Pengaruh Pajanan Timbal Akibat Kerja Terhadap Kejadian Hipertensi Pada Pekerja: Laporan Kasus Berbasis Bukti

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Abstrak

Pendahuluan: Timbal merupakan salah satu bahan penting yang banyak digunakan di industri. Industri baterai timbal-asam menggunakan timbal dalam jumlah besar yang meningkatkan pajanan timbal ditempat kerja dan diperkirakan dapat mempengaruhi tekanan darah selama bertahun-tahun. Tujuan dari laporan ini adalah untuk menyajikan bukti tentang pengaruh pajanan timbal ditempat kerja terhadap kejadian hipertensi pada pekerja. **Metode:** Pencarian literatur dilakukan melalui basis data elektronik dari PubMed, Scopus dan Cochrane. Kriteria inklusi yang diterapkan yaitu tinjauan sistematis, meta analisis, studi kohort, studi kasus kontrol, studi potong lintang, pekerja dengan pajanan timbal ditempat kerja dan dampak hipertensi atau tekanan darah tinggi. Artikel terpilih kemudian dinilai secara kritis menggunakan kriteria yang relevan dari Oxford Centre for Evidence-Based Medicine. **Hasil:** Tiga studi potong lintang yang relevan disertakan. Studi oleh Thongsringklee M. dkk, Singamsetty dkk serta Sudjaroen dkk menunjukkan bahwa pekerja dengan paparan timbal secara langsung memiliki risiko lebih tinggi untuk terjadi hipertensi dibandingkan dengan pekerja dengan paparan tidak langsung (OR adj 1.38, 95% CI 1.01-1.89; OR 1.97, 95% CI 1.96-2.17; dan OR 1.4, 95% CI 0.97-1.73, secara berurutan) dan bermakna secara statistik, meskipun studi oleh Sudjaroen dkk tidak. **Kesimpulan dan rekomendasi:** Bukti saat ini tidak memberikan bukti yang kuat untuk mengkonfirmasi bahwa paparan timbal dapat menyebabkan hipertensi pada pekerja. Disarankan bagi pekerja yang terpapar timbal secara langsung untuk lebih waspada karena dua dari tiga studi melaporkan kemungkinan timbal meningkatkan risiko hipertensi. Diperlukan penelitian lebih lanjut dengan desain penelitian yang lebih baik untuk memberikan bukti yang kuat bahwa paparan timbal dapat meningkatkan risiko hipertensi pada pekerja.

Kata kunci: hipertensi, pajanan timbal, pekerja

The Effect of Occupational Lead Exposure on The Incidence of Hypertension in Worker: An Evidence Base Case Report

Abstract

Introduction: Lead is one of the essential materials in many industries. The lead-acid battery industry consumes the largest amount of lead which make lead exposure increases at the workplace and has been suspected to influenced blood pressure for many years. The aim of this report is to present the evidence about the effect of occupational lead exposure on the incidence of hypertension in worker. **Method:** The literature searching was conducted through PubMed, Scopus and Cochrane Library. The inclusion criteria were Systematic Review, Meta-Analysis, Cohort Study, Case-control Study, Cross-sectional Study, worker with occupational lead exposure and hypertension or high blood pressure outcome. The selected articles were then critically appraised using relevant criteria by the Oxford Center for Evidence-Based Medicine. **Result:** Three relevant cross-sectional studies were included. Studies by Thongsringklee M. et al, Singamsetty et al. and Sudjaroen et al. showed that workers with direct-lead exposure have more risk for hypertension than workers with indirect-lead exposure (OR adj 1.38, 95% CI 1.01-1.89; OR 1.97, 95% CI 1.96-2.17; and OR 1.4, 95% CI 0.97-1.73, respectively) and significant statistically, although the last study wasn't. **Conclusion and recommendation:** The current evidences do not show strong evidence to ensure that lead exposure can cause hypertension in worker. It is recommended to be more alert for workers with direct-lead exposure because two out of three studies reported the possibility that lead increase the risk of hypertension. Further research with better study design is needed to provide strong evidence that lead exposure can increase the risk of hypertension in worker.

Keywords: hypertension, lead exposure, worker

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Introduction

Lead has been used for thousands of years. Until now, lead is still one of the essential materials in many industries, including battery, paint, ceramic and tile factories(1), electrical equipment, manufacturing industry and mining industry(2). Adults are mainly exposed to lead

at their workplaces(3). Inhalation, ingestion and dermal absorption are the main routes of lead exposure, and inhalation is the primary route of occupational exposure(2). Like the other heavy metals, lead has been shown to cause various health problems in humans(3). It has been demonstrated that acute and chronic occupational lead exposure can cause progressive health effects on several human organs and systems including the nervous, haematopoietic, cardiovascular systems, gastrointestinal and reproductive systems, as well as the kidney and bones(1,2).

Recently, some studies have revealed the role of lead exposure in the induction of hypertension(4–6). Hypertension is a serious risk factor for myocardial infarction, heart failure, vascular disease, stroke, and renal failure(7). But the relationship between occupational lead exposure-induced hypertension remains poorly recognized(1,2,7). The probable mechanisms that cause hypertension due to lead exposure may include physiological changes of the muscular and endothelial layers induced by the disturbance in the renin-angiotensin-aldosterone system which plays an important role in the regulation of blood pressure(2). The aim of this report is to present the evidence about the effect of occupational lead exposure on the incidence of hypertension in worker.

Case

A 28-year-old male came to the clinic with the results of his medical check-up. From those results, it was found that the patient has hypertension. The patient said that he never smoked or got alcohol drink, rarely ate fast food, exercised regularly three times a week and never stayed up late. There is no family history of hypertension, coronary heart disease, stroke, diabetes mellitus or renal failure. Physical examination is within normal limits, except his blood pressure is 152/95 mmHg. The patient said that the results of his medical check-up in the previous year also showed that he has hypertension without any other abnormalities. The previous doctor recommended the patient to take anti hypertensive drugs, but the patient refused.

The patient is a worker in a battery factory. Every day, the patient works in the battery assembly section. He works 8-9 hours/day, five days a week. He has been worked there for eight years. The patient said that he always use a respirator when working. But he also admitted that he often took off the respirator even for a moment when working because of discomfort. The patient asked the doctor for possible causes of his hypertension, whether it can be caused by work related to the battery. The question arose because his colleagues in the same section also suffer from hypertension without any other symptoms like himself.

Method

The literature searching was performed via electronic databases from PubMed, Scopus and Cochrane Library. The keywords used were “work*”, “occupation* lead exposure”, “lead exposure”, “hypertension and blood pressure” and combined with Boolean operation “OR” and “AND” (Table 1). The inclusion criterias were Systematic Review, Meta-Analysis, Cohort Study, Case-control Study, Cross-sectional Study, workers with occupational lead exposure and hypertension/high blood pressure outcome. The exclusion criterias were inaccessible article, article is not in English and statistical value data is not available (Figure 1). The selected articles were then critically appraised to determine whether the article is valid, important and applicable to the patient using relevant criteria by the Oxford Center for Evidence-Based Medicine.(8)

Table 1. Searching Strategy Using Keywords

Database	Keyword	Finding
PubMed	((work*) OR (occupation* lead exposure)) AND (lead[MeSH Terms]) AND (exposure) AND ((hypertension[MeSH Terms]) OR (blood pressure[MeSH Terms]))	141
Scopus	(TITLE-ABS-KEY (*"work*"* OR *"occupation* lead exposure"*)) AND (TITLE-ABS-KEY (*"lead"* AND *"exposure"*)) AND (TITLE-ABS-KEY (*"hypertension"* OR *"blood pressure"*))	455
Cochrane Library	((work*) OR (occupation* lead exposure)) AND (lead) AND (exposure) AND ((hypertension) OR (blood pressure))	557

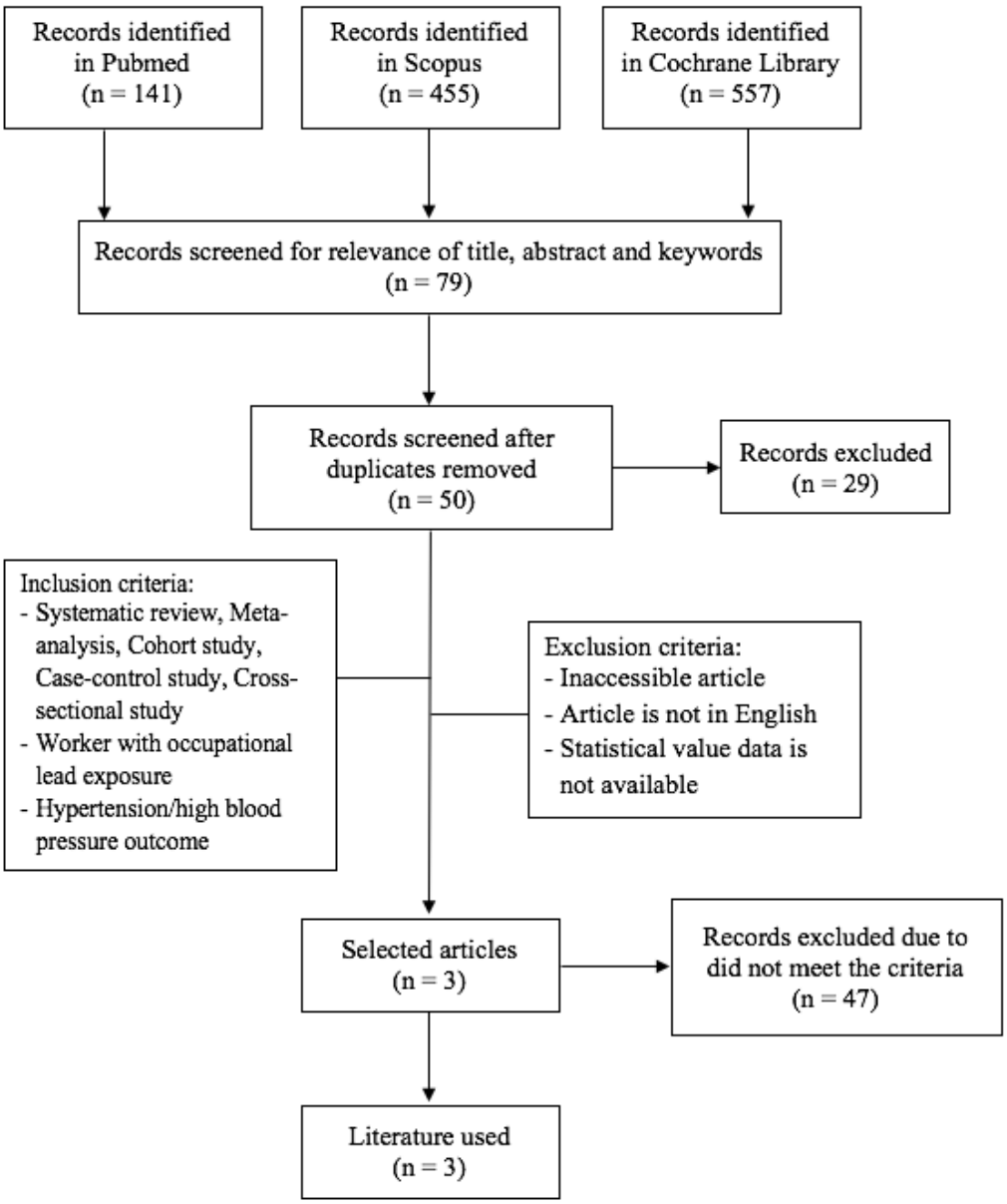

Figure 1. Literature Searching Chart

Result

The online searching resulted three selected articles that fit the inclusion and exclusion criteria, i.e. the study conducted by Thongsringklee M, et al.(4), Singamsetty et al.(5) and Sudjaroen et al.(6) The first study, conducted by Thongsringklee M, et al. (2020)(4) was a cross-sectional study that aimed to investigate the occupational health effects of lead exposure–on blood pressure, hepatic function and kidney function–among the communication radio-repair workers in Thailand. All male workers who had worked for at least three months were recruited as the subject. The workers with cardiovascular disease, hepatic disease, renal dysfunction, anemia, and cancer before working in the plant and those who had hobbies or extra jobs related to lead were excluded. The subjects were divided into two groups, direct exposed group (66 communication radio repair workers who use lead for soldering or direct exposure to lead) and indirect exposed group (54 clerks who work inside the same plant building with the communication radio repair workers or indirect exposure to lead). All subjects were given structured-questionnaire of personal characteristics consist of age, marital status, body mass index (BMI), education levels, working experience, working hours (hour/day), smoking, drinking alcohol and exercise. Blood samples were drawn and blood pressure was also measured.

The study provided the differences of general information between exposed and low exposed groups. There were significantly different variables of personal characteristics between both groups which were age and working hours. Other variables such as BMI, education levels and working experience were not statistically different between two groups. Blood pressure was classified as high blood pressure by using systolic (≥140 mmHg) and or diastolic (≥90 mmHg) blood pressures. About 30% of both groups had high blood pressure (p 1.00). Then, the study adjusted for all symptoms of lead exposure for age (years), BMI (kg/m^2), smoking status, alcohol drinking, milk drinking, seafood consumption (days/week), exercise (days/week) and working hours (hour/day). There was a significant association between lead exposure and hypertension among workers (p 0.04) with OR adj 1.38 and 95% CI 1.01-1.89.(4)

The second study, conducted by Singamsetty et al.(5) was also a cross-sectional study that aimed to emphasize the health profile of workers in a battery factory and with reference to their blood lead levels and correlation with signs and symptoms of lead toxicity. A total of 254 workers including all official staffs and workers were included and socio demographic data of every subject with respect to age, socio economic status, BMI, risk factors were noted. Clinical examination (blood pressure, heart rate, etc.) for all the subjects and necessary laboratory investigations, visual acuity testing and audiogram for selected study subjects were performed and results were noted. Based on nature of work, subject were categorized into direct exposed group, because they have greater chance of exposure to lead (119 workers) and indirect exposed group (135 workers). Among study subjects 20% were hypertensive's. Majority of hypertensive's were working in battery structuring unit (33.33%). The prevalence of lead hypertension was found to be more in the direct exposed group (11%) than in indirect exposed group (7.48%). The proportion of hypertensives was significantly higher in the direct exposed group (p ≤ 0,05) with OR 1.97 and 95% CI 1.96-2.17.

The third article was also a cross-sectional study conducted by Sudjaroen et al.(6) that aimed to detect health impact caused by lead poisoning among indirect exposed group (n = 33), including human resource staffs, transport drivers, stock checkers and QC staffs, and battery workers (as direct exposed group, n = 30) who working with smelting lead, repaired batteries and recycled lead for new batteries production at Nakhon Chaisri district, Nakhon Pathom, Thailand. A structured questionnaire filled in by the subjects, consists of demographic data. After taking a brief history, height and weight of each subject were recorded to calculate the BMI. General and work-related symptoms of each subject were noted prior to the blood pressure measurement and blood sampling. The demographic characteristics of study subjects showed that there were no significant differences between two groups.

Among the battery workers, the work-related sign to hypertension was 20% and not significantly different in the two groups studied (p 0.35) with OR 1.4 and 95% CI 0.97-1.73.

For the purpose of this report, the outcome of lead exposure were discussed only hypertension. The other outcomes were not discussed in this report. The following are the results of the critical appraisal from the three articles.

Table 2. Characteristics of The Study

Author	Study Design	Subject	Intervention	Outcome and Result	Similarity measurement	Follow up	Causal diagnostic study	Level of Evidence
Thongsring klee M., Robson MG., Siriwong W. (2020)(4)	Cross sectional	120 communi-cation radio repair workers: 66-direct exposed group 54-indirect exposed group	Lead exposure	<u>Outcome</u> Health effect of lead exposure: hypertension <u>Result</u> Hypertension: - Direct exposed group: 20 from 66 (30.3%) - Indirect exposed group: 16 from 54 (29.6%) - p = 1.00 Hypertension adjusted by age, BMI, smoking status, alcohol drinking, milk drinking, seafood consumption, exercise: OR 95% CI = 1.38 (1.01 – 1.89), p = 0.04	Yes	No	Yes	4
Singamsetty B., Gollapalli PK. (2017)(5)	Cross sectional	254 battery factory workers: 119-direct exposed group 135-indirect exposed group	Lead exposure	<u>Outcome</u> Health effect of lead exposure: hypertension <u>Result</u> Hypertension: - Direct exposed group: 29 from 119 (24.37%) - Indirect exposed group: 19 from 135 (14.07%) - OR 95% CI = 1.97 (1.96 – 2.17), p ≤ 0,05	Yes	No	Yes	4
Sudjaroen Y., Suwannahong K. (2017)(6)	Cross sectional	63 industrial batteries workers: 30-direct exposed group 33-indirect exposed group	Lead exposure	<u>Outcome</u> Hypertension <u>Result</u> Hypertension: - Direct exposed group: 6 from 30 (20%) - Indirect exposed group: 5 from 33 (15.15%) - OR 95% CI = 1.4 (0.97 – 1.73), p = 0.35	Yes	No	Yes	4

Table 3. The Critical Appraisal of The Study

	Study by Thongsringklee M, et al.(4)	Study by Singamsetty et al.(5)	Study by Sudjaroen et al.(6)
Title	Health Effects of Low Level Exposure to Lead Among Communication Radio Repair Workers at Samutsakhon Province, Thailand	A study on health profile of workers in a battery factory with reference to lead toxicity: six months study	Biomarker Related Lead Exposure of Industrial Battery's Workers
Study Design	Cross-sectional	Cross-sectional	Cross-sectional
Population	Communication radio repair workers	Battery factory workers	Industrial batteries workers
Intervention	Direct lead exposure	Direct lead exposure	Direct lead exposure
Comparison	Indirect lead exposure	Indirect lead exposure	Indirect lead exposure
Outcome	Health effects of lead exposure (hypertension)	Health effects of lead exposure (hypertension)	Biochemical and hematological markers of lead exposure (hypertension)

Question	Study by Thongsringklee M, et al.	Study by Singamsetty et al.	Study by Sudjaroen et al.
Is the result of this harm study valid?			
Were there clearly defined groups of patients, similar in all important ways other than exposure to the treatment or other cause?	No	No	Yes
Were treatments/exposures and clinical outcomes measured in the same ways in both groups (was the assessment of outcomes either objective or blinded to exposure)?	Yes	Yes	Yes
Was the follow-up of study patients sufficiently long and complete?	No	No	No
Do the results satisfy some “diagnostic tests for causation”?			
Is it clear that the exposure preceded the onset of the outcome?	Not stated clearly	Not stated clearly	Not stated clearly
Is there a dose-response gradient?	Not analyzed	Not analyzed	Not analyzed
Is there positive evidence from a “dechallenge-rechallenge” study?	No	No	No
Is the association consistent from study to study?	Yes	Yes	Yes
Does the association make biological sense?	Yes	Yes	Yes
Are the valid results from this harm study important?			
What is the magnitude of the association between the exposure and outcome?	OR adj = 1.38	OR = 1.97	OR = 1.4
What is the precision of the estimate of the association between exposure and outcome?	95% CI 1.01-1.89	95% CI 1.96-2.17	95% CI 0.97-1.73
Should these valid, potentially important results change the treatment of your patient?			
Do the results apply to our patient?	Yes	Yes	Yes
Is our patient so different from those in the study that its results don’t apply?	No	No	No
What are our patient’s risks of the adverse event?	PEER = c/(c+d) = 0.34*	PEER = c/(c+d) = 0.34*	PEER = c/(c+d) = 0.34*
To calculate the NNH (number of patients we need to treat to harm one of them) for any odds ratio (OR) and our patient’s expected event rate for this adverse event if they were **not** exposed to this treatment (PEER):	NNH = 14 (It need 14 workers with direct-lead exposure to add 1	NNH = 6 (It need 6 workers with direct-lead	NNH = 12 (It need 12 workers with direct-lead exposure to add 1

$NNH = \frac{PEER(OR-1)+1}{PEER(OR-1)\times(1-PEER)}$	occurrence of hypertension case)	exposure to add 1 occurrence of hypertension case)	occurrence of hypertension case)
What are our patient's preferences, concerns and expectations from this treatment?	Patient concern: how much lead exposure can effect hypertension.	Patient concern: how much lead exposure can effect hypertension.	Patient concern: how much lead exposure can effect hypertension.
What alternative treatments are available?	-	-	-

***** We used the prevalence value of hypertension in the general population in Indonesia as a PEER value (34%)(9), assumed that the population was not from worker population who was exposed to lead.

Discussion

The heavy metal lead is a common occupational and environmental pollutant. Damage caused by lead exposure is still a major public health problem(10). Lead exposure is estimated to account for 0.6% of the global burden of disease, with the highest-burden in developing regions, such in Indonesia(11). The lead-acid battery industry consumes the largest amount of lead which make lead exposure increases at the workplace(10). Among all heavy metals, lead has been suspected to influenced blood pressure for many years. The three selected studies involved workers with lead exposure in the workplace and clearly stated the outcome, which is increasing in blood presssure or hypertension in workers.

The studies conducted by Thongsringklee M., et al. (4), Singamsetty et al.(5), Sudjaroen et al.(6) aimed to investigate the occupational health effects, one of which is hypertension, due to lead exposure among workers. The result from all three studies showed that the proportion of hypertension was higher in the direct exposed group. Workers with direct-lead exposure were more at risk to developed hypertension than workers with indirect-lead exposure. Lead exposure can cause physiological changes in the muscular and endothelial layers induced by disturbance in the renin-angiotensin-aldosterone system, which plays an important role in the regulation of blood pressure(2). We chosed to use terms 'direct exposed group' for workers with direct-lead exposure, and 'indirect exposed group' for workers with indirect-lead exposure in this report in the two study groups. Because we considered the similarity of the terms being used between the articles and those terms also didn't replace the true meaning or definition from the source articles.

All three studies used a cross-sectional study design. Ideally, to find a causal relationship, the best study design is the Randomized Controlled Trial (RCT), because the determination of subjects in the two study groups is carried out randomly, so it is unlikely that there are differences in the characteristics of the subjects being studied. However, in the case of exposure to hazardous materials RCT are not possible. The cross-sectional study design can still be used with some modifications in determining the odds ratio or relative risk values to measure the relationship between exposure and the outcome. But there is no time dimension so it is weak in ensuring that exposure precedes the diseases.

Subject characteristics between study groups, direct exposed group and indirect exposed group, in the firts study, showed that there were characteristics differences between two groups, on age and working hours/day variables. This could be due to the study design used, where there were criteria for determining the subject into the group, that is based on the type of work, direct-lead exposure or indirect-lead exposure. Those characteristics differences were feared to have an effect on the outcome. However, this study then made adjustment. The relationship of hypertension due to lead exposure is adjusted by age and working hours/day variables (also adjusted to other variables– BMI, smoking status, alcohol drinking, milk drinking, seafood consumption, and exercise–

although there is no difference between the two groups), so it can be believed that the relationship that occurs was based on the individual subject being studied.

In contrast to the first study, the second study did not show the similarity characteristics between groups, or it was not clear whether the characteristics of the subjects were similar between the two groups. This study involved all workers in the battery factory, and the determination of the group of subjects studied was also based on the nature of work, direct exposure to lead or indirect exposure to lead. So, there was a possible difference in subject characteristics between the two groups, which was feared to affect the relationship to the outcome. While the third study clearly showed the similarity characteristics of the subjects and the results were no differences between the two groups. The similarity of subject characteristics is needed in the study of causal relationships with a cross-sectional design, so the causal relationships that occurred were truly based on the exposure being studied.

Exposure and clinical outcome were measured in the same way between the two study groups, in all three studies. The first study determined the assessment of the outcome of hypertension by using an objective standard based on the National Heart, Lung, and Blood Institute (NHLBI) where systolic blood pressure ≥140 mmHg and or diastolic blood pressure ≥90 mmHg was considered to be hypertension. As well as the second and third study, the assessment of the outcome of hypertension used an objective standard from the WHO guidelines where the category to begin hypertension when the systolic blood pressure ≥140 mmHg and or diastolic blood pressure ≥90 mmHg(13). These three studies were not clearly defined as the assessment of outcomes blinded to exposure.

There was no follow up in those studies because the study design in these studies was cross-sectional, so only one measurement was taken during data collection and there was no subsequent follow-up. The three studies also did not state clearly whether exposure preceded the onset of outcome. The first study stated that at the time of collection of study subjects, the recruited subjects had worked for at least three months without cardiovascular disease, hepatic disease, renal dysfunction, anemia, and cancer before working in the plant and those who had hobbies or extra jobs related to lead were excluded. From this, it can be assumed that the researchers intend to see for the relationship of lead exposure in the workplace with the incidence of hypertension (and other outcomes) in workers due to working in that factory. However, this is not stated clearly in the article. While the other two studies did not mention about the inclusion criteria which illustrated that the subjects recruited for the study did not have any conditions prior lead exposure in the workplace.

Dose-response gradient was not analyzed in those studies so was dechallenge-rechallenge study. Dechallenge-rechallenge study is not possible to do in a cross-sectional study with causal relationship between lead exposure in the workplace with the incidence of hypertension in worker. According to Kosnett et al(14), hypertension is a long-term health risk that can be caused by lead exposure. The long-term here refers to lead exposure of more than one year.

The first and second study showed that workers with direct-lead exposure have more risk for hypertension than workers with indirect-lead exposure and this result was significant statistically (OR adj 1.38, 95% CI 1.01-1.89 and OR 1.97, 95% CI 1.96-2.17, respectively). While the last study also showed that workers with direct-lead exposure have more risk for hypertension than workers with indirect-lead exposure (OR 1.4, 95% CI 0.97-1.73) but this result was not significant statistically. This can be caused by the number of study subjects were too small. The association makes biological sense that lead exposure can cause physiological changes in the muscular and endothelial layers induced by disturbance in the renin-angiotensin-aldosterone system which plays an important role in the regulation of blood pressure.

Our patient is a worker in the battery factory, at the battery assembly section and

exposed to lead every day at workplace and has hypertension. Those studies use a similar population, workers with lead exposure in the workplace. However, from the three studies with cross-sectional design, two studies showed a significant relationship between lead exposure in the workplace and the risk of hypertension in workers and one study did not show a statistically significant relationship. Thus, that indicates that the current evidences have not shown sufficient evidence to be able to ensure that lead exposure can cause hypertension in worker. The other evidence is needed with a better study design to provide strong evidence that lead exposure can cause hypertension in worker.

Conclusion

Two from three studies with a cross-sectional design showed a significant relationship between lead exposure in the workplace with the incidence of hypertension in worker and one study showed a relationship that was not significant statistically. Therefore, it can be concluded that the current evidences do not show sufficient evidence to ensure that lead exposure increased the risk of hypertension in worker. It is recommended for workers with direct-lead exposure to be more alert of the risk of hypertension. In addition, further research with better study design, such as cohort prospective, is needed to provide strong evidence that lead exposure can increase the risk of hypertension in worker.

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