THE EFFECT OF INCREASED MANGANESE CONTENT IN DRINKING WATER ON THE BALANCE OF SOME NEUROMEDIATORS IN CHILDREN

Name: Yuliya Koldibekova, PhD; Nina Zaitseva MD, PhD; Marina Zemlianova MD, PhD

FBSI "FSC for Medical and Preventive Health Risk Management Technologies", Perm, Russia

ABSTRACT

Quality of drinking water is becoming especially vital in industrially developed cities in Russia, USA, Germany as it exerts considerable influence on population health. Manganese (Mn) is among priority contaminants which pollute drinking water. We performed our research on samplings created as per randomized clusterization technique with approximated modeling strategy. Our samplings were made up of children aged 4-7 years who drinking water with increased Mn contents. Mn content assessment results revealed persistent occurrence of this metal in drinking water in quantities equal to 0.81 mg/l or up to 0.4 RfDcr. Chronic exposure of children population was characterized with daily Mn dose being up to 0.002 mg/(kg·day) introduced orally with drinking water. Approximately 2.000 children aged 0-14, were an exposed sub-population. We detected 1.3-1.4 higher average Mn concentration in blood of children from the focus group against the same parameter in children from the reference group and the reference level (p=0.0001-0.010). On the basis of a relevant model, an increased Mn content in the blood which was higher than the reference level was validated as an oral exposure marker. In assessing the biochemical parameters characterizing the balance of the neuromediators, an increase in glutamic acid and dopamine (excitation neurotransmitters) in blood serum of children from the focus group was found 1.4–1.5 times higher and a decrease in -aminobutyric acid (inhibiting neurotransmitter) was found 1.8 times lower than the same indicator in the control group (p=0.0001-0.001). We proved that increase in glutamic acid and decrease in -aminobutyric acid depended on Mn content in blood (OR = 3.4–4.5; 2.2 < DI > 5.8; p=0.0001–0.002; 0.64 < R2 > 0.80; p=0.0001). Chronic exposure to Mn in drinking water causes an increase in the incidence of diseases of the central nervous system in children (about 100 additional cases/1000 children) in the form of an astheno-vegetative syndrome, attention deficit hyperactivity disorder associated with external exposure of Mn to drinking water.

INTRODUCTION

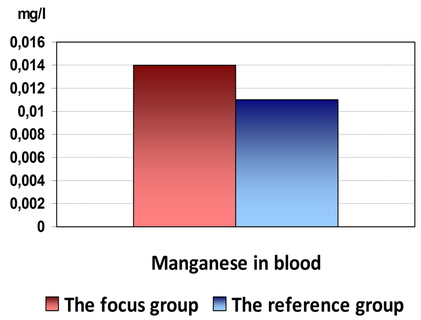
- Manganese (Mn) is the main indicator of water quality according to the requirements of sanitary norms of the Russian Federation, WHO, US Environmental Protection Agency [1, 2].
- In Russia an increased Mn content in drinking water samples of centralized water supply systems at the level of up to 3.6 RfDcr has been observed [2].
- According to World Health Organization there is a stable amount of manganese in groundwater and open water bodies at the level of 1 RfDcr in the United States and Germany [1,3].
- Mn is characterized by the development of specific effects of damaging action to central nervous system (CNS) [4]. Mn penetrates the blood-brain barrier, affects directly neurons, disrupts their metabolism and initiates lipid peroxidation of the cell membrane, damages astrocytes (glial cells), leads to glial dysfunction.
- Chronic manganese exposure to drinking water might increase CNS diseases in children.

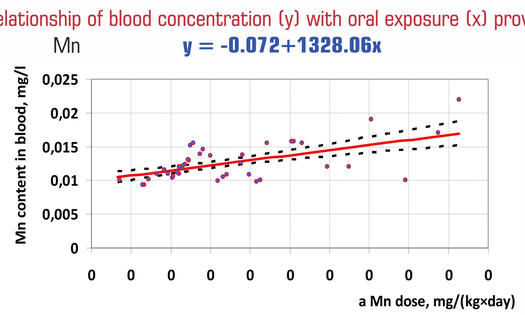
METHODS AND MATERIALS

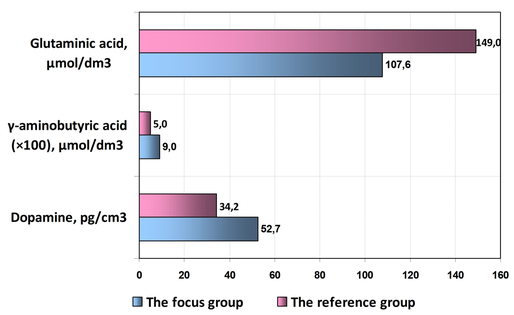
Hygienic assessment of drinking water quality according to manganese content	
Data from monitoring and actual studies ND14.1:2:4.139-98 "Quantitative chemical water analysis using Atomic Absorption Spectrometry"	▹ Observation area ▹ Comparison area ▹ Mn content in drinking water compared with RfDcr oral intake (RfDcr=0.14 mg/kg) according to Guidelines (R 2.1.10.1920-04).
In-depth examination of 204 children aged 4-7 years	
Observance of ethical principles in the Declaration of Helsinki (1975) with amendments of 2013 Russian National Standard "Good Clinical Practice" (ICH E6 GCP)	▹ **147** children constantly consuming drinking water with high Mn content in drinking water (focus group). ▹ **57** children living in the territory with satisfactory drinking water quality on Mn content (reference group).
Chemical and analytical blood study in children	
According to current Methodology Guidelines4.1.3230-14	▹ Mn in blood using inductively coupled plasma mass spectrometry.
Biochemical examination of children	
According to test systems: Glutamate Kit, GABA ELISA Kit, Dopamine ELISA Fast Track	▹ Glutamic acid in blood serum ▹ y-aminobutyric acid in blood serum ▹ Dopamine in plasma
Epidemiological and statistical study methods	
Fletcher R. Clinical epidemiology Glantz S. Medical and biological statistics	▹ Mathematical modeling ▹ Calculation of odds ratio (OR) and confidence interval (DI) ▹ Nonlinear regression analysis method

RESULTS

The assessment of manganese content in drinking water of the observation area has shown a stable amount of this metal at the level of 0.81 mg/l or up to 0.4 RfDcr. Chronic exposure of children in the observation area is characterized by an average daily Mn dose up to 0.002 mg / (kg·day), intaking orally from drinking water. About 2 thousand children aged 0 to 14 years presents exposed subpopulation. In children of the focus group, the average Mn concentration in the blood was 1.3-1.4 times higher than in the blood of children in the reference group and the reference level. Based on an adequate model of dependence, the increased Mn content in the blood respective to the reference level was proved as a marker of oral exposure. When assessing biochemical indicators characterizing the functional state of central nervous system, the neurotransmitter imbalance was established (an increase in glutamic acid level by 1.4 times, a decrease in γ-aminobutyric acid by 1.8 times and dopamine by 1.5 times respective to similar indicators in children of the reference group). The association of increased glutamic acid level and reduced γ-aminobutyric acid level in blood serum with Mn content in blood was determined (OR = 3.4–4.5; 2.2 ⩽ DI ⩾ 5.8; p=0.0001–0.002; 0.64 ⩽ R2 ⩾ 0.80; p=0.0001).







CONCLUSIONS

In children consuming drinking water with a stable amount of manganese at the level up to 0.4 RfDcr, it was found that the concentration of this metal in the blood is up to 1.4 times higher than the reference level and the same indicator in children of the reference group. The established dependence of manganese content in the blood on manganese dose in drinking water enabled to prove the increased manganese concentration in the blood as a marker of exposure. In children with increased manganese content in the blood the CNS neurotransmitter imbalance (an increase in glutamic acid level by 1.4 times, a decrease in -aminobutyric acid by 1.8 times respective to similar indicators in children of the reference group) was determined. The dependence of indicator deviation probability characterizing the state of excitation and inhibition in CNS in addition to increased manganese content in the blood was proved.

Contact Information

Yuliya Koldibekova

FBSI «FSC for Medical and Preventive Health Risk Management Technologies» Perm, Russia

Email: koldibekova@fcrisk.ru Website: http://fcrisk.ru/ Phone: +7 (342) 237-18-15

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