

Copper Concentration in Body Tissues and Fluids in Normal Subjects of Southern Poland

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Abstract Data on the concentration of the elements in the human body are important, for example, to estimate the amounts required to maintain a good healthy state or find their connections with morbidity and mortality. In this paper, the concentration of copper (by flame atomic absorption spectrometry) in material obtained from autopsy cases of nonpoisoned people ($n=130$), aged from 14 to 80 years, between 1990–2006, is presented. The following values were found (mean \pm SD in micrograms of copper per gram or per milliliter): brain 3.32 ± 1.50 ($n=43$), liver 3.47 ± 1.51 ($n=79$), kidney 2.15 ± 0.90 ($n=76$), stomach 1.10 ± 0.76 ($n=65$), intestines 1.54 ± 1.19 ($n=25$), lung 1.91 ± 1.30 ($n=27$), spleen 1.23 ± 0.28 ($n=3$), heart 3.26 ± 0.59 ($n=5$), bile 3.60 ± 1.67 ($n=13$), and blood 0.85 ± 0.19 ($n=73$).

Keywords Copper concentration · Autopsy tissue · Bile · Blood

Introduction

Copper is widely distributed in nature and is an essential element. It is a constituent of every tissue and is stored mainly in the liver, brain, heart, kidney, and muscles. Copper can be absorbed from the stomach to the distal small intestine (with typical diet, the average copper absorption is in the range of 30–40%). The distribution of copper throughout the body is mediated by ceruloplasmin, albumin, and other copper binders [1].

Copper is involved in many biochemical processes that support life. This trace element is essential for various enzyme systems (e.g., ferroxidases, cytochrome oxidase, superoxide dismutase, tyrosinase, and dopamine β -hydroxylase) and normal cell homeostasis. A finely balanced level of copper in the body is essential for health. Deficiency, excess intake, or disturbances in its metabolism lead to disease and toxicity [1–6].

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Disturbances in copper metabolism are found, for example, in Wilson's disease [2, 5, 7]. As a result of these disturbances, copper accumulates in excess amounts in the liver, the brain, the kidneys, the cornea, and other tissues, thereby damaging them [5–7]. Copper accumulation manifests itself in severe pathologies, including neurodegeneration, liver lesions, and behavioral abnormalities [3, 7]. Other disturbance of copper metabolism occurs in Menkes disease in which copper deficiency is associated with symptoms from the CNS, vascular tissues, and bones [6, 8, 9].

Excess intake of copper, as a result of exposure (e.g., dietary) or poisoning, also leads to elevated concentrations in internal organs and body fluids and detrimental effects on the body (e.g., liver damage, gastrointestinal disturbances, blood hemolysis, kidney failure, and, in severe cases, coma and death) [5, 6].

Data of the copper concentration in the human body are important to estimate the amounts required to maintain a good healthy state or to find their connections with morbidity and mortality. There is little data on current reference values for copper in the human body (internal organs, blood, and urine). The data reviewed are rather old and originate mainly from early papers from the 1960s to the 1980s [10–14]. Some earlier data may be burdened with analytical problems resulting, among other things, from the lack of biological reference materials, which are very important in the determination of trace elements [15].

The aim of this study was to evaluate the copper concentration in human tissues and body fluids of normal subjects in Poland.

Material and Methods

Copper, in human tissues and body fluids (blood and bile), of normal subjects was determined in autopsy material subjected to forensic examination at the Institute of Forensic Research, Kraków, Poland, between 1990 and 2006. The investigated group consisted of 130 nonpoisoned people (44 women and 86 men), aged from 14 to 80 years (mean±SD 33.6±18.0 years), who are inhabitants of southern Poland.

Determination of copper was carried out by flame atomic absorption spectrometry (SP-9 800 spectrometer, Pye Unicam, Cambridge, Great Britain). Before determination, samples of investigated material were digested (20 g of internal organs were digested by nitric and sulfuric acids in closed glass apparatus; 2 ml of blood or bile were digested by nitric acid and hydrogen peroxide in a microwave system). Suprapure quality concentrated acids from Merck (Darmstadt, Germany) and deionized water (obtained from apparatus supplied by Barnstead, Dubuque, IA, USA) were used in the analysis. Characteristics of the used analytical method were relative standard deviation 4.1%, at a concentration of 4.3 µg Cu/g wet weight; detection limit (three times the standard deviation of the mean of the blank) 0.024 µg Cu/g. The accuracy of the method was checked out through the use of standard reference material, bovine liver, 1577b (Gaithersburg, MD, USA).

Results

The results obtained for the concentration of copper in tissues, bile, and blood from autopsy material are presented in Table 1. The mean concentration of copper is less or more similar to median. Reference levels of copper found in biological material by some other authors are listed in Table 2 (tissues) and Table 3 (blood and bile).

Table 1 Concentrations of Copper (Arithmetic Mean±SD, Median, and Range [$\mu\text{g Cu/g}$ wet weight or $\mu\text{g Cu/ml}$]) in Internal Organs, Bile, and Blood in Normal Subjects of Southern Poland

Material	Number of Subjects	Mean±SD	Median	Range
Brain	43	3.32±1.50	3.11	0.67–7.51
Liver	79	3.47±1.51	3.20	1.10–7.70
Kidney	76	2.15±0.90	1.90	0.26–5.59
Stomach	65	1.10±0.76	1.00	0.24–4.87
Intestines	25	1.54±1.19	1.30	0.65–6.80
Lung	27	1.91±1.30	1.35	0.51–4.50
Spleen	3	1.23±0.280	1.25	0.94–1.50
Heart	5	3.26±0.59	3.38	2.64–3.86
Bile	13	3.60±1.67	3.28	1.30–7.36
Blood	73	0.85±0.19	0.83	0.57–1.31

Table 2 Normal Levels of Copper ($\mu\text{g/g}$ wet weight) in Human Tissues Found by Various Authors

Material	Parameters	Sumino et al. 1975 [12]	Iyengar et al. 1978 [13]	Versieck 1985 [14]	Lyon et al., 1989 [21]	Bem et al., 1993 [16]	Hamilton et al., 1994 [11]	Yoo et al., 2000 [18]
Brain	<i>n</i>	20	84					91
	Mean±SD	5.1±1.4						3.1±0.92
	Median	4.7						
	Range	2.9–8.4	5.0–10.6					
Liver	<i>n</i>	30	133		12	79	8	90
	Mean±SD	9.9±5.5	7.37		6.1±2.3	4.0±2.1	7.8±1.4 ^a	5.6±2.8
	Median	8.0						
	Range	2.1–23	3.2–10.6		3.2–9.7			
Kidney	<i>n</i>	29	221		12	79	8	88
	Mean±SD	2.6±0.28	2.95		2.2±0.4	2.6±2.5 ^b	2.1±0.4 ^a	1.8±0.54
	Median	2.6						
	Range	1.8–3.4		2.0–2.76	1.7–3.0			
Small intestine	<i>n</i>	26						
	Mean±SD	2.1±0.48						
	Median	2.1						
	Range	1.4–4.4						
Lung	<i>n</i>	30	102					87
	Mean±SD	1.3±0.24	3.1					0.97±0.57
	Median	1.3						
	Range	0.81–1.9	1.1–4.8					
Spleen	<i>n</i>	20	59					
	Mean±SD	1.2±0.23						89
	Median	1.1	2.62					0.88±0.42
	Range	0.83–1.7	0.80–8.67					
Heart	<i>n</i>	29	59		12			90
	Mean±SD	3.3±0.67	4.0		3.3±0.3			2.4±0.59
	Median	3.4						
	Range	2.2–4.6	1.9–4.4		2.9–3.8			

^aData from 1972–1973^bRenal cortex

Table 3 Normal Concentration of Copper ($\mu\text{g/ml}$) in Blood and Bile (mean, mean \pm SD, range) Found by Various Authors

Material	Iyengar et al. 1978 [13]	Haswell 1991 [23]	Hamilton et al. 1994 [11]	Tietz et al. 1995 [19]	Yoo et al. 2000 [18]	Piekoszewski et al. 2000 [24]	Barany et al. 2002 [20]
Blood	1.01 (0.64–1.8)	(0.70–1.27) ^a	1.20 \pm 0.020	(0.90–1.50) (0.80–1.55) ^a F (0.70–1.40) ^a M	0.97 \pm 0.46	1.11 \pm 0.12 ^a (0.90–1.32) ^a	0.95 \pm 0.1 (0.61–1.9) 1.1 \pm 0.2 ^a (0.55–2.6) ^a
Bile	1.18–6.20						

F = Female, M = male

^a Serum

Discussion

Copper concentrations in internal organs determined in this work for the adult human population are consistent, in general, with other published findings, but there are some differences, particularly in liver levels, which are slightly lower than those found by other authors, except for the concentrations found by Bem et al. [16]. Bem et al. found quite similar copper levels in liver and kidneys of the inhabitants of northeastern Poland. In the oldest papers [11–13], about twice higher copper levels in human liver are reported.

The examined material in this study originated from nonpoisoned subjects. Data on the copper concentration in tissues of exhumed cadavers, subjects with cirrhosis, or very young children were excluded from statistical analysis. In these cases the levels of copper were high. For example, the copper level in liver from an exhumed body was 9.69 $\mu\text{g/g}$, in liver with cirrhosis 13.5 $\mu\text{g/g}$, and in liver and kidney of a 2-month-old girl 33.2 and 5.59 $\mu\text{g/g}$, respectively.

Increased levels of copper in liver in young children, and in cases of cirrhosis, are also reported by other authors. Asseth and Morseth [6] give a level of about 30 $\mu\text{g/g}$ wet weight in liver of the newborn. According to Jonas et al. [17], the copper concentration in normal liver was 4.06 \pm 1.6 $\mu\text{g/g}$ wet weight ($n=8$), whereas in cirrhotic liver without Wilson's disease 12.69 \pm 5.5 $\mu\text{g/g}$ wet weight ($n=4$).

The mean blood concentration of copper in our study was 0.85 \pm 0.19 $\mu\text{g/ml}$, ranging from 0.57 to 1.31 $\mu\text{g/ml}$, and was somewhat lower than that given by Hamilton et al. [11], Iyengar et al. [13], Yoo et al. [18], Tietz [19], and Barany et al. [20].

When comparing data obtained by various authors, it is important to take into consideration that many factors can influence the concentration of trace elements in the body, e.g., age, state of health, living environment, and dietary habits [15, 21, 22]. Furthermore, effects because of the whole analytical procedure (sampling, determination, etc.) should also be taken into account. The differences mentioned above, between our results and the results reported by other authors, may be because of various investigated population and different analytical procedures. Moreover, some differences may originate from excluding results obtained from extremely high values (concerning exhumed cadavers, subjects with cirrhosis, or young children).

Conclusion

Copper concentrations in internal organs determined in this work for the adult polish subpopulation are consistent, in general, with other published findings. There are some differences, however, particularly in liver levels, which are slightly lower than those reported by other authors and even nearly twice lower than those given by authors of papers from the seventies and the eighties.

The mean normal blood concentration of copper was somewhat lower than that given by other authors.

The various factors (investigated population, analytical methods, and rejected extreme results) may influence the final results.

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