blood) with genotoxic effect (comet tail length and MN frequency). Result showed that, both personal air Cr and Ni concentrations exceeded the reference value. Besides, blood and urine Cr and Ni in the machinists also exceed the reference value.

Table 1: The personal sampling and biological monitoring of Ni and Cr among machinist

Parameter(s)	Mean (SD)	Reference value
Personal Air sampling [a]		
Chromium (mg/m^3)	1.57 (0.63)	NIOSH:0.5mg/m^3 ACGIH:0.5mg/m^3
Nickel (mg/m^3)	0.34 (0.22)	NIOSH: 0.015mg/m ACGIH: 0.1mg/m^3
Biomarker of exposure [b]		
Blood Chromium (µg/L)	0.85(0.27)	<0.05 µg/100 ml
Blood Nickel (µg/L)	0.15 (0.06)	<0.05 µg/100 ml
Urine Chromium (µg/L)	80 (30)	<5 µg/g
Urine Nickel (µg/L)	36 (90)	<2 µg/g
Biomarker of (genotoxic) effect [c]		
Comet Tail Length (µm)	25.08 (8.79)	N/A
Micronuclei frequency (1,000 cells)	21.85(12.99)	N/A

[a] From NIOSH Method 7300 (2003)

[b] Taken from Hoet et al., (2011)

Table 2 and Table 3 describe the relationship of personal air sampler and biomarker of exposure to the genotoxic effect. Both linear regressions indicated that Cr and Ni in the blood and urine are the significant predictor factors for comet tail length and MN formation among machinists.

Table 2: The relationship between personal exposure levels with genotoxic effect (comet tail length formation)

Variables		SLR (ENTER)	
		b (95% CI)	*p*
Personal Air	(Cr) (mg/m^3)	0.82 (-3.11,4.73)	NS
	(Ni) (mg/m^3)	-3.88 (-15.16,7.40)	NS
Biomarker of exposure	Blood (Cr) (µg/L)	0.01 (0.001,0.018)	0.029**
	Blood (Ni) (µg/L)	0.03 (-0.01, 0.07)	NS
	Urine (Cr) (µg/L)	0.11 (0.03,0.19)	0.006**
	Urine (Ni) (µg/L)	0.02 (-0.01, 0.04)	NS

NS: Non-significant

Multiple Linear Regression (MLR) (Method=STEPWISE) Comet tail length (µm) = 5.912 + 0.125 (Cr in urine) + 0.011 (Cr in blood), R^2=0.356

** Significant at p<0.01

Table 3: The relationship between personal exposure levels with genotoxic effect (micronuclei frequency)

Variables		SLR (ENTER)	
		b (95% CI)	*p*
Personal Air	(Cr) (mg/m^3)	2.82 (-2.93,8.59)	NS
	(Ni) (mg/m^3)	-2.92 (-19.64,13.8)	NS
Biomarker of exposure	Blood (Cr) (µg/L)	0.02 (0.002,0.027)	0.024**
	Blood (Ni) (µg/L)	0.02 (0.044,0.082)	NS
	Urine (Cr) (µg/L)	0.17 (0.05,0.29)	0.005**
	Urine (Ni) (µg/L)	0.02 (-0.02,0.05)	NS

NS: Non-significant

Multiple Linear Regression (MLR) (Method=STEPWISE) Micronuclei (1000 cells) = -7.386 + 0.191 (Cr in urine) + 0.017 (Cr in blood), R^2=0.373

** Significant at p<0.01

Discussion

Past studies suggested that many industrial-used metals are stable and persistent environmental contaminants; they have the potential to cause genetic alterations in the target tissues of exposed humans. The purpose of this paper is to evaluate the genotoxic effects of Cr and Ni among machinists who are exposed to MWF.

Personal and Biological Exposure Monitoring

Findings of the personal and biological (urine and blood) showed a relatively higher body burden of the total Cr and Ni. It is hypothesized that, the elevated aerosols of WMF could be attributed to the evaporation and condensation that occurs during the working process and due to the emission of aerosols by the impact force. Result showed that, exposed machinists who worked at a closed environment have the accumulation of Cr and Ni present in the air exceeded the time-weighted average (TWA). It was consistent with past studies which showed that lung inhalation is the major route of occupational exposure for Ni and Cr-induced toxicity among exposed machinists (Vitayavirasuk *et al*., 2005; Oudyk *et al*., 2003). This causes the increased level of Cr and Ni concentrations in blood and urine due to the presence of Cr and Ni in the workplace atmosphere. In fact, biological monitoring of urine and blood levels of Cr and Ni have the scientific support as an indicator to

determine the occupational exposure level among exposed machinists (Wu and Liu, 2013; Chen *et al*., 2007).

Biological Effect Evaluation (Genotoxicity)

The mechanisms of Cr and Ni toxicity have been recently reviewed (Nickens *et al*., 2010). Past studies indicated that the available scientific information on potential genotoxic effects of chemicals are often far from definitive, particularly when the toxicological mechanisms are subject to a wide variety of influences. On the other hand, Cr and Ni could disrupt DNA strands, DNA crosslinks, and DNA repair; and oxidative stress has been found to play a key role in metal induced genotoxicity (Valko *et al*., 2006). Nevertheless, it is fairly elusive to answer that these toxicological mechanisms are capable to induce definite genotoxicity among exposed machinists who are exposed to Ni and Cr from the aerosol of WMFs from their work process.

A continuum from exposure to effects is established to evaluate the potential genotoxic effects due to Ni and Cr in MWFs exposure among exposed machinists. Result showed that only Cr-urine and Cr-blood has positive relationship with MN and comet tail length formation. This may be due to the fact that the dramatic increase in potential biomarkers hasn't been matched by a rise in useful and validated biomarkers (Schmidt, 2006) and risk factors that influence or are associated with genotoxic (Vivien *et al*., 2015). In fact, a broad genotoxicity risk assessment shall be considered except considering the single causal-interpretation on exposure-effect continuum.

Conclusion

This study showed that machinists were at an increased risk of genotoxic effects due to occupational exposure to Cr. The integration of personal and biological monitoring is an efficient way to measure the metal exposure and genotoxic effects among exposed machinists. Even though the result of this study is not sufficient enough to establish the definite causal relationship of the exposure-effect continuum, it suggests the necessary to include both exposure-effect biomonitoring in any toxicological study.

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