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Biomarker of occupational airways inflammation for exposure to inorganic dust

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Abstract

Occupational airways inflammation occurs when the bronchial tubes airways have become swollen and oversensitive due to unwanted particles gases and particulate matter of inorganic dust such as asbestos, silica and coal dust. Workers' biomarker of airways inflammation is used as tools to interpret their lung metabolism and toxic mechanism reaction with pollutant exposed by industrial process. The aim of this review is to determine compatible biomarker that is used in diagnosis occupational airways inflammation from the exposure of inorganic dust. This review summarize the outcome of workers' biomarkers that indicate airways inflammation caused by occupational exposure to the industrial pollutant. Relevance online database and data from previous epidemiological studies have been used in this study. Previous study found that Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and Interleukin-8 (IL-8) in spontaneous sputum, induced sputum, nasal wash and bronchoalveolar Lavage (BAL) have significantly correlate with symptoms of occupational asthma among the workers. Few studies have examined on non-invasive methods of EBC and FENO as biomarkers because of their reliability and sensitivity screening tools to diagnosed occupational asthma by determined eosinophil level in airway inflammation with a significant correlation of asthma severity. Several studies of occupational asthma had also suggested the combination use of different biomarker or pulmonary analysis such as lung function test for better results. Workers' biomarkers indicate occupational disease regarding their airways inflammation and guiding the clinician on decisions for further treatment. IL-6 and IL-8 mostly used as the biomarker of occupational asthma to indicate the exposure of industrial pollutant.

Keywords: Occupational asthma, Airways biomarker, Inorganic dust

Introduction

Exposure to dust is one of the major chemical hazards in the industries to the workers respiratory health. Inorganic dust is generated by vary industrial activities such as building construction, manufacturing, mining, and agriculture. The amount of dust that emitted from the activities depends on the physical characteristics of the material, process occur and the way of the material is handling. Dust particles that emitted from the industries vary in size thus, the smaller or fine particles are invisible that may penetrate into lungs. Occupational airways inflammation or known as Occupational Asthma (OA) occurs when someone

inhaled unwanted particle or gases that causes the bronchial tubes airways responding to become inflamed, swollen and oversensitive (Tarlo *et al*., 2010). Workers' biomarker of airways inflammation is used as a biological tools to indicate their lung metabolism and toxic mechanism reaction or respond to the pollutant exposed by the industrial process while working. The aim of this review is to determine the convenient biomarker that is used in diagnosis occupational airways inflammation from the exposure of inorganic dust among workers.

Materials and Methods

This review is based on a systematic search on previous studies that are relevant with the topic of biomarker for occupational airways inflammation by inorganic pollutant. Journal articles have been retrieved including case study, cross-sectional, case control, cohort or experimental design studies. The articles were selected for final selection were screened according on the following criteria: the article was published between 2000 until 2015, published in English, related to occupational dust exposure focussing on inorganic dust inhalation, workers sample biomarker and used quantitative design that report on the performance of the workers biomarker due to occupational exposure to inorganic dust.

This review has been conducted by using the online databases from scientific journal search engines, which were Science direct, Springerlink, Pubmed, and Google Scholar. The identified papers were chosen by three keywords search were used "biomarker", "occupational asthma" and "inorganic dust exposure" with associated synonyms. The journal were filtered by the used of biomarker method. The article that is fulfilled the criteria were reviewed in full. A total of 850 related publications to the topic of interest were identified while 156 paper title and abstracts have been reviewed. The full content of 63 was reviewed but 12 papers were included in this systematic reviewed.

Results

This biomarkers study on occupational asthma regarding to the exposure of inorganic dust in working area had been found from all over the world that fulfilled the reviewed criteria.

The study on cement workers exposure to silicosis by determine the level of plasma malondialdehyde (MDA) and erythrocyte glutathione (GSH) by Orman *et al*., (2004) shows that MDA level were significantly higher in the 48 production workers comparing to 28 of office worker . However, the GSH level shows the contrary results where it is significance lower in production workers compared to the control group. The pulmonary function test in the workers did not show any abnormalities of the lung function.

A cross-sectional study by Fell *et al*., (2010) to determine the association of cement aerosol exposure with the percentage of neutrophils cells responded from airway inflammation in cement production workers. This study involving 3 non-smoking male respondent categories which are direct exposure group of 35 cement production workers, non-direct exposure group of 15 cement office workers, and control group of 39 students and hospital workers. The exposed group shows significantly high percentage of neutrophils cell associated with the cement aerosol exposure. From the sputum analysis, there is only IL-1β concentration was higher in the exposed worker.

Adelroth *et al*., (2006) in the study of the association between miners airway inflammation causes from the iron ore quarry exposure to dust and diesel exhaust by determining the level of Fibronectin and Interleukin 10 (IL-10). The miners was found having high level of Fibronectin, Interleukin 10 (IL-10) and matrix metalloproteinase (MMP)-9 in their sputum compared to control group. However the level of MMP-9 were decreasing within 3-month period of working. This study involved 22 person who are never or ex-smoker male of miners and 24 person as a control group who are non-smoking male research workers that is not associated in this study, technical staff and office workers. However, the lung function test shows no abnormalities associated with the exposure to dust and diesel exhaust on both groups.

The study to determine the effect of inorganic dust exposure on retired workers that can cause Chronic Obstructive Pulmonary Disease (COPD) and pulmonary inflammatory by obtaining blood serum was conducted by Hwang *et al*., (2013). 39 of retired workers who had been diagnosed COPD and 39 retired worker who had not been diagnosed COPD had been recruited in this retrospective cohort study. Six biomarkers had been studied which are high sensitive C-Reactive Protein (hsCRP), interleukin (IL)-6, Clara Cell secretary proteins (CC-16), tyrosine lysine leucine 40 (YKL-40) Surfactant protein D (SP-D), and Serum Amyloid protein A

(SAA) in blood serum. Three of the biomarkers; IL-6, hsCRP and YKL-40 were found significantly higher in the COPD group. Thus, another three biomarkers; SP-D, IL-6, and SAA were found not having significant association to the cause of COPD.

94 retired male coal miner workers were selected in the cross sectional study conducted by Lee *et al*., (2014). This study is to determine the biomarkers concentrations of interleukin-6 (IL-6), tyrosine lysine leucine 40 (YKL-40) and tumor necrosis factor-alpha (TNF-α) in blood serum causes by exposure of inorganic dust. Serum YKL-40 was found significantly higher in the workers who have pneumoconiosis. The concentration of serum YKL-40 and IL-6 was found significantly higher in workers who have normal in lung function test. The concentration of IL-6 showed significant association with the workers lung function test.

Lee *et al*.,(2010) in the retrospective cohort study by following of one-year study among coal workers' pneumoconiosis (CWP) by determined the serum levels of Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-8 (IL-8). The study found that 88 of male retired coal miners having significantly high level of TNF-α with low predicted of Forced Expired Volume in first second (%FEV1) of lung function test. The level of TNF-α and IL-8 were found significantly higher in CWP and progressive CWP workers respectively. Therefore, the level of TNF-α and IL-8 were directly correlated with the presence of CWP and progression of CWP respectively.

According to the study of Tolinggi *et al*., (2014) on 9 miner workers and 9 district office worker to determine the effect of inhalation limestone dust to the level of Interleukin 8 (IL-8) serum and pulmonary function test. IL-8 was significantly higher especially after working period and pulmonary function level was lower in the miner workers compared to office worker. The personal dust exposure between the miners and the office workers was significantly difference.

Malaysian cross sectional study among bus drivers to determine the relationship between exposure to particulate matter and biomarkers in Klang Valley by Kavitha *et al*., (2011) was observed on 62 non-smoking male of public bus driver and administrative staff respectively. Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6) in their sputum was analyzed. The level of TNF-α and IL-6 concentration were significantly difference between the bus driver and administrative staff where the mean level of biomarker in public bus driver was significantly higher. Thus, the increasing of particulate matter exposure level had significantly correlate with the increasing concentration of TNF-α and IL-6.

Hilt *et al*., (2002).was conducted a study on tunnel construction workers that had been exposure to dust and the relationship with the increasing of interleukin-6 and fibrinogen. This study found that there was a significant increase in IL-6 concentration in workers during the shift while fibrinogen was significantly increased during 24 hours period from Monday to Tuesday afternoon. The IL-6 concentration had a significant positive correlation on the night after the shift work.

The cross-sectional study in five photocopy centers in Coimbatore, India to determine the cause of oxidative stress and systematic inflammation among photocopier operators by chronic exposure to gases and inorganic emissions from photocopy machine had been performed by Elango *et al*., (2013). Blood sample from 81 photocopy operator and 43 control group was obtained. The result showed that plasma ICAM-1, LTB4, ECP and IL-8 were significantly higher in the photocopier operator group compared to control group. For the lung function test, there was a positive association on plasma CC-16 and negative correlation between plasma CRP levels with predicted Forced Vital Capacity (%FVC) while. The decreasing of lung function test is significantly correlate with the increasing of the exposure to ultra-fine particle in photocopier industry (Bahruddin *et al*., 2013)

Codorean *et al*., (2011) had conducted a study on power plant workers who are exposed to particulate coal in power plant by obtaining multiplex cytokine profiling in blood. From the biomarkers analysis, serum cytokines TNF-α, GM-CSF, MCP-1, IL-6, IL-8, and IL-1β were significantly increase in workers exposed 20 years compared to workers exposed 10 years and control group.

According to Tungu *et al*., (2012) in his cross sectional study on Fractional Exhaled Nitric Oxide (FENO) among 127 male cement factory workers, the FENO level is not significantly different between smoking and non-smoking either for exposed workers or control group. Moreover, there was no significant difference in nitric oxide concentration between exposed workers in different stages of cement production.

Discussion

Based on this reviewed papers, three main biomarkers that were usually used to determine airways inflammation that was caused by the industrial inorganic dust which were Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and Interleukin-8 (IL-8). A significant increase of Interleukin-6 (IL-6) in exposed group sample as compared to comparative group sample was seen in several study (Hwang *et al*., 2013; Lee *et al*., 2014; Kavitha *et al*., 2011; Hilt *et al*., 2002; Codorean *et al*., 2011). However, the exposed group of inorganic dust was found had significantly higher of Interleukin-8 (IL-8) compared to comparative group (Lee *et al*., 2010; Tolinggi *et al*., 2014; Elango *et al*., 2013; Codorean *et al*., 2011). According to Codorean *et al*. (2011), Lee at al. (2010) and Kavitha *et al*. (2011), Tumor Necrosis Factor-Alpha (TNF-α) was found significantly higher in the exposed worker compared to non-exposed worker. Previous study showed connection the exposure of air particle with the respiratory health by using biomarkers Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and Interleukin-8 (IL-8) (Suhaimi and Jalaludin, 2014). Most of the studies on industrial worker used semi-invasive method by obtaining blood serum and induced sputum to determined biomarker.

The determining of Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and Interleukin-8 (IL-8) have been widely used as biomarker response in airways inflammation. This pro-inflammatory biomarkers produce as a mechanism defense from unwanted particle. The longer period of exposure with fine particles may trigger in the high level production of Tumor Necrosis Factor-Alpha (TNF-α) (Jalaludin *et al*., 2014). Despite, Eosinophil Cationic Protein (ECP) levels in nasal swab have been determined as a useful biomarker for upper respiratory inflammation (Andrew and Jalaludin, 2015). However, the used of non-invasive method to determine biomarker of airways inflammation such as Exhaled Nitric Oxide and Exhaled Breath Condensate (EBC) for the nitric oxide biomarker which is simple and fast to use in clinical study and is not widely used among industrial workers. Despite, Exhaled Nitric Oxide has been recognized and recommended as useful method in determining airways inflammation by American Thoracic Society (ATS).

Biomarker for airways inflammation can be divided into three methods of categories which are non-invasive; example, Fractional Exhaled Nitric Oxide (FENO), exhaled breath condensate (EBC) and spontaneous sputum. Semi-invasive; example induced sputum, nasal wash and large airways secretions. The invasive methods will be the Bronchoalveolar Lavage (BAL), and lung biopsies. Biomarkers in peripheral blood has been widely used as a good alternative to study specifically on airway inflammation, compared to other less invasive method.

Most of the studies are comparing between the biomarkers that exist in the same sample for the inflammation response. Respiratory system can be divided into upper and lower airways. The upper and lower airways might indicate different severity level of inflammation according to the exposure and sociodemographic factors of the subject. The comparative study between upper and lower airways biomarker would indicate respiratory health status along the airways

Some of the previous studies obtained pulmonary test to determine the association of the airways inflammation with the pulmonary function test whereby this test should be carried out to represent an early stage of respiratory disease and as complimentary of the biomarkers result (Fell *et al*., 2010). The ventilator function test level for exposed cement workers was significantly lower compared to not exposure worker (Al-Neaimi *et al*., 2001). Besides, the decreasing ventilator function level of subject showed the prevalence of cough, chest tightness and phlegm (Noor *et al*., 2000). There are significant association between the lower pulmonary function level with the elevated biomarkers concentration whereby, the coal workers showed the elevated of TNF-α level (Lee *et al*., 2010) while the miners concentration of IL-8 was significantly higher (Tolinggi *et al*., 2014). Thus, lung function test is associated with the personal exposure where from the study on the traffic policeman and metal welders was found that the decreases of lung function level can be associated with the increases in the personal exposure to the working air pollutant (Muhammad *et al*., 2014; Aziz and Jalaludin, 2014). Despite, the reduction of lung function level contribute with the presence of airways inflammation symptoms such as cough, phlegm, wheezing and chest tightness (Hussin and Jalaludin, 2016).

Conclusion

Workers' biomarkers can indicate occupational disease regarding their airways inflammation and

guiding the clinician on decisions for further treatment. There are various biomarkers that can be used to indicate airways inflammation. Cytokines such as TNF-α and IL-6 have been widely used while for chemokines mediator of IL-8, it is mostly used as the biomarker of occupational asthma to indicate the exposure of industrial pollutant. Non-invasive method for obtaining biomarkers is more practically suitable for workers especially those in production line.

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