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Effects of Metal Welding Fumes on Kidney Function Parameters in Male Albino Rats

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Welding is described as one of the most hazardous occupations. The study aims to determine the influence of metal welding fumes on kidney function parameters in blood of the exposed animals. The fumes were collected from welding sites during the activity by a skilled welder. One hundred thirty experimental animals were used and made into 13 groups. Twelve groups were given dosages calculated to correspond to real life workers exposure regimes and 1 group served as control. The dosages were administered intratracheally after been anesthetized weekly for 12 weeks. The animals were sacrificed and whole blood samples were taken. Serum was used to determine urea, chloride (Cl), Sodium (Na), Potassium (K) and the activity of creatinkinase (CK). The values of Urea and Creatinine in the treatment groups have exceeded the control values and slightly significant. Values of electrolytes Cl, K and Na in all the treatment groups have exceeded the control. Thus, it shows impairment of the kidney by elevated serum levels of the metabolites and probable damage in the kidney function. Benchmark dose and standard limits should be proposed for such occupations in Kano.

Keywords: *Effects, Evaluation, Kidney function, Metal welding fumes*

Introduction

Welding is an industrial process which is common, and use excessively high temperatures to join metals. Importantly, the process produces metallic fumes and gases that are potentially hazardous (Gordon 2004, Antonini et al. 2004). Tierney (1977) described welding as one of the most hazardous occupations. There are several reasons why welding is regarded as dangerous occupation: workers suffer excessive heat, burns, radiation, noise, fumes, gases, electrocution, and even the uncomfortable postures involved in the work; the different chemical composition of welding fumes, work piece, method employed, and surrounding environment; and lastly the routes of entry or surface exposed to these harmful agents access the body (Zakhari and Anderson 1981). There is some suggestion that Manual Metal Arc welding may result in acute decreased lung function compared to other processes (Leonard et al. 2004). Generation of Reactive Oxygen Species (ROS) is theorized as one mechanism for welding fume acute adverse health effects, (Taylor et al. 2003) with stainless steels containing chrome and nickel producing more reactive oxygen species (ROS) than mild steel (Leonard et al. 2004). Health authorities in Kano focus more attention on communicable diseases such as malaria, typhoid, etc. caused by vectors or water borne as environmental health problems. However, many deaths in the metropolis could be as a result of ailments from hazardous compounds/substances that destroy tissues and organs which

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existing laboratory practices and techniques cannot diagnose correctly and efficiently. Are the metal fumes toxic? What organ(s) are the most susceptible to the metal fumes? What concentration of the metal fumes can cause damage to human tissue/organ? Answers to these questions are not only important but necessary in order to broaden the scope of environmental health issues in urban Kano. Thus, the present study was aimed at determining the kidney function parameters (Chloride, Sodium, Potassium, urea, creatinine) of the experimental animal groups.

Materials and Methods

Collection of Welding Fumes

The metal fumes were generated in a cubical open front fume chamber (volume=1m^3) by a skilled welder performing manual metal welding (shielded manual metal arc welding) process using a stainless-steel hard surfacing electrode (Hyundai Welding electrode low hydrogen E 7018 3.2mm) and collected on 0.2µm nuclepore filters. They were collected in significant amount just before the start of the study. The particle size of the collected fume sample was determined using scanning electron microscopy (SEM) and found to be within the respirable size range with a mean diameter of <1µm (Popstojanov et al. 2014).

Experimental Design

Experimental activity requires the use of appropriate lab animals. Albino rats were chosen for this study. The rats were obtained and housed at the Animal house, Department of Pharmacology, Aminu Kano Teaching Hospital, Kano, Nigeria. Randomized block design was adopted for this study. A total of 130 laboratory rats (*Rattus norvegicus*) were utilized for the study. The animals were maintained in the animal room and were allowed to acclimatize for two weeks before treatment. The animals weigh between 210-250g. The animals were divided into 13 experimental groups with each group composing of 10 albino rats.

Housing and Feeding Conditions for Experimental Animals

The animal house has restricted access, free from pathogens and other extraneous factors. They were placed in cages with each cage housing 5 animals. The animals were marked on their tails for identification. The temperature in the experimental animal room was maintained at about 22°C (± 3°C) and the relative humidity was at least 30%. For lighting, the sequence was 12 hours light and 12 hours dark. They were given a conventional laboratory diet for rats bought from Vital Feeds Kano with water ad libitum. Existing protocols for the use of lab animals were adhered to strictly and ethical approval for the study was obtained

from College of Health Sciences Research Ethics Committee (CHS-REC), Bayero University, Kano (OECD 2018).

Preparation of the Test Substance

The dosing paradigm employed in this study was related to workplace exposures of metal workers. A mathematical calculation was utilized to determine the daily lung burden of a metal worker on a specified number of hours work schedule (Antonini et al. 2010, Sriram et al. 2010). Below are the factors that were taken into consideration during the calculation:

- Fume concentration (5mg m^{-3}, threshold limit value for welding fumes).
- Human minute ventilation volume (20,000mlmin^{-1}×$10^{-6}m^3ml^{-1}$).
- Exposure duration (no. of hr day^{-1}×60min h^{-1}).
- Deposition efficiency (15%) (ICRP 1994, Antonini et al. 2006).

With reference to the above factors, metal workers daily burden for various hours per day.

1. Metal worker daily burden (2hrs/day)=Fume concentration (5mg/m^3)× Human minute ventilation volume (20,000ml/min×10-6m^3/ml)×Exposure duration (2hr/day×60min/hr)×Deposition efficiency (15%)=1.8mg.

Using surface area of alveolar epithelium (rat=0.4m^2; human=102m^2) as dose metric (Stone et al. 1992). Rat daily burden of exposure was taken as 0.0070mg.

Then, similar exposure in rats for 3 years, 5 years, 10 years and 20 years will be 7.66mg, 12.77mg, 25.55mg and 51.10mg, respectively at 365 days per year. Each of these concentrations was then divided into 12 which was administered weekly for the period of the study (12 weeks).

2. Metal worker daily burden (4hrs/day)=Fume concentration (5mg/m^3)× Human minute ventilation volume (20,000ml/min×10-6m^3/ml)×Exposure duration (4hr/day×60min/hr)×Deposition efficiency (15%)=3.6mg.

Using surface area of alveolar epithelium (rat=0.4m^2; human=102m^2) as dose metric (Stone et al. 1992). Rat daily burden of exposure was taken as 0.0141mg.

Then, similar exposure in rats for 3 years, 5 years, 10 years and 20 years will be 15.44mg, 25.73mg, 51.46mg and 102.93mg, respectively at 365 days per year. Each of these concentrations was then divided into 12 which were administered weekly for the period of the study (12 weeks).

3. Metal worker daily burden (8hrs/day)=Fume concentration (5mg/m^3)× Human minute ventilation volume (20,0000ml/min×10-6m^3/ml)×Exposure duration (8hr/day×60min/hr)×Deposition efficiency (15%)=7.2 mg.

Using surface area of alveolar epithelium (rat=0.4m^2; human=102m^2) as dose metric (Stone et al. 1992). Rat daily burden of exposure was taken as 0.0282mg.

Then, similar exposure in rat for 3 years, 5 years, 10 years and 20 years will be 30.88mg, 51.46mg, 102.93mg and 205.86mg, respectively at 365 days per year. Each of these concentrations was then divided into 12 which was administered weekly for the period of the study (12 weeks).

Table 1 describes the working concentrations (dosage) of metal fumes administered to test animals for 12 weeks. Each concentration was given per animal per week.

Table 1. *Working Concentration for Test Substances Administered to Groups of Animals used for the Study*

Groups		
I	**II**	**III**
Group IA (0.64 mg/animal/week)	Group IIA (1.29 mg/animal/week)	Group IIIA (2.57 mg/animal/week)
Group IB (1.06 mg/animal/week)	Group IIB (2.14 mg/animal/week)	Group IIIB (4.27 mg/animal/week)
Group IC (2.13 mg/animal/week)	Group IIC (4.29 mg/animal/week)	Group IIIC (8.56 mg/animal/week)
Group ID (4.26 mg/animal/week)	Group IID (8.58 mg/animal/week)	Group IIID (17.16 mg/animal/week)

The metal fumes sample was prepared in sterile saline and sonicated for 1min to disperse the particulates. Rats were anaesthesized with ketamine (0.1ml/100g b.w IP) and after passing out, immediately followed by intratracheal instillation of the respective dose per animal once a week for 12 weeks. Control animals were given 200µl of sterile saline via intratracheal route after been anaesthesized.

Administration and Dosage of Test Substances

The study involved chronic toxicity testing of the metal fumes in albino rats which lasted for 12 weeks and treatment was administered weekly by intratracheal instillation (Antonini et al. 2013).

Collection of Blood Samples of Treated Animals

Animals were euthanized 1 week after the 12 weekly treatments. Blood samples were collected from jugular vein into an EDTA container for biochemical analysis. However, the blood sample was centrifuged at 3000rpm to obtain the serum for subsequent analysis (Hoff and Rlagt 2000, Antonini et al. 2013).

Kidney Function Tests

Biochemical parameters were determined in serum photometrically. Concentrations of urea, chloride (Cl), Sodium (Na), Potassium (K) and the activity

of creatinkinase (CK) were determined using Pliva Lachema test kits (Czech Republic).

Data Analysis

Sigmastat v.3.5 statistical tool was employed to analyze data or results obtained from the study. Means of various parameters were analyzed statistically to test for statistical difference by one-way analysis of variance (ANOVA) and level of significance was taken at $p<0.05$ indicating significance.

Results

Tables 2-4 show the kidney function parameters in blood of experimental animals in groups I (A, B, C, D), II (A, B, C, D) & III (A, B, C, D). The parameters include Urea, creatinine and electrolytes which are potassium, chloride and sodium.

Table 2. *Mean Values of Kidney Function Parameters of Blood Samples of Animals Exposed to lower Metal Welding Fumes for 12 Weeks*

Test animal groups	Urea (mg/dl)	Creatinine (µmol/l)	Potassium (mmol/l)	Chloride (mEq/l)	Sodium (mEq/l)
IA	222.5±12.58	31.37±4.25^{a}	4.16±0.33	93.92±5.51	50.95±3.91^{a}
IB	268.35±11.21	30.94±3.91^{b}	4.25±0.41	99.6±5.84	58.15±5.03^{bc}
IC	313.35±15.27	34.85±4.53^{c}	4.41±0.52	102.77±6.36	60±4.62^{abd}
ID	327.77±14.04	45.73±4.33^{abc}	4.47±0.43	116.98±6.76	90.3±4.88^{cd}
Control	183.35±10.37	28.02±2.40	4.1±0.42	97.2±5.44	49.6±4.73
P value	**>0.05**	**<0.05**	**>0.05**	**>0.05**	**<0.05**

p<0.05: there is significant difference.
p>0.05: there is no significant difference.
Means±SD values with same letters as superscript indicate significance.

Table 3. *Mean Values of Kidney Function Parameters Blood Samples of Animals Exposed to moderate Metal Welding Fumes for 12 Weeks*

Test animal groups	Urea (mg/dl)	Creatinine (µmol/l)	Potassium (mmol/l)	Chloride (mEq/l)	Sodium (mEq/l)
IIA	295±11.02	34.35±2.88	4.84±0.31	107.31±8.04	59.56±3.47^{ab}
IIB	320.85±14.75	36.1±3.55	4.79±0.24	121.77±7.22	76.45±4.24^{a}
IIC	361.1±13.33	39.73±4.01	4.51±0.30	122.98±7.64	80.85±4.53
IID	386.65±18.21	46.1125±4.44	4.56±0.26	132.99±7.08	98.1±4.71^{d}
Control	183.35±10.37	28.02±2.40	4.1±0.42	97.2±5.44	49.6±4.73
P value	**>0.05**	**>0.05**	**>0.05**	**>0.05**	**<0.05**

p<0.05: there is significant difference.
p>0.05: there is no significant difference.
Means±SD values with same letters as superscript indicate significance.

Table 4. *Mean Values of Kidney Function Parameters of Blood Samples of Animals Exposed to High Metal Welding Fumes for 12 Weeks*

Test animal groups	Urea (mg/dl)	Creatinine (µmol/l)	Potassium (mmol/l)	Chloride (mEq/l)	Sodium (mEq/l)
IIIA	339.35±13.30[a]	36.56±3.61[ab]	5.52±0.31	117.43±4.41	68.23±4.54[ac]
IIIB	361.1±11.10[b]	39.73±2.15[c]	4.61±0.22	142.98±4.55	84.3±4.88[abd]
IIIC	392.65±12.36	48.61±3.41[ad]	4.56±0.19	152.99±3.99	101.5±5.05[bc]
IIID	430.83±15.27[ab]	57.36±3.68[bcd]	5.07±0.34	199.09±6.71	112.43±5.04[d]
Control	183.35±10.37	28.02±2.40	4.10±0.42	97.20±5.44	49.60±4.73
P value	**<0.05**	**<0.05**	**>0.05**	**>0.05**	**<0.05**

p<0.05: there is significant difference.
p>0.05: there is no significant difference.
Means±SD values with same letters as superscript indicate significance.

Discussion

The mean values of Urea for groups IA, IB, IC & ID range from 222.5 to 327.77mg/dl as shown in Table 2. Group IA has the least mean value of 222.5mg/dl while Group ID has the highest mean value of 327.77mg/dl. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 183.35mg/dl. There is no significant difference statistically between the groups (p>0.05).

The mean values of Urea for groups IIA, IIB, IIC & IID range from 295 to 386.65mg/dl as shown in Table 3. Group IIA has the least mean value of 295mg/dl while Group IID has the highest mean value of 386.65mg/dl. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 183.35mg/dl. There is no significant difference statistically between the groups (p>0.05).

The mean values of Urea for groups IIIA, IIIB, IIIC & IID range from 339.35 to 430.83mg/dl as shown in Table 4. Group IIIA has the least mean value of 339.35mg/dl while Group IIID has the highest mean value of 430.83mg/dl. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 183.35mg/dl. There is a significant difference statistically between the groups (p<0.05). Similarly, in another study, treatment with the mixture of metals arsenic (As), cadmium (Cd) or lead (Pb) in rats has resulted in a significant increase in urea and a significant decrease in protein and albumin levels, indicating a systemic toxic effect of the treatment (Choudhuri et al. 2016).

The mean values of Creatinine for groups IA, IB, IC & ID range from 30.94 to 45.73µmol/l as shown in Table 2. Group IA has the least mean value of 30.94µmol/l while Group ID has the highest mean value of 45.73µmol/l. The mean values are increasing across IB, IC & ID. The values of all the groups have exceeded the control mean value of 28.02µmol/l. There is significant difference statistically between the groups (p<0.05).

The mean values of Creatinine for groups IIA, IIB, IIC & IID range from 34.35 to 46.11µmol/l as shown in Table 3. Group IIA has the least mean value of 34.35µmol/l while Group IID has the highest mean value of 46.11µmol/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 28.02µmol/l. There is no significant difference statistically between the groups ($p>0.05$).

The mean values of Creatinine for groups IIIA, IIIB, IIIC & IIID range from 36.56 to 57.36µmol/l as shown in Table 4. Group IIIA has the least mean value of 36.56µmol/l while Group IIID has the highest mean value of 57.36µmol/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 28.02µmol/l. There is a significant difference statistically between the groups ($p<0.05$). Similarly, treatment with the mixture of metals arsenic (As), cadmium (Cd) or lead (Pb) in rats has resulted in a significant increase in serum cholesterol and creatinine levels (Choudhuri et al. 2016).

The values of Urea and Creatinine in the treatment groups have exceeded the control values thus it shows impairment of the kidney by elevated serum levels of these metabolites. Similarly, Afify et al. (2007) found a statistically significant correlation between the level of blood chromium and renal insult represented by the affection of urinary beta-2 microglobulin, urea, and creatinine. An increase in serum urea and creatinine level in the animals, treated with mixture of heavy metals (As, Cd and Pb), relative to control animal and animal treated with individual metal As, Cd or Pb indicated nephrotoxic effect of metals treatment. In addition, Samir et al. (2015) revealed also an increase in serum creatinine concentration in cadmium group and no changes was signalized in the others treated groups, while serum urea concentration was increased in cadmium and combined treated rats and no change was observed in mercury treated rats.

Kareem et al. (2015) showed that renal parameters in terms of serum creatinine level and proteinuria were deranged evident on biochemical analysis. When group B and C were compared to group A (Control), a statistically significant difference ($p<0.05$) was noticed in terms of renal parameters.

Serum levels of creatinine increased as a result of copper exposure in comparison to the control group. These observed changes are in accordance with other authors' results (Wang et al. 2014, Onwuka 2005). Both urea and creatinine are excreted through kidney. In fact, urea is the first acute renal marker which increases during any kind of kidney injury. But, creatinine is the most trustable renal marker which increases only due to loss of major renal function (Peres et al. 2013).

The mean values of Potassium (K) for groups IA, IB, IC & ID range from 4.16 to 4.47mmol/l as shown in Table 2. Group IA has the least mean value of 4.16mmol/l while Group ID has the highest mean value of 4.47mmol/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 4.1mmol/l. There is no significant difference statistically between the groups ($p>0.05$).

The mean values of Potassium (K) for groups IIA, IIB, IIC & IID range from 4.51 to 4.84mmol/l as shown in Table 3. Group IIA has the least mean value of 4.51mmol/l while Group IID has the highest mean value of 4.84mmol/l. The mean

values are decreasing across the groups. The values of all the groups have exceeded the control mean value of 4.1mmol/l. There is no significant difference statistically between the groups ($p>0.05$).

The mean values of Potassium (K) for groups IIIA, IIIB, IIIC & IIID range from 4.56 to 5.52mmol/l as shown in Table 4. Group IIIC has the least mean value of 4.56mmol/l while Group IIIA has the highest mean value of 5.52mmol/l. The mean values have decreased from IIIA, IIIB, IIIC. The values of all the groups have exceeded the control mean value of 4.1mmol/l. There is no significant difference statistically between the groups ($p>0.05$). Similarly, the results of De Jong et al. (2019) have shown that levels of potassium increased as a result of Cu exposure in comparison to the control group.

The mean values of Chloride (Cl) for groups IA, IB, IC & ID range from 93.92 to 116.98mEq/l as shown in Table 2. Group IA has the least mean value of 93.92mEq/l while Group ID has the highest mean value of 116.98mEq/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 97.2mEq/l. There is no significant difference statistically between the groups ($p>0.05$).

The mean values of Chloride (Cl) for groups IIA, IIB, IIC & IID range from 107.31 to 132.99mEq/l as shown in Table 3. Group IIA has the least mean value of 107.31mEq/l while Group IID has the highest mean value of 132.99mEq/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 97.2mEq/l. There is no significant difference statistically between the groups ($p>0.05$).

The mean values of Chloride (Cl) for groups IIIA, IIIB, IIIC & IIID range from 117.43 to 199.09mEq/l as shown in Table 4. Group IIIA has the least mean value of 117.43mEq/l while Group IIID has the highest mean value of 199.09mEq/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 97.2mEq/l. There is no significant difference statistically between the groups ($p>0.05$).

The mean values of Sodium (Na) for groups IA, IB, IC & ID range from 50.95 to 90.30mEq/l as shown in Table 2. Group IA has the least mean value of 50.95mEq/l while Group ID has the highest mean value of 90.30mEq/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 49.6mEq/l. There is significant difference statistically between the groups ($p<0.05$).

The mean values of Sodium (Na) for groups IIA, IIB, IIC & IID range from 59.56 to 98.1mEq/l as shown in Table 3. Group IIA has the least mean value of 59.56mEq/l while Group IID has the highest mean value of 98.1mEq/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 49.6mEq/l. There is significant difference statistically between the groups ($p<0.05$).

The mean values of Sodium (Na) for groups IIIA, IIIB, IIIC & IIID range from 68.23 to 112.43mEq/l as shown in Table 4. Group IIIA has the least mean value of 68.23mEq/l while Group IIID has the highest mean value of 112.43mEq/l. The mean values are increasing across the groups. The values of all the groups have exceeded the control mean value of 49.6mEq/l. There is

significant difference statistically between the groups ($p<0.05$). However, the results have shown that levels of urea, sodium and protein decreased as a result of Cu exposure in comparison to the control group. Significant effects were seen already at a dose and Cu toxicity on serum parameters related to renal function (Babaknejad et al. 2015).

The values of these electrolytes (Cl, K, Na) in all the treatment groups have exceeded the control which indicates probable damage in the kidney function. In another study, predominant renal injury among welders is tubular, and this injury is correlated with the blood chromium level (Afify et al. 2007). Powers et al. (1986) said that glomerular injury has been noted in chromium workers, the predominant renal injury is tubular, with low doses acting specifically on the proximal convoluted tubules and this injury is correlated with the blood chromium level as low-dose, chronic chromium exposure typically results only in transient renal effects. They also reported that elevated urinary B2-microglobulin levels (an indicator of renal tubular damage) have been found in chrome platters, and higher levels have generally been observed in younger persons exposed to higher Cr (VI) concentrations. As the kidneys are highly sophisticated transport organs, they excrete metabolic waste. Such a function is optimised by a special circulatory structure in the kidney, which has a remarkable ability to adjust the haemodynamic inputs in order to maintain renal circulation (Burkitt et al. 2000).

Some studies have shown that recurrent exposure to metal fumes could result in the urinary excretion of low molecular weight proteins (Wedeen and Qian, 1991, Petersen et al. 1994, Ding et al. 2011) although this state might be reversible at the onset unless there is already established renal impairment as evident by decreasing glomerular filtration rate. Chronic exposure to heavy metals like lead, chromium and cadmium may produce insidious, yet progressive tubulointerstitial nephropathy often leading to renal failure (Petersen et al. 1994, Garcon et al. 2007). In contrast to tubular proteinuria in which low molecular weight proteins are seen, glomerular proteinuria is readily detected by testing for urinary albumin using albustix (Wedeen and Qian 1991).

Among possible target organs of heavy metals liver, kidney and neural systems appear to be the most sensitive one (Flora and Pachauri 2010). Chronic exposure to Pb showed nephropathy, including nephromegaly and dysfunction of proximal tubules in animal studies (Liu et al. 2012).

Conclusions

The values of Urea and Creatinine in the treatment groups have exceeded the control values thus it shows impairment of the kidney by elevated serum levels of these metabolites. The values of the electrolytes Cl, K and Na in all the treatment groups have exceeded the control which indicates probable damage in the kidney function. Benchmark dose and standard limits should be proposed for such occupations in Kano.

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