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Evaluation of Liver Biochemical Parameters in Manganese Miners

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Abstract

***Background*:** Manganese (Mn) related jobs may cause manganism especially in miners. Side effects include neural and pathological disorders. In spite of liver is the main organ that filters Mn (99%) but few studies has performed about Mn toxicity in liver so no specific biochemical indicator is available (Gunnar). In this study, the relation between blood, urine and saliva Mn level and its hepatotoxic effects is evaluated.

***Materials and Methods*:** Blood, urine, saliva of 50 accidently selected miners collected in acid washed tubes for an experience study. Samples were used to evaluation not only biochemical parameters by pars azmoon kits but also Mn concentration by mass spectroscopy.

***Results*:** Manganese concentration in all miners in addition to blood AST, ALT, ALP increased significantly (p<0.001) related to controls. Miners with 10-15 years background had higher blood total, direct & indirect billirubin and ALP levels compared to others. Mn concentration in serum declined but in urine and saliva had no changes by working in mine. AST & ALT increased significantly in miners with 300 µg/L serum Mn concentration. Mn concentration in various samples and serum AST & ALT level were higher in native miners than non-native but in both not related to background.

***Conclusion*:** Significantly higher levels of billirubin, AST & ALT in miners compared to controls revealed Mn hepatotoxic effects in them. Also significant ALP increasing showed cholestasis in miners that supported by AST, ALT level. Significant billirubin, AST, ALT, ALP in miners with 10-15 years background revealed the importance of this period in miners liver check up. Higher Mn levels in different sources of native miners can be due to more environmental contact. Higher AST, ALT and lower ALP level in native miners indicate more hepatastoxic and less cholestasis and therefore arthrosclerosis and parkinson risk in these workers.

Introduction

Manganese is the 12th plenty element of the earth's crust. It is also a rare and essential element in plants and animals, so that human body needs 3-9 mg of it to grow properly [1, 2]. Manganese exists in the most of the body tissues like liver, pancreas, kidney and especially bones. Not only does manganese work as a cofactor for some enzymes like arginase, coline esterase, phosphoglucomutase, pyruvate carboxylase and most of phosphatases and peptidases, but also participates with vitamine B to make prothrombin. Its mineral form is used in Iron melting industries, alloys, steel, glass, dry batteries, ceramic and colors production and its organic form is used to prepare chemicals like pesticides, fuel additives, photography materials, MRI materials. To prepare Mn and make industrial use of it, should extract and inspissate the quarry [2, 3]. This operation leads to the production of dust containing Mn which can be dangerous for the health of the people who are expose to it [4, 5]. Although Mn for its less absorption and fast repelling, has less poisoning effects on human comparing with other metals and its acute poisoning is less observed, chronic entering Mn to the body more than usual amounts has some pathologic effects that are called manganism [6, 7]. Manganism is a forerunner and irreversible brain disease which its symptoms are like parkinson [8, 9]. Thanks to its small dimension, Mn can pass through brain-spinal barrier and gathers in the mitochondria of cells of some parts of the brain that controls movement actions, as their damage are predicted to be the result of oxidative effect of the free radicals produced by Mn. Because of this, the most manganism cases can be seen in the Mn miners [10-12]. Mn is repelled by faces, urine, milk, and sweat, but the main place to filtrate Mn is the liver (99%) so that after excretion in bile, it is finally repelled by feces [13-15]. In spite of the different researches which are done related to the repellence of Mn from body, this process is not clear yet [16]. Lots of studies are done about the neurotoxicity of the Mn and its effects on behavior changes [8,12], fertility [3, 17], humoral hoemostasis [18], calcium & iron uptake [19-21], serum lipoproteins [22-25], lipoprotein lipase activity [26, 27]. In high concentrations, Mn makes some disorders on fatty acids elongation and saturation in the liver [27-29]. It also leads to increase the liver lipids peroxidation [30, 31]. Studies show that cholesterol accumulation in brain and serum lead to read decreasing

[27]. On the other hand the low uptake of Mn leads to decreasing appoprotein and HDL synthesis in the liver [27]. Some other studies are done about the effects of Mn on it's liver pathology but there is no specific biochemical indicator for prediction and diagnosis of Mn toxic effects yet [13]. In this research has been tried to assess the probable relation between the Mn concentration in blood, urine and saliva of miners related to hepatotoxic effects of its particles

Materials and Methods

Sample gathering: To do this experimental applicatory research, we selected 25 persons of miners randomly. In the morning and before working, for two successive days, workers blood, urine and saliva were collected. At the same time, we gave them a questionnaire to file, obtaining miner's information such as age, background, pathologies, drugs etc. On the other hand the same samples of five health 25-40 years old men living in qom was collected and evaluated as control group. Samples were received in nitric acid and then distilled water washed glass tubes and transferred to Lab. in dry ice. Some of the prepared serum was used for biochemical parameters evaluation. The rest serums with urine and saliva samples were freezed in -20ºC until used for Mn assay by atomic absorption. Liver biochemical functional indicators such as total, direct and indirect billirubin, AST and ALT were measured by autoanalyzer and Pars Azmoon kits. Mn measurement: Mn was measured by VARIAN AA240 atomic absorption equipment [30]. Samples was thawed in Lab temperature, then for preparing a clear solution, 0.5 cc serum were mixed with 1.5cc nitric acid in capped tubes and put in the microwave at 200ºC for 10 minutes. Tubes were saved in 4°c. Standard curve was aligned by 0.02, 0.2, 2, 5 ppm manganese chloride [30, 31]. Data processing: prepared information was analyzed by ANOVA test using SPSS-11.5 software.

Results

Total data obtained of this research are presented in table 1 as data average and limits. Also differential data presented in compare with normal men and native miners and miners back ground. Mn and biochemical parameters concentration in biological fluids: according to results, no meaningful difference observed between serum total, direct and indirect billirubin concentration in control men and miners, although all values were higher in miners. Enzymes SGOT (serum glutamate oxaloacetate transaminase) (OT) and SGPT (serum glutamate pyruvate transaminase) (PT) showed meaningfull (p<0.001) elevation in miners. Also serum ALP (alkaline phosphatase) level had no significant (p<0.001) difference in miners related to control (Fig. 1). Liver injuries are supported by elevation of PT/OT. The higher Mn level in miners serum, saliva and urine observed in significant range (p<0.001) as was expected. Figure 1 shows these variations related to control men.

Biochemical parameters variation related to miners background: total, indirect and especially direct billirubin elevation in serum of miners with 10-15 yrs background was more considerable than other miners.

Also miners with 10-18 yrs background had higher serum alkaline phosphatase levels and miners with 13-15 yrs had significantly higher OT, PT and PT/OT level. Based on the results serum Mn level reduces with working in the mine but saliva and urine Mn level has no significant change. Also miners with 200-400 serum Mn have higher serum OT and PT levels. Manganese concentration and biochemical parameters differences between native and non-native miners: figures 2 to 4 show native miners have higher urine and saliva and especially serum Mn levels related to non-natives but both of them have the same diagram of changes with working in the mine. OT, PT and PT/OT in native and ALP in non-native miners have higher degrees but both have the same levels of serum different billirubin forms.

Table 1. Average and limits of collected datas

Number of Workers			50
Age (year)		Mean±SD	40.3958±2.4
		Range	30 - 66
Background		Mean±SD	14.85714±0.73
		Range	5 - 19
Manganase concentration	Serum(µg/L)	Mean±SD	307.6626±18
		Range	105.6995 - 611.399
	Saliva(µg/L)	Mean±SD	65.12953±5.8
		Range	30.05181 - 67.87565
	Urine(µg/L)	Mean±SD	45.45553±4.6
		Range	20.72539 - 88.0829
Total bilirubin (mg/dL)		Mean±SD	0.946735±0.24
		Range	0.4 - 2.8
Direct bilirubin (mg/dL)		Mean±SD	0.26898±0.09
		Range	0.11 - 0.53
Indirect bilirubin (mg/dL)		Mean±SD	0.677143±1.5
		Range	0.2- 2.37
AST (IU/L)		Mean±SD	32.52083±4.4
		Range	18- 49
ALT (IU/L)		Mean±SD	40.58333±5.1
		Range	14 - 97
ALT/AST		Mean±SD	1.212917±0.86
		Range	0.46 - 3.13
ALP (IU/L)		Mean±SD	247.1667±35
		Range	113 - 470

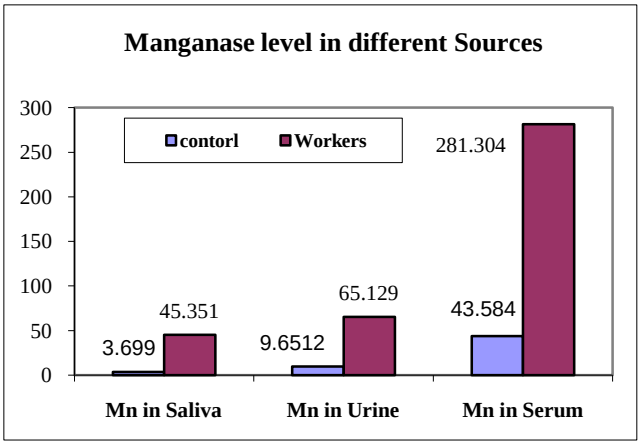

Figure 1. Serum, urine and saliva Mn levels of miners and normal men

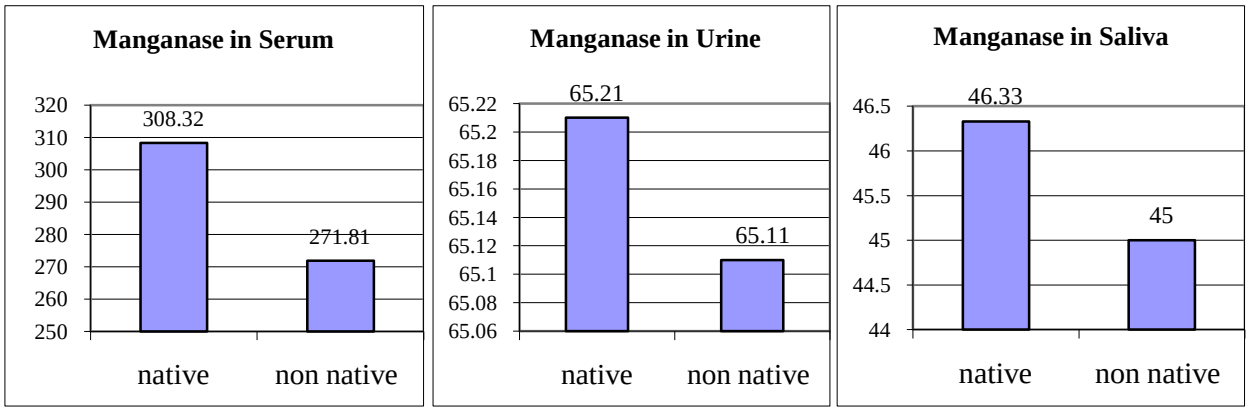

Figure 2. Serum, urine and saliva Mn concentration in native and non-native miners

Discussion

Results showed not only the hepatopathologic effects of Mn but also cholestasis parallel to working in Mn mines. More spread hepathotoxic effects in miners with 10-15 yrs background and native miners on one hand and less cholestasis and therefore less artherosclerosis, nerupathologic conditions and parkinsonism in native miners on the other hand revrale the relation between Mn effects and background and living near the mine. Also higher serum billirubin, OT and PT levels in miners related to controls confirmed hepatopathologic effects of Mn as Davis is mentioned [14]. Higher ALP level in miners serum was similar to Davis's results that emphesized on relationship between cholestasis and Mn accumolation in miners [14]. Because cholestasis can lead to liver injuries in long terms, hepatotoxic effects of Mn and then high OT and PT levels are predictable. Although various studies introduce Mn as a external inducer for lipids vacuole synthesis in hepatocytes, Roby [26] and Kawano et al. [25] eported hypocholestrolemia in order to lack of Mn. Amdur et al. [21] has introduced Mn as inducer of mevalonate kinase, Benedict et al. [22] as inducer of farnesyl pirophoaphate synthetase and they mentioned these enzymes as the reasons for hypercholestrolemia after accumolation of Mn. On the other hand Zwingmann et al. [16], Akoume et al. [20], Jonkins et al. [24] and Senturk et al. [27] have shown Mn can lead to bile duct closing and inhibition of bile acids transfer to gall bladder and accumolation of them in the liver lead to hypercholestrolemia.

On the other hand Senturk [27] suggested high cholestrol is the reason for toxic effects of Mn in brain. Also hypercholestrolemia can lead to higher artherosclerosis risk in the miners (Farrokhi). Pleban and Pearson [31] and Wang et al. [10] sentenced normal ranges of Mn is 2-8 µg/dl in serum, 0.1-0.8 µg/dl in urine and 1.2 µg/dl in CNF. As we expected and according to Pleban and Pearson results [31], Mn concentration in serum, urine and saliva of miners increased. Significant billirubin increasing in miners with 10-15 yrs, ALP in 10-18 yrs and AST and ALT in 10-15 yrs background as mentioned by Zwingmann et al. [16] is in order to hepato-billiary injuries and cholestasis of Mn.

Therefore hepato-billiary injuries in miners after 10 yrs working in Mn mines start and after 15 yrs reach to highest degree and then have a constant condition. Also although Mn concentration in urine and saliva had no changes, but eleated in serum with working in Mn mine. Wang et al. [10] has stated there are no direct relation between duration of working in Mn mine and parkinsonism rate. Higher levels of Mn in native miners can be relation to long term approximation and Mn receiving by water. Although higher serum AST, ALT and ALT/AST levels in native miners indicate wider liver injuries in them lower ALP levels lead to lower cholestasis and artherosclerosis and therefore parkinsonism risk, a cocept the native people refer to it: native miners more resistance. Based on results liver injuries and cholesthasis are happened in miners specially after 10-15 yrs working and therefore not only periodically medical chek up are recomended but also the place of miners working should be changed periodically. Also the evaluation of Mn effects on other organs such as kidney and bone marrow should keep in mind. This research has performed as a research project supported by IAU (Qom branch) and should say thanks to the persols that aided us.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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