CORRELATION AMONG THE ROUTINE BIOCHEMICAL ANALYSIS DATA AND HAIR TRACE ELEMENT CONTENTS

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SUMMARY: On the point of view that elemental hair content can reflect the general physiological and pathological processes in organism the macro- and trace elements hair profiles, estimated by combination of ICP-AES and ICP-MS methods and routine clinical laboratory data in 120 middle-aged men and women before starting of rehabilitation courses in clinical sanatorium were compared. The largest correlation between hair element level and blood biochemical parameters for Ca, Mg and Se was revealed. Hair Ca was interconnecting with erythrocytes quantity, hemoglobin level, ALT, TG and VLDL index, Mg – with WBC count, ALT, TG and VLDL index and Se – with erythrocytes and monocytes quantity, AST, ALT level, serum Mg concentration, speed of erythrocytes sedimentation and prothrombin index.

Supposed, that the obtained data reflect the more or less close relations among the elemental status of human body, estimated by multielement hair analyses, and general physiological mechanisms of human health support.

Introduction

There were a lot of publications dedicated to the diagnostic use of human scalp hair multielement analyses in recent decades (Anke, Risch, 1979; Passwater, Cranton, 1983; Haaranalyze… 1987; Katz, Chatt, 1988; Skalny, Bykov, 2003 etc.). Some investigators tried to find any correlations among hair elemental content and different biochemical and physiological parameters including macro- and trace element concentrations in body fluids and their hair levels (Golubkina et al., 1996; Momcilovic et al., 2004; Skalny, 2005).

Hower till now there were limited and fragmentary data concerning investigations of constellations or correlations among the hair element analyses data and laboratory findings routinely used in clinical practice. Possibly, this fact reflects the prevalence of narrow view on biological significance of trace elements, "expecting of expected" results in investigators. Nevertheless, more wide researches can reveal a lot of interesting suggestions or denials, and these data can be very useful for understanding and clinical interpretation of hair elemental analyses.

Materials and methods.

Trace element profiles estimated by combined ICP-OES and ICP-MS methods (Skalnaya et al., 2004) and routine clinical laboratory data (such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), whole bilirubin, glucose, Ca, Mg, P, cholesterol, triglycerides (TG) and very low, low and high-density lipoproteins – VLDL, LDL, HDL levels, prothrombin index, blood cells count) was compared in 112 middle-aged men and women before starting rehabilitation courses in sanatorium.

Statistical calculations were made using Microsoft Excel XP application package.

Results and discussion.

It was established, that hair Ca level negatively correlated to erythrocytes count ($r = -0.27$, $p < 0.01$) and hemoglobin's level ($r = -0.25$, $p < 0.01$), ALT, TG, VLDL ($r = -0.27$, $r = -0.29$, $r = -0.28$, respectively, $p < 0.05$) (Fig. 1). So, hair Ca elevation can be associated with risk of anemia and disturbances of lipid metabolism. Increased hair Ca and decreased triglyceride levels occur with hyperthyroidism, hyperparathyroidism (Skalny, 1999; Fischbach, 2004). Low TG level can be due to low VLDL (80% of TG are in VLDL), which are major carriers of TG. Decreased VLDL can occur in hyperthyroidism and chronic anemias (Fischbach, 2004). Low hair Ca can correspond to increased RBC and Hb count (polycytemia, renal, pulmonary, cardiovascular diseases etc.), TG, VLDL (occur with hyperlipoproteinemia, liver and renal damage, hypothyroidism, poorly controlled diabetes mellitus, pancreatitis, myocardial infarction etc.), ALT level (usually reflects liver damage, biliary obstruction, pancreatitis, heart failure). It is known, that ALT level is higher in males (Fischbach, 2004) and this fact associates with lower hair Ca in males, as compared to females (Skalny, 2000). So, there are lots of data, which reciprocally suggest the same pathologic conditions.

Hair Mg content negatively correlated to WBC count ($r = -0.22$, $p < 0.05$) and TG, VLDL ($r = -0.25$, $p < 0.05$) and ALT ($r = -0.21$, $p < 0.1$) levels, similarly to hair Ca (Fig. 2). It supports numerous data, regarding

Erythrocytes quantity	⇦			
Hemoglobin level	⇦			
ALT	⇦	–	**Ca**	+
TG	⇦			
VLDL	⇦			

Fig. 1. Correlation between hair calcium level and routine biochemical parameters of blood

WBC quantity	⇦			
ALT	⇦	–	**Mg**	+
TG	⇦			
VLDL	⇦			

Fig. 2. Correlation between hair magnesium level and routine biochemical parameters of blood

on simultaneous increasing or decreasing of Ca and Mg in hair (Haaranalyze…, 1987; Pangborn, 1994). But the hair Mg level is not correlated to any red blood cell parameters in contrast to Ca. Elevation of Mg in hair is related to leukocytosis and a decrease of it can be related to leucopenia. It is interesting that a tendency to hyperglycemia decline while hair Mg decreasing ($r = -0.20$, $p < 0.1$). So, hair Ca, Mg can be some of good non-direct indicators of lipid status and related diseases, including liver damage, cardiovascular failures, pancreatitis, hyperthyroidism and hyperparathyroidism, and also erythro- (Ca) and leuko- (Mg) cytoses or penias.

It is interesting to declare the absence of any correlations between Fe content in hair and red blood parameters in contrast to white blood parameters. There were the relatively strong positive correlations to basophils and young neutrophils count ($r = 0.76$ and $r = 0.73$, $p < 0.001$), also to eosinophils count ($r = 0.30$, $p < 0.01$). Both basophils' and eosinophils' function is to combat allergic disorders and parasitic infections (infestations), neutrophils' function is to combat the pyogenic (bacterial) infections. So, it can be supposed that increased hair Fe can correspond to allergic and inflammatory predisposition, sometimes due to parasitic invasion, and liver damage (any metabolic intoxication including Fe overloading). We observed a similar combination in alcoholic patients (Skalny, 1990): increased hair Fe and increased transferrin saturation with Fe were combined with liver damage and inflammations. Also, it is known that increased transferrin saturation increases the susceptibility to bacterial infections.

The above-presented data are good corresponding to direct correlations between hair Fe and total bilirubin level ($r = 0.49$, $p < 0.001$), which allows to evaluate liver function and hemolytic anemia. Also, there were revealed negative correlations among hair Fe and serum Ca ($r = -0.43$, $p < 0.001$) or cholesterol ($r = -0.2$, $p < 0.1$) levels. Its can be associated to interelemental antagonism and well-known phenomenon of decreased atherosclerotic signs (atherosclerosis morbidity) in alcoholics, usually demonstrating elevated hair Fe.

Similarly to Fe data, the levels of Mn in hair were correlating significantly to white blood parameters such as basophils, young neutrophils, stab neutrophils and eosinophils ($r = 0.67$, $r = 0.60$, $p < 0.0001$, $r = 0.30$, $p < 0.01$, $r = 0.29$, $p < 0.001$). These data correspond to described participation of Mn in regulation of inflammatory, allergic, oxidative processes (Avtsyn et al., 1991; Ermidou-Pollet, Pollet, 1999; Biesalski et al., 2002).

Hair Zn was also negatively correlated to TG, VLDL ($r = -0.28$, $p < 0.05$, $r = -0.32$, $p < 0.01$), demonstrated the tendency to correlation to ALT and AST ($r = -0.20$, $p < 0.1$).

Hair Cu correlated positively to LDL ($r = 0.23$, $p < 0.05$), and non-significantly to cholesterol ($r = 0.22$, $p < 0.1$) levels in serum. 60 to 70% of the total serum cholesterol consist in LDL. LDL is the cholesterol-rich remnant of VLDL lipid transport vehicle. LDL is more prevalent in blood and it is mainly catabolized in the liver and possibly in nonhepatic cells as well. Degradation of VLDL is a major source of LDL (Fischbach, 2004). Elevated hair and blood Cu such as LDL or "bad cholesterol" are closely associated with increased incidence of atherosclerosis and CHD (Juchheim, 1991; Zimmermann, 2003; Skalny, Rudakov, 2004). Now the test of choice in CHD is LDL because it has a longer half-life as compared to VLDL and it is easier to measure (Fischbach, 2004). Except atherosclerosis and CHD there are some other clinical "similarities" between hair Cu and serum LDL levels: both are usually increased in hepatic obstruction or diseases, hypothyroidism, nephrotic syndrome, chronic renal failure, multiple myeloma, diabetes mellitus, some kinds of neuroses (Passwater, Cranton, 1983; Juchheim, 1991; Zimmermann, 2003; Fischbach, 2004 etc.), and decreased in chronic anemias, hyperthyroidism, inflammatory joint disease, severe hepatocellular disease. It is interesting to decline the controversial associations between hair Cu and Zn to lipids metabolism (one of suggestion of its functional antagonism).

Additionally, the negative correlation of hair Cu to the thrombin time (TT) ($r = -0.25$, $p < 0.05$) was revealed. It signs the possibility of Cu involvement in pathogenesis of anticoagulant defects. Both such Cu parameters and TT changes are typical for the same pathologies such as liver diseases, multiple myeloma, elevated hematocrit conditions, uremia (Passwater, Cranton, 1983; Avtsyn et al., 1991; Zimmermann, 2003 etc.).

As it was established in our investigation, hair Se level positively associates to RBC and monocytes count in blood ($r = 0.21$, $r = 0.30$, $p < 0.05$ and $p < 0.01$, respectively), ALT and AST activity ($r = 0.35$, $p < 0.01$, $r = 0.24$, $p < 0.05$), serum Mg concentration ($r = 0.23$, $p < 0.1$). A negative correlation to a white blood parameter (segmentoyadernie neutrophils) was revealed ($r = -0.22$, $p < 0.05$). Also, negative correlations to erythrocytes' sedimentation rate (ESR) ($r = -0.31$, $p < 0.01$) and prothrombin time (PT) ($r = -0.44$, $p < 0.001$) were found. In general, all these data evidently suggest the anti-inflammatory, antioxidant properties of Se, its protective role against liver damage, myocardial failure, rheumatic (systemic derangement of connective tissue) diseases (Oberleaset al., 1999; Golubkina et al, 2003 etc.) (Fig. 3).

According to obtained data, in cases of decreased hair Se we can expect the RBC, monocytes counts (monocytes' function is to combat severe infections by phagocytosis), elevated neutrophils (reflects pyogenic infections, inflammation, metabolic intoxications, chemical and drugs-caused tissue destruction, myeloproliferative disease, malignant neoplasms), ESR and PT. ESR is the rate at which erythrocytes settle out of

					⇨	Erythrocytes quantity
Erythrocytes sedimentation	⇦				⇨	Monocytes quantity
Prothrombin index	⇦	–	**Se**	+	⇨	AST
					⇨	ALT
					⇨	Serum Mg concentration

Fig. 3. Correlation between hair selenium level and routine biochemical parameters of blood

anticoagulated blood in 1 hour and this test is based on the fact that inflammatory and necrotic processes cause an alteration in blood proteins, resulting in aggregation of RBCs, which makes them heavier and more likely to fall. Increased ESR is found in all collagen diseases, rheumatoid arthritis, arthritis, polymyalgia rheumatica, hypo- and hyperthyroidism, gout, different infections and inflammatory diseases, carcinoma, lymphoma, neoplasms, heavy metal poisoning, cell or tissue destruction, myocardial infarction, nephritis, nephrosis, anemia, subacute bacterial endocarditis. Prothrombin is a protein produced by liver for clotting of blood. PT is one of the most important screening tests used in diagnostic coagulation studies. It directly measures a potential defect in extrinsic coagulation system through analysis of the clotting ability of 5 plasma coagulation factors (prothrombin, fibrinogen, factors V, VII, X). Conditions that cause increased PT include, for example, liver damage or disease, biliary obstruction, celiac disease etc. (Fischbach, 2004). So, this picture suggests that Se deficiency, reflected in decreased hair Se level, can "open the door" for severe infection, anemia, neoplasms, intoxications, myocardial necrosis, rheumatic, liver and renal diseases.

Also, low serum Mg reflects decreased action of numerous ADP-related enzyme systems, regulation of contraction of muscular tissue, neuromuscular irritability and the clotting mechanism. This is why its decrease also corresponds to Se deficiency and other observed parameters.

It is very interesting that increased hair Se, which occurs in some oncological diseases, severe liver damage and intoxications, skin diseases (Passwater, Cranton, 1983; Juchheim, 1991; Semikopenko et al., 2004; Skalnaya, 2005), correlated positively to ALT and AST levels, which are sensitive detectors of liver and heart failure, myocardial infarction. It suggests the necessity to differentiate clinical significance of low and high hair Se content, due to different causes: nutritional over- or underconsumption, or metabolic derangements, leading to increased elimination of Se, or tissue destruction and necrosis in severe damages, including congestion, cancer.

In case of As, an evident direct correlation between its hair content and thymol test ($r = 0.41$, $p < 0.001$), reflecting the liver damage (Nazarenko, Kishkun, 2002) was estimated. This fact corresponds to well-known As role as thiol poison very well. Also, at increasing of hair As the calcium serum concentration decreased ($r = -0.30$, $p < 0.05$). A decrease of serum albumin will result in a decrease in total serum Ca (Fischbach, 2004). Among the different reasons this situation is typical in reduced albumin level, hypoparathyroidism, hyperphosphatemia, due to renal failure or cytotoxic drugs, malabsorption, malnutrition and liver damage (toxic hepatitis, cirrhosis). At least some of these conditions can be caused by As overaccumulation.

An increase in hair Hg content correlated to elevated AST, ALT ($r = 0.44$ and $r = 0.37$, $p < 0.001$) and glucose ($r = 0.36$, $p < 0.01$) levels. This triad is possible in cases of advanced liver disease, myocardial infarction, pancreatitis, chronic renal disease, poisonings (Fischbach, 2004) and we can suppose the increased hair Hg in result of decreased activity of detoxification, or urinary elimination mechanisms in these conditions and excessive intake of Hg with fish etc.

Hair Pb content correlated only with young neutrophils count ($r = 0.32$, $p < 0.01$), similarly to Fe. But hair Cd, Cr, Al levels revealed no significant correlation to investigated parameters.

If assume the observed situation with potentially toxic elements and their correlations to routine laboratory tests, we can suppose current underestimation of clinical significance of even minimal rising of Hg and As in human hair.

So, the obtained data are a clear demonstration pro hair elemental analysis as a modern efficient diagnostic tool in permanent discussion, presented in literature (Anke, Risch, 1979; Haaranalyze.., 1987; Drasch, Roider, 2002; Bass et al, 2001; Zimmermann, 2003 etc.).

Our opinion is that the obtained data clearly demonstrate that hair analysis in cases of Ca, Mg, Fe, Zn, Cu, Mn, Se, As, and, possibly, some other elements, is a very useful source of knowledge for clinical practice and scientific investigations, reflecting long-term systemic derangements in human body.

Conclusion

So, it can be assumed that comparison of hair elemental analyses data and routine laboratory findings in patients with chronic diseases are reciprocally useful: it can influence on diagnostic validity of the medical investigation, to help in differential diagnostics of diseases relation to deficiency or excess of elements, to improve the understanding of pathochemical pathways of disadaptation, start and development of different diseases. Also, such approach, when used not only in case of hair, but other diagnostic samples, can find some new aspects of biological significance of macro- and trace elements.

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