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The effect of manganese exposure on erythropoietic and reproductive system parameters

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Abstract

The aim of this study is determining the effect of manganese (Mn) exposure on erythropoietic and reproductive system. A study group consisting of 51 non-smoking welders older than 18 years old with Mn exposure, who visited Ankara Occupational and Environmental Diseases Hospital, and a control group consisting of 79 healthy office employees without Mn exposure, were chosen as study group. Blood Mn level, total testosterone (TT), freetestosterone (FT), alanine aminotransferase (ALT), aspartate aminotransferase(AST), thyroid stimulant hormone (TSH), triiodothyronine (T3), thyroxine (T4), uric acid, creatinine, complete blood count (CBC), prolactin, follicle stimulating hormone (FSH), luteinizing hormone (LH) levels were analysed along with the demographic data of the patient. The study and control groups consisting of a total of 130 persons were all male, 39.2% (n=51) of which represented the study group with manganese exposure and 60.8% (n=79) of which represented the healthy control group. A significant difference was identified statistically between Mn (t= 4,501, p= 0,000), FT (t= -6.959, p=0.000), TT (t= -2.835, p=0.005) values of those with and without manganese exposure. AST and ALT levels were not found significant although they were higher in the exposed group. When the values are examined according to uric acid, creatinine, TSH, T3, T4and complete blood count, it was observed that the values of exposure group and control group were almost identical. Although FHS, LH and PRL values were high in the study group, the differences were not found significant. Consequently, although Mn is a trace element, it was concluded that, in high levels,it might reduce the testosterone synthesis with direct toxic effect on the testicle in the long-term exposures leading.

Keywords: Manganese, prolactin, FSH, LH, testosterone, reproductive dysfunction

Introduction

Manganese is a metal naturally occurring in the earth's crust, available in both organic and inorganic forms. Pure manganese is silver colored, but it does not occur naturally. They are available in organic compounds as they combine with the substances such as oxygen, sulphur and chlorine. Manganese is used in the industry as an oxidising agent to improve the steel production and to plate the welding rods and also used in the production of fireworks, battery, fertilizer, glass, paint, cosmetics, as a textile decolourant, as an imaging agent in medicine and as an additive some drugs and gasoline [1-3].

Daily intake of Mn with food is 2-9 mg and as a trace element it is necessary for various metabolic functions, such as energy metabolism in the growth of the metabolism, activation of metalloenzymes, reproduction hormone and antioxidant enzyme functions [3-9]. There are studies which have determine that serum prolactin and cortisol levels increased [10] in those with chronic Mn exposure, and high Mn exposure can cause sexual dysfunction [11-15].

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Material and Method

Study Groups

51 welders with Mn exposure, having an average age of 38.90, who visited Ankara Occupational and Environmental Diseases Hospital, were selected as the study group and 79 healthy office employees without any Mn exposure, having an average age of 38.26, were selected as the control group. In each group, the males above 18 years of age are non-smokers. The Decision of the Ethical Committee of Ankara Keçiören Training and Research Hospital is available for the study.

Measurements

The haematological analysis were made with Cell-Dyn Emerald Hematologic Analyser with blood samples taken in the tubes containing Ethylene Diamine Tetra Asiatic acid (EDTA), the manganese results, with Inductively Coupled Plasma – Mass Spectrometer (ICP-MS) Agilent 7.700 from the blood samples taken in the tubes containing EDTA and FSH, LH, PRL, TST analysis, with Abbott Architect i2000 Immunoassay device from blood samples taken in the tubes containing EDTA.

Statistical Analysis

SPSS22.0 software was used in statistical analysis. Data distribution was determined with Kolmogorov-Smirnow test. In the study, the statistical significance level of which was accepted as 0.05, the difference between the averages of two independent variables was evaluated with t-test; the difference between more than two variables was evaluated with two-way analysis of variance (ANOVA) and additionally with Pearson Correlation analysis. The averages are given with the standard deviations.

Result

The study and control group are male, 39.2% (n=51) were manganese exposed and 60.8% (n=79) is non-exposed.

A significant difference was identified statistically between Mn (t= 4.501, p= 0,000), FT (t= -6.959, p=0.000), TT (t= -2.835, p=0.005) values of those of exposed and non-exposed group. AST and ALT levels were also higher in the exposed group (23.76 and 54.82) then in the non-exposed group (18.81 and 22.91) but the differences were not significant. When the values are examined according to uric acid, creatinine, TSH, T3, T4 and complete blood count, it was observed that the values of exposure group and control group were almost identical.

Although FHS, LH and PRL values were high in the exposed group, the differences were not found significant (Table 1).

Table 1. The Statuses of Continuous Variables, Based on Manganese Exposure

	Group	N	Mean	Std. Deviation	t	p
Age	Exposed	51	38.90	8.02	0.413	0.680
	Control	79	38.26	8.90		
Mn (µg/L)	Exposed	51	22.99	22.11	4.501	0.000
	Control	79	8.97	2.96		
FT (ng/ml)	Exposed	51	9.00	2.67	-6.959	0.000
	Control	79	13.38	3.95		
TT (ng/ml)	Exposed	51	5.21	2.51	-2.835	0.005
	Control	79	6.42	2.26		
ALT (U/L)	Exposed	51	26.66	15.85	1.589	0.115
	Control	79	22.91	11.08		
AST (U/L)	Exposed	51	20.92	7.32	1.831	0.071
	Control	79	18.81	4.66		
TSH (µıu/ml)	Exposed	51	1.62	0.94	-0.192	0.848
	Control	79	1.65	0.97		
CREATININE (mg/dl)	Exposed	51	0.82	0.09	-0.128	0.899
	Control	79	0.82	0.10		
T3 (pg/ml)	Exposed	51	3.00	0.55	0.073	0.942
	Control	79	3.00	0.39		
T4 (ng/dl)	Exposed	51	1.02	0.15	-0.050	0.960
	Control	79	1.02	0.13		
URIK ACID (mg/dl)	Exposed	51	5.65	1.32	1.536	0.127
	Control	79	5.32	1.11		
WBC (x109/L)	Exposed	51	7.15	1.83	-0.691	0.491
	Control	79	7.38	1.82		
RBC(x1012/L)	Exposed	51	5.22	0.57	-0.906	0.367
	Control	79	5.30	0.47		
HGB (g/L)	Exposed	51	15.30	1.51	-1.115	0.267
	Control	79	15.58	1.32		
MCV (f/L)	Exposed	51	87.70	4.94	-0.188	0.851
	Control	79	87.88	5.58		
HCT (%)	Exposed	51	45.64	4.58	-1.176	0.242
	Control	79	46.52	3.88		
MCHC (g/L)	Exposed	51	33.51	0.96	0.061	0.951
	Control	79	33.52	1.05		
MCH (pg/cell)	Exposed	51	29.42	1.96	-0.121	0.904
	Control	79	29.46	2.24		
RDW (%)	Exposed	51	15.63	1.19	-0.490	0.625
	Control	79	15.74	1.39		
PLT (K/uL)	Exposed	51	219.17	62.15	-0.486	0.628
	Control	79	223.94	49.24		
NEU (x109/L)	Exposed	51	4.03	1.21	-0.398	0.691
	Control	79	4.12	1.32		
LYM (x109/L)	Exposed	51	2.25	0.64	-1.459	0.147
	Control	79	2.44	0.76		
MPV (fL)	Exposed	51	8.10	1.42	0.541	0.589
	Control	79	7.97	1.33		
PDW (%)	Exposed	51	17.97	1.52	-0.663	0.509
	Control	79	18.14	1.34		
PCT (%)	Exposed	51	0.17	0.05	-0.104	0.917
	Control	79	0.17	0.03		
FSH (mlu/ml)	Exposed	51	4.14	1.74	1.712	0.089
	Control	79	3.55	2.21		
LH (mlu/ml)	Exposed	51	4.11	1.67	0.572	0.568
	Control	79	3.94	1.61		
PROLACTINE (mlu/ml)	Exposed	51	13.06	6.09	0.348	0.729
	Control	79	12.65	6.95		

The Pearson correlations between ages, manganese level, duration of employment, free testosterone, FSH, LH, PRL are given in Table 2. The strongest correlation was observed to be between FSH and LH and the free testosterone had a negative correlation with PRL and manganese level.

Table 2. Pearson Correlations of Continuous Variables

N=130	Age	Mn	Working Time	FT	FSH	LH	PRL
Age	1	-.042	.192*	-.262**	.312**	.247**	-.007
Mn		1	-.125	-.214*	.012	-.011	.028
Working Time			1	-.156	.227**	.041	-.048
FT				1	-.165	-.037	.185*
FSH					1	.458**	.030
LH						1	.288**
PRL							1

While the testosterone levels varied according to the age groups ($p<0.001$) and whether there was any exposure ($p<0.001$) in the investigation conducted with two-way ANOVA, the collective effect of each variant was not found significant statistically ($F=2.844$ $p=0.062$) (Figure 1).

The statistical study suggested a positive correlation between the Manganese level for the control group without any Mn level and HGB ($r= 0.228$, $p=0.044$), MCV ($r=0.231$, $p=0.041$), MCH ($r=0.222$, $p=0.049$).

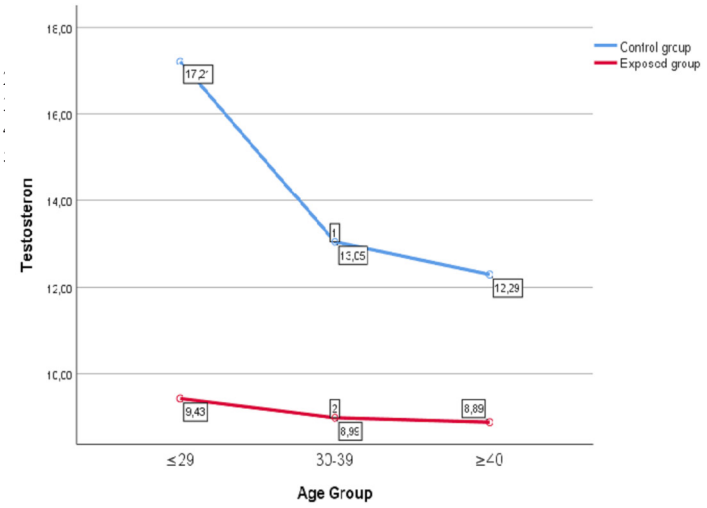

Figure 1. Two-way ANOVA analyse

Discussion

This seem to be the first study which investigated the correlation between Mn exposure and testosterone levels according to literature search. The mechanism of toxic effect of Mn exposure on the endocrine system is not very clear. However, oxidative stress is thought to be one of the important reasons in metal exposures [16-21].

It was found out that manganese caused maturation delays in the reproductive organs. Testosterone levels reduced following the manganese application and LH levels remained considerably unchanged. Manganese seems to target the Leydigcells [3,22].We found out similar results in our study. Nevertheless, the positive correlation between Mn and Hgb in the healthy control group that we have detected in our study accounts for the essential properties of Manganese at low levels.

Kim et al. found out that FSH, LH and testosterone levels increased in the workers exposed to Mn, in the study they conducted on 251 welders to examine the effect of Mn exposure on the neuroendocrine system. In another study, no correlation was found between FSH, LH or testosterone levels in the welders [23].

In a study conducted on the employees working at a dry alkaline battery manufacturing plant, all erythropoietic parameters and serum iron concentrations is lower in Mn exposed group. On the other hand Ca, prolactin, FSH or LH levels were found to be similar in exposed group and control group [24]. Another study discovered that FSH, LH and testosterone levels have decreased [9].

The studies conducted on people with chronic Mn exposure at the workplace showed no haematological effect in high Mn levels [3,25-28], similar to our study.

The liver has an active role in transport of manganese. A recent study revealed no pathological finding in the liver biopsy in a group consisting of 13 patients who have been monitored for chronic Mn intoxication [3,25].

The animal studies showed an increase in the liver enzymes following the long-term Mn exposure and when exposure was discontinued, liver enzymes were found to recovering different periods [3,29-32].Although, in our study, the levels of AST and ALT were high in Mn exposed group, they were found insignificant.

Conclusion

Testosterone is known to play a role in regulating the sexual activity, libido, social behaviors, cognitive functions, sleep control and wellbeing in males and females. We think that the effect of Mn exposure on the endocrine parameters needs to be reviewed in comprehensive studies which will also include the clinical reflections.

Competing interests
The authors declare that they have no competing interest

Financial Disclosure
The financial support for this study was provided by the investigators themselves.

Ethical approval
The Decision of the Ethical Committee of Ankara Keçiören Training and Research Hospital is available for the study.

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