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RESEARCH ARTICLE

Prevalence of Toxic Parkinsonism among Welders

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Abstract

The actual cause of Parkinson's disease is not known. The disease etiology appears to be multifactorial. The role of environmental factors as manganese toxicity has been proposed in the pathogenesis of Parkinson's disease. *Objectives:* To detect the association between heavy metals exposure and the effect on nervous system among welders, suggesting the hypothesis that welders are at increased risk for neurological disorders, including Parkinson's disease. *Subjects and methodology:* Seventy four (74) workers involved in welding process were recruited from four workshops in major industrial facilities in the 10th of Ramadan Industrial area, Cairo Egypt. Full clinical examination for detecting early manifestations of Parkinsonism was performed. Blood levels of heavy metals as manganese; lead, cadmium and Chromium were measured. *Results:* Parkinsonism manifestations were demonstrated in 11 out of 74 examined subjects. These manifestations revealed statistically significant positive relations with blood levels of lead, manganese and cadmium levels. *Conclusion:* welders are at increased risk for neurological disorders, including Parkinson's disease. Exposure to heavy metals is a great hazard for developing early Parkinsonism. *Recommendations:* Environmental control measures should be enforced at the work place. Periodic medical checking for early manifestations of Parkinsonism should be done.

Introduction:

The discovery of novel gene mutation has recently accelerated the research into the causes of Parkinson disease. The majority of PD cases remain idiopathic and in those cases, environmental causes should be considered. Several research studies were carried out to explore the mechanisms by which environmental exposures were related to occurrence of the disease. **(Alcalay et al., 2010; Furbee, 2011; Racette et al.,2012).** Gene environment interaction is implicated so that the impact of risk factor genes is likely mediated through complex interactions with previous environmental exposures, such as pesticides and heavy metals **(Edwards and Myers, 2007; Klein et al., 2009; Willis et al., 2010).** Parkinson's disease (PD) is a chronic, progressive, movement disorder. Its prevalence is estimated to be as high as 329 people in 100 000 population. Prevalence varies greatly throughout the world, ranging from 14/100,000 in China to 328/100,000 in Bombay, India **(Parkinson's disease News, 2012).** In Egypt, the prevalence rate of PD is 557 per 100,000 populations **(Khedr et al., 2012).** This makes Egypt the country with the world's second highest prevalence of Parkinson's disease behind Albania **(Parkinson's disease News, 2012).**

Parkinson's disease is one of the most common neurodegenerative disorders, affecting approximately 1 million Americans and one to 2% of those over age 60 worldwide **(Strickland and Bertoni, 2004).** Welding smoke is a mixture of particulate fumes and gases. **Haung, (2007),** documented the potential relation of inhaling welding fumes and the early onset of PD. The fumes released from the welding rod during melting process include relatively high levels of manganese. Several reports have focused on welding and manganese toxicity as potential risk factors for Parkinsonism and some have even proposed that welding is a risk factor for PD **(Jankovic, 2005; Finkelstein and Jerrett 2007)**. Recognition of that manganese (Mn), one of the metals found in welding fume is a neurotoxin and can lead to a neurologic syndrome with Parkinson features. It has led to speculation that manganese exposure through welding fumes might result in PD **(Kieburtz and Kurlan, 2005**; **Racette et al., 2012).** A review published by **Guilarte in 2010**, discussed if chronic manganese exposure produces dopamine neuron degeneration and PD or not. It concluded that there was an over whelming evidence showing that Mn-induced Parkinsonism, did not involve degeneration of midbrain dopamine neurons and that l-dopa was not an effective therapy. Exposure to metals in general has been considered as a possible etiologic factor in the development of PD. The welding process consists of different metal fumes as Manganese, lead, cadmium and chromium. Recently, **Weuve et al., 2013**, has provided evidence suggesting that cumulative exposure to lead may result in worsened cognition function among persons with PD. A case report by **Okuda et al., 1997**, found that acute cadmium intoxication may damage the basal ganglia, resulting in Parkinsonism. Moreover, numbers of experimental studies **(Lukawski et al., 2005; Rai et al., 2010; Yan et al., 2012)** have demonstrated that cadmium can induce cytotoxic cerebral cortical neurons damage.

From the occupational safety aspects, welders with early symptoms of Parkinsonism as bradykinesia, tremor and emotional disturbances, should be paid a lot of concern as they are more prone to accidents. Studies in occupational medicine investigating PD in welders were not conclusive. Putting the hypothesis that welders are at increased risk for neurological disorders, including Parkinson's disease, we undertook this study aiming to assess the possible link between heavy metal exposures during the welding process and neurodegenerative disorders as Parkinsonism disease. This link is assessed through evaluating environmental and biological levels of four heavy metals: Lead Cadmium, Manganese and Chromium which are present during the welding process.

Subjects and Methods:

Study setting: This is a cross section study. This study was carried out in different welding workshops in the 10th of Ramadan Industrial area, Cairo Egypt in the period from March 2011 to October 2011. The study was approved by ethical committee of the Department of Occupational and Environmental Medicine, Cairo University, Egypt.

Sample selection: After applying the inclusion and exclusion criteria, seventy four (74) workers involved in a welding process were recruited from four workshops in major industrial facilities in this city. The workers included in the study were all men, who had been employed for at least one year. The inclusion criteria included workers who have been employed for at least one year. The exclusion criteria, on the other hand included those workers with history of head injuries and / or history of neurologic diseases.

Welding processes involved the use of welding combustibles and welding filler materials. In these workshops, there are variety of welding processes used; shielded metal arc welding; arc welding; stand welding; oxyacetylene welding; oxygen cutting and torch brazing. Different welding processes produce big amounts of welding fume. During the process of melting the parent metal and the consumable produce concentrated particulate fumes and gases. These fumes contain a number of elements, including Manganese (Mn), Lead (Pb), Cadmium (Cd) and Chromium (Cr).

Methods

A-Environmental monitoring: the proposed study assessed air levels of heavy metals (manganese, lead, chromium and cadmium) in the breathing zone of welders during the process of welding. Air samples were collected using personal and area samplers. Measurements were taken during shift time from welding workshops. Three measurements were taken and the mean values are calculated. Levels of heavy metals in air were estimated by graphite furnace atomic absorption spectrometry. Samples of indoor air were collected in welding units by active sampling on 8 × 110mm adsorbent tubes containing activated charcoal at a flow rate of 200 mL/min, using an air sampling pump with electronic flow control. The flow of the pump was calibrated using a mini, Buck optical calibrator. After 4h sampling was stopped by placing caps on both ends of the tubes. The tubes were covered with aluminum foil and stored at 4 °C until analysis.

B-Clinical assessments and investigations: All studied subjects were personally interviewed via face to face interview. An informed consent was obtained regarding participation in the study and blood investigations. Workers were adequately oriented by the research team regarding the aim and importance of the study. Strict confidentiality was considered throughout sample collection, coding, testing, and recording of the results. The questionnaire consisted of mainly closed questions but included some explorative questions for detailed occupational and medical histories. On average, the interview lasted between 40 and 60 minutes. Information included demographic and clinical patient data, assessment of current occupation, duration in years and hours /day. Also inquiries about use of personal protective equipment are involved in the questionnaire. Each of the 74 welders underwent a comprehensive physical examination for detecting early manifestations of Parkinsonism as resting tremors, swinging movement, loss of concentration, decreased memory and bradykinesia. Blood samples were collected for measuring blood level of heavy metals and trace elements (lead, cadmium, manganese and chromium). Heavy metals concentrations were estimated by graphite furnace atomic absorption spectrometry

Statistical Analysis:

Data collected from the study was coded and entered using the statistical package SPSS version 16. The mean values and standard deviation (SD) were then estimated for quantitative variables. As for the qualitative variables, the frequency distributions were calculated. Compared demographics and characteristics of welding workers using unpaired t-test and fisher exact test were used when appropriate. p values less than 0.05 were considered statistically significant.

Results

Tables (1), lists the characteristics of studied group, all were men working in welding and their mean age was 34.42±8.4 years. The mean duration of their employment was 11.73±9.17 years. The frequencies of smokers among the welders' were 42(56.8%). Table (2), showed air levels of measured heavy metals in the working environment of welders. All air concentrations were above maximum allowable concentrations, according to the Egyptian law and international regulations except for chromium. The frequency of using personal protective equipment (PPE) (gloves, goggles and aprons) among welders showed that 55(74.3%) used PPE. This work revealed that 11 (14.9%) out of 74 workers performing electrode fixation or welding developed Parkinsonism. Five of those Parkinsonism cases were below 40 years old, but the rest were between 44 and 52 years old. They were exposed for at least 30 minutes each day, seven days a week, to high concentrations of air lead, manganese and cadmium. The highest manifestations encountered were decreased memory 11 (14.9%), followed by loss of concentration 8 (10.8%), resting tremors and swinging movement 5(6.8%), bradykinesia 3 (9.4%) and lastly changes in hand writing 2 (2.7%) (table3). For the eleven diagnosed patients with Parkinsonism in our study, there was loss of memory and two of the others mentioned signs as resting tremors, swinging movement, bradykinesia or changes in hand writing. Lower extremity rigidity was more common than upper extremity rigidity. Postural/action tremor was more common than rest tremor. None of the subjects in this study were taking Parkinson medications. Prevalence of Parkinson's manifestations was classified according to the duration of employment, table (4). It demonstrated a relation between the duration of employment in years to welding fumes and extrapyramidal manifestations. Both motor and non-motor dysfunctions were manifested after 5 years of employment as welder. The mean values of lead, cadmium and manganese in blood were statistically significantly higher (P <0.001) table (5), among subjects suffering from Parkinson manifestations compared to mean levels among those without these manifestations. However the mean level of chromium showed no statistically significant difference between the two groups. But it is still higher than normal serum levels that range from less than 0.05 up to 0.5 µg /mL.

Table (1) General characteristics of the studied group

	Mean	±SD
Age (years)	34.42	8.4
Duration of employment (years)	11.73	9.17
	N=74	**%**

Marital status		
Married	54	72.98
Unmarried	20	27.02
Smoking habit		
Smoker	42	56.8
Nonsmoker	32	43.2

Table (2) Air levels of measured metals in the working environment

Air levels of Heavy metals	**Welding site**		**Recommended OSHA level***
	Min Max.	**Mean± SD**	
Lead μg/m^3	0.8 – 1.2	0.87±0.30	0.15μg/m^3
Manganese mg/m^3	6.2 – 7.1	6.73±0.47	5 mg/m^3 Ceiling , TWA
Cadmium mg/m^3	1.01-2.5	1.73±0.74	0.2 mg/m^3
Chromium μg/m^3	1.0 – 1.6	1.28±0.28	2.5 μg/m^3

*Recommended OSHA level **(ACGIH, 1999)**.

Table (3) Prevalence of parkinson's manifestations among the studied group:

	N=74	%
Motor Dysfunction:		
Resting tremors	5	6.8
Swinging movement	5	6.8
Bradykinesia	3	9.4
Changes in handwriting	2	2.7
Non- Motor Dysfunction:		
loss of concentration	8	10.8
Decreased memory	11	14.9

Table (4) Prevalence of parkinson's manifestations according to the duration of employment

	<5 yrs		5-10 yrs.		>10 yrs.	
	N=11	%	N=31	%	N=32	%
Motor Dysfunction:						
Resting tremors	0	0	1	3.2	4	12.5
Swinging movement	0	0	0	0	5	15.6
Bradykinesia	0	0	0	0	3	9.4
Changes in handwriting	0	0	0	0	2	6.3
Non- Motor Dysfunction:						
loss of concentration	0	0	2	6.5	6	18.8
Decreased memory	0	0	3	9.7	7	21.9

Table (5) Level of measured metals among sufferers of Parkinson's manifestations compared to non-manifesting subjects

Level of heavy metals	Subjects with parkinson's manifestations (N=11) **Mean±SD**	Subjects without parkinson's manifestations (N=63) **Mean±SD**	**Unpaired t-test**	**P value**
Lead	42.8±12.3	26.7± 6.8	6.3171	<0.001
Manganese	1.3 ± 0.24	0.92±0.16	6.7089	<0.001
Cadmium	2.3± 0.3	0.9± 0.21	19.0696	<0.001
Chromium	8.2± 1.3	7.6± 1.02	1.7268	0.085

Discussion

In this study, we have found a relatively high prevalence (14.9%) of Parkinsonism in welding exposed workers. There was increase in the mean blood levels of heavy metals as lead, cadmium and manganese among workers suffering from extrapyramidal manifestations. These findings were in consistence with **Racette et al., 2005**, who reported increased prevalence (12.8%) of Parkinsonism in welders relative to a non-exposed reference population in a cross-sectional study of Parkinsonism in Alabama's welders. However, **Goldman et al., 2005**, found no relations between occupational welding exposure and PD in movement disorders clinic based case control study. Also, a cohort study by **Kenborg et al., 2012,** investigated the risk for Parkinson's disease and other neurodegenerative disorders among 5867 Danish welders and 1735 non-welding metal workers exposed to welding fume. They concluded that those welders are not at increased risk for Parkinson's disease. Parkinson's disease is caused by the progressive destruction of nerve cells that control muscle movement. Recently **Racette et al., 2012,** conducted a work-site based study among welders and demonstrated that the overall prevalence of Parkinsonism was 15.6% in welding exposed workers compared to 0% in the reference group. This study also showed similarity between welders and newly diagnosed idiopathic Parkinson disease (PD) patients, except for greater frequency of rest tremor and asymmetry in PD patients. There is no OSHA standard for total welding smoke, but OSHA sets standards for individual components of welding smoke. Local exhaust or general ventilation must be provided to keep exposure to toxic fumes, gases or dusts below the OSHA permissible exposure limits (PELs). However the National Institute of Occupational Safety and Health (NIOSH) had concluded that welders could be harmed by welding smoke even when the concentrations of the individual components were well below the OSHA PELs. While exposure to manganese can disrupt normal neurological processes, welding fumes contain other metals such as lead, cadmium, and chromium which may also be risk factors in the development of Parkinson's disease. Other issues, such as how much manganese must be present in welding fumes to insure toxic effects and the duration of exposure to these fumes, are still under debate. Some suggest that Parkinson's disease may actually encompass a combination of symptoms that have overlapping characteristics. In our work we measured air level of heavy metals in the work place during performing the welding process, table (2). All measured elements are above the recommended OSHA levels described by the **ACGIH in 1999**, except for chromium. We have documented in our study the lack of knowledge of safety measures among workers and hence the importance of implementing a strategy for raising the awareness of safety culture. NIOSH recommends that welding emissions should be reduced to the lowest feasible concentrations using engineering controls and work practices. In the current study, the highest manifestations encountered were decreased memory (14.9%), followed by loss of concentration (10.8%), resting tremors and swinging movement (6.8%), bradykinesia (4.1%) and lastly changes in hand writing (2.7%) (table3). In accordance with our results, **Sinczuk-Walczak et al., (2001)** assessed the effects of manganese on the nervous systems of 62 welders and 13 battery production workers. They found increased emotional irritability, memory impairment, concentration difficulties, sleepiness and limb paresthesia in the manganese-exposed workers. A retrospective study by **Sanchez-Ramos et al. (2011)**, determined the utility of tremor analysis in distinguishing tremors among workers exposed to welding fumes, patients with Idiopathic Parkinson's Disease (IPD) and Essential Tremor. They concluded that a quantitative tremor analysis can provide additional objective information to the clinical evaluation of patients with possible manganese-induced Parkinsonism. The degree and duration of exposure in relation to the risk of manganese-induced Parkinsonism have not been well studied, but they are based on our findings shown in table (4). It is clear that both motor and non-motor dysfunctions were manifested after 5 years of employment as welders. A study of 39 cases, dated back to 1919 was conducted by **Edsall** and his coworkers and reached this conclusion after 4 months of exposure to manganese. There were 9 to 12% increases in the levels of blood manganese required to produce permanent deficits. Our study has explained the development of Parkinson manifestations by the state of heavy metals overload manifested among the studied welders group. Mean values of measured heavy metals (lead, manganese and cadmium) were statistically significantly higher among subjects suffering from extra-pyramidal manifestations compared to mean levels among those without these manifestations, table (5). In accordance with our findings a study conducted by **Zayed et al., 1990** in southern Quebec(Canada), involving 42 Parkinsonism patients compared with a group of 84 matched controls, a slightly increased risk for PD was found to be associated with occupational exposure to manganese, iron, and aluminum, but this association did not reach statistical significance . **Racette et al. 1999**, demonstrated that clinically idiopathic Parkinson's cannot be distinguished from manganese (Mn) induced Parkinson's, but imaging studies of the brain were not conclusive. The article by **Josephs et al. 2005**, describes neurologic syndromes in welders who had evidence of hyper intensity in the pallidum on T1-weighted MR images. Such imaging abnormalities have been seen in individuals with presumed manganese intoxication. Two recent imaging studies by **Criswell et al., 2011; 2012,** among workers exposed to welding fume containing Mn. They used structural and molecular imaging. They demonstrated neurotoxic injury to the basal ganglia in these workers with minimal neurologic abnormalities. They concluded that workers with very mild Parkinson signs have evidence of dopaminergic dysfunction in the caudate nucleus with positron emission tomography. In consistent with our finding **Weisskopf et al.,** 2010, found evidences that higher cumulative exposure to lead is associated with an increased risk of PD. Our results agreed with **Yan et al., 2012**, who demonstrated that Cd can induce cytotoxic cerebral cortical neurons damage. Accordingly, in the current study, there are reasons to believe that welding fumes may have different neurotoxic effects than the largely pure manganese exposures since welding fume includes not only manganese but also a complex mix of other heavy metals and substances.

Conclusion and recommendations:

Limitation of this study includes the difficulty in interpreting the results of such a small case series with the coexistence of welding and Parkinson disease manifested by extrapyramidal symptoms and signs. Moreover, it is clear that welding produce a working environment rich in heavy metals as lead, cadmium, manganese and chromium. We have concluded an association between exposures to Mn and other welding metals fume and Parkinsonism among welders. Neurobehavioral tests to identify early signs of Parkinsonism are recommended for workers exposed to welding fumes. However, a follow-up study is needed. The magnitude of this problem has to be studied on large scale to support our findings. Environmental control measures should be enforced at the work place. Health surveillance should be carried out regularly for early detection of these manifestations and before the development of functional disability. In general we can recommend detoxifying protocol that may give hope to future treatment of Parkinsonism cases proved to be caused by chronic toxicity of heavy metal.

Conflict of interest: There is no conflict of interest in this research.

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