ORIGINAL REPORT

Urinary β_2 Microglobulin in Workers Exposed to Arc Welding Fumes

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Abstract- Welding is a process in which two or more metals are attached by the use of heat and, in some cases, pressure. Direct exposure and inhalation of welding fumes causes acute and chronic side effects in humans. Kidney damage is one of these important side effects. β_2 microglobulin is an 11.8 kilodalton protein and levels increase in the case of some inflammatory and viral diseases, or kidney malfunction and autoimmune diseases. In this study measurements of β_2 microglobulin were used as a criterion for assessing effects on the kidneys of workers exposed to welding fumes. The study population were electric arc welders in an industrial plant in Tehran, Iran. For control we selected workers who did not have any exposure to welding fumes. Both groups were selected on the basis of a questionnaire and the consideration of criteria for inclusion and exclusion. In the end 50 cases and 50 controls were chosen. A urine sample was collected from all participants and urinary *p*H was set to between 6-8 using NaOH (1M). Sample transportation to the laboratory complied with the related standards. The samples were assessed using the ORG 5BM kit. For quantitative assessment of β_2 microglobulin we used the Enzyme-linked Immunosorbent Assay (ELISA) method. The ages of the welders ranged from 21 to 48 years (mean=30.5±5.9 yrs) and of controls from 23 to 56 years (mean=31.8±5.9 yrs). Mean employment duration was 7.86±5.01years (range 2 to 27 years) for welders. Mean β_2 microglobulin level was 0.10±0.096 µg/ml in welders and 0.11±0.06 in controls. This difference was not statistically significant (P=0.381). In conclusion we don't find that exposure to electric arc welding fumes cause a significant change in urinary β_2 microglobulin compared to the control group.

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Keywords: *β_2* microglobulin/urine; Welding fumes; Occupational exposure

Introduction

Welding is a joining process of two or more metals with a lightweight bond by using heat or pressure with strength, elasticity and resistance approaching that of the parent metal (1) and electric arc welding is one the most common welding methods in which different iron electrodes with different coatings are used. The thick electrode coverings preserves the welding metal from oxidation and also hardens the metal surface (2,3).

Welding fumes in electric arc welding are composed of 14 different metals, i.e. manganese (Mn), beryllium (Be), cadmium (Cd), chromium (Cr), cobalt (Co), copper (Cu), iron (Fe), lead (Pb), mercury (Hg), molybdenum (Mo), nickel (Ni), antimony (Sb) and vanadium (V)(4,5) and this fumes cause acute and chronic illnesses in humans through direct contact and inhalation. Examples for acute effects are upper respiratory tract irritation and metal fume fever. For chronic effects we can name siderosis, lung cancer and pathologic effects on different body organs such as kidney (1,6,7). According to International agency for research on cancer welding fumes are classified as possible human carcinogens, i.e. group 2B (8). Monitoring workers for possible renal effects of occupational exposure to welding fumes is difficult, since there are few sensitive and specific tests for screening kidney damage. Traditional tests such as BUN and creatinine are insufficient since they change when some significant damage has already been done to the kidneys (9).

β_2 microglobulin is an 11.8 kilodalton protein containing 100 amino acids, without covalent binding in the heavy chain. β_2 microglobulin exists in eukaryotic

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cells and increases due to some inflammatory, viral and autoimmune diseases, kidney malfunction and aging (10-13). Recently β_2 microglobulin measurement has been noticed as a sensitive test for evaluation of renal tubular malfunction (14) and the usage is evaluation of workers who are exposed to heavy metals which may affect their kidneys (15). Kidney effects of cigarette smoking have also gained attention recently (16). Studies have shown that smoking has few effects on kidney function in those without renal risk factors (17,18). Smoking and Nicotine reduce the Glomerular Filtration Rate (GFR) in non-smokers and those who only smoke occasionally (17). On the other hand, chronic smoking does not cause kidney malfunction in the normal population (18). One of the major problems with smoking is the presence of nephrotoxic agents such as Lead, Cadmium and Mercury in tobacco (19,20).

The renal tubule impairment was evaluated by determination of urinary β_2 microglobulin in workers who are exposed to heavy metals and exposure to chromate seems to induce an enhanced level of urinary β_2 microglobulin concentration because chronic occupational exposure to chromate causes tubular malfunction (29), higher β_2 microglobulin concentrations (>200µg/g creatinine) were found in the population with urine concentrations of cadmium greater than 2.5µg/L. this finding indicate that malfunction in the reabsorption capacity of the renal tubules (30). .

Materials and Methods

This was a descriptive-analytic, cross sectional study. The inclusion criterion was history of welding for at least 2 years. Exclusion criteria were: (1) collagen-vascular diseases such as rheumatoid arthritis and Sjogren's Syndrome; (2) kidney problems such as nephrocalcinosis, interstitial nephritis, upper urinary tract infections and kidney transplant; (3) renal toxicity due to treatment with aminoglycosides, cisplatin and cyclosporin; (4) viral diseases such as Infectious Mononucleosis and Hepatitis C; and 5-lymphoproliferative disorders such as Multiple Myeloma and Hodgkin's Lymphoma (11, 14).

The study population were electric arc welders in an industrial plant in Tehran. Controls were selected from workers without exposure to welding fumes. Both groups were selected through a questionnaire and applying inclusion and exclusion criteria. 50 cases and 50 controls were selected.

A urine sample was collected from all participants and, by using 1 molar NaOH, urinary *p*H was set to between 6-8. Sample transportation to the laboratory complied with the related standards. The samples were assessed using the ORG 5BM kit (IBL-America). For quantitative assessment of β_2 microglobulin we used the Enzyme-linked immunosorbent assay (ELISA) method.

In this method a specific human antibody attached to microplates through β_2 microglobulin molecule is used. In a first step when the sample is added, the β_2 microglobulin molecule binds to the antibody. In the following step the microplate is washed over and the non-specific antibodies are removed. A yellow colour is produced by adding a conjugated enzyme, which is a β_2 microglobulin specific antibody bound to peroxidase, and then additional washing and adding the substrate. In the final step, by adding an acidic solution, the reaction is stopped and the yellow colour changes to blue. The strength of colour is assessed spectroscopically at a 450 nm wavelength, and can be directly related to the amount of β_2 microglobulin in the urine. The normal range is between 0-0.3 µg/ml. Metal fumes, such as Iron, Lead, Zinc, Copper and Manganese, in the ambient working environment were assessed through the atomic absorption method. A personal sampling pump(model SKC 224-PCXR4 ; SKC, Inc ,UK) with an membranous filter was used and the NIOSH 7300 method was applied. Their levels were all below permissible limits.

Data were analysed using statistical software SPSS version 16, continuous variables were compared between the two groups using the *t*-test for normally distributed variables and *Chi*-square test was used to compare binomial variables between the two groups. P value of less than 0.05 was considered statistically significant.

Results

The mean age of welders was (30.5±5.9) and of controls (31.8±5.9) years which showed no statistically significant difference (Table 1).

Table 1. Demographic data in welders and controls

	Welders (n=50)		Controls (n=50)		
	mean ± SD	**range**	**mean ± SD**	**range**	
Age(year)	30.5 ± 5.9	21-48	31.8 ± 5.9	23-56	NS
Work duration	7.86 ± 5.1	2-27	8.29 ± 5.2	3-28	NS

NS: *P* >0.05

Table 2. Comparison of urine β_2 microglobulin, BUN and Creatinine in welders and controls

	Welders (n=50)			Controls (n=50)			P
	mean ± SD	**Median**	**Range**	**mean ± SD**	**Median**	**Range**	
BUN (mg/dl)	13.4 ± 3.3	13	7.9-25	14.5 ± 3.5	13.3	8-22	0.21
Cr (mg/dl)	1 ± 0.17	1	0.7-1.3	0.96 ± 0.13	1	0.7-1.2	0.32
β_2 micro (μg/ml	0.1 ± 0.09	0.12	0.05-0.58	0.11 ± 0.06	0.1	0.06-0.32	0.38

Employment duration was (7.86±5.01) years for welders and (8.29±5.2) years for controls which showed no statistically significant difference (Table 1).

The mean BUN of welders was (13.4±3.3) and of controls (14.5±3.5) mg/dl, and the mean creatinine was (1.006±0.17) for welders and (0.96±0.13) mg/dl for controls which showed no statistically significant difference (Table 2).

10 welders and 6 controls were smokers with no statistically significant difference (P>0.05).

Mean β_2 microglobulin was (0.1±0.096) μg/ml for welders and (0.11±0.06) μg/ml for controls which showed no statistically significant difference (Mann Whitney test, Table 2).

2 welders and 1 control had abnormal β_2 microglobulin higher than 0.3 μg/ml, which showed

no statistically significant difference in Fisher exact test (P=0.54).

Also the association of age, employment duration and exposure to welding fumes with increased levels of urinary β_2 microglobulin in welders was not statistically significant (P>0.05).

The mean urinary β_2 microglobulin of 16 smokers was (0.108±0.09) and of 84 non-smokers was (0.107±0.08) μg/ml which showed no statistically significant difference (P>0.05).

Discussion

In this study we assessed the relationship between exposure to welding fumes, which contained metals such as iron, copper, lead, manganese and subtle amounts of cadmium, and changes in urinary β_2 microglobulin between welders and controls. No statistically significant difference was noticed.

Toda *et al.* (21) studied 22 welders who had exposure history of 7 months to 22 years to cadmium and observed no adverse kidney effects.

In a study conducted by Littorin *et al.* (22) on 17 male manual metal-arc stainless steel welders (mean exposure time 20 years) with far higher levels of chromium in urine than individually matched controls, there were no signs of kidney damage in tests of function of tubuli or glomeruli. Wael *et al.* (23) studied kidney effects of exposure to cadmium, lead and mercury from cigarette smoking. In spite of high blood cadmium and lead levels and high hair lead levels in smokers, there were no signs of nephrotoxicity. In our study no statistically significant difference was observed between smoking and changes in urinary β_2 microglobulin. Vittinghus *et al.* (24) compared biological markers of glomerular filtration (Kampmann clearance) and tubular function (urinary concentration of albumin, IgG, transferrin, orosomucoid and β_2 microglobulin) among 102 ever-welders, who were exposed to dust particulates containing chromium, nickel and manganese and 33 non-welders (mostly electricians). The number of welding years taken as a measure of cumulative welding exposure was not related to levels of proteins in urine when adjusting for the effect of age. In addition, no alteration of urinary proteins was found among the ex- welders apart from slightly elevated albumin. Vyskocil *et al.* (25) examined the biochemical markers of kidney damage in 52 male stainless steel welders (manual coated metal arc welding) exposed to chromium and nickel. No difference was found in the mean urinary excretion of total proteins, albumin, protein 1, transferrin, retinol-binding protein, lactate dehydrogenase, lysozyme, or beta-N-acetylglucosaminidase in a comparison with matched controls. β_2 microglobulin was slightly increased in those welders with a urinary chromium concentration of greater than 64.5 nmol/mmol creatinine. The prevalence of abnormal values did not differ from those observed in the control group. No correlation was found between the concentrations of chromium or nickel in urine and that of urinary proteins or enzymes. Roels *et al.* (26) concluded that there is a critical concentration of heavy metals to induce tubular dysfunction and low molecular weight proteinuria. For example, this critical concentration is more than 50 μg Hg/g creatinine for mercury, more than 70 μg Pb/dl for lead and more than 10 μg Cd/g creatinine for cadmium. In a study conducted by Nakajima *et al.* (27) on the association between urinary excretion of cadmium, copper and zinc in cadmium exposed subjects and the increase of urinary excretion of β_2-microglobulin, it was suggested that urinary cadmium and urinary copper was affected by dysfunction in renal tubular absorption (indicated by urinary β_2-microglobulin), whereas not only urinary cadmium and urinary copper but also urinary zinc appear to be a function of renal cellular desquamation (indicated by urinary metallothionein).

Garcon *et al.* (28) conducted a study on 35 workers exposed to lead and cadmium. They suggest the use of alpha-glutathione S-transferases excretion in urine as a hallmark of early changes in the proximal tubular integrity that could later lead to clinical disease if exposure is not reduced.

Honda *et al.* (31) concluded increased urinary levels of β_2 microglobulin and N-acetyl-beta-d-glucosaminidase with the increase in urinary Cd, indicating tubular impairment associated with increase in Cd body burden. However, this study was limited by being a cross-sectional study, which cannot yield a causal inference and urine β_2 microglobulin was not measured in pre placement examination.

No significant association between duration of exposure to welding fumes, age and urinary β_2-microglobulin levels was found in our study. This can be due to the fact that the level of cadmium, chromium and lead, which have considerable effect on tubular function, is not high enough in welding fumes. Although the study population had considerable exposure to welding fumes, we still did not detect any significant change in urinary β_2-microglobulin levels. We believe more studies on urinary β_2-microglobulin levels and other low molecular weight proteins are required to determine the effects of welding fumes on renal function. Also the appropriateness of using urinary β_2-microglobulin levels as a biomarker for tubular dysfunction in welders deserves more research.

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