Southern Adventist University [KnowledgeExchange@Southern](https://knowledge.e.southern.edu?utm_source=knowledge.e.southern.edu%2Fsenior_research%2F61&utm_medium=PDF&utm_campaign=PDFCoverPages)

[Senior Research Projects](https://knowledge.e.southern.edu/senior_research?utm_source=knowledge.e.southern.edu%2Fsenior_research%2F61&utm_medium=PDF&utm_campaign=PDFCoverPages) [Southern Scholars](https://knowledge.e.southern.edu/southern_scholars?utm_source=knowledge.e.southern.edu%2Fsenior_research%2F61&utm_medium=PDF&utm_campaign=PDFCoverPages)

2002

Concentrations of Hair Minerals Determined by Inductively Coupled Plasma-Mass Spectrometry in People with Headaches

Joel R. Mundall

Follow this and additional works at: [https://knowledge.e.southern.edu/senior_research](https://knowledge.e.southern.edu/senior_research?utm_source=knowledge.e.southern.edu%2Fsenior_research%2F61&utm_medium=PDF&utm_campaign=PDFCoverPages) Part of the [Medicine and Health Sciences Commons](http://network.bepress.com/hgg/discipline/648?utm_source=knowledge.e.southern.edu%2Fsenior_research%2F61&utm_medium=PDF&utm_campaign=PDFCoverPages)

Recommended Citation

Mundall, Joel R., "Concentrations of Hair Minerals Determined by Inductively Coupled Plasma-Mass Spectrometry in People with Headaches" (2002). *Senior Research Projects*. 61. [https://knowledge.e.southern.edu/senior_research/61](https://knowledge.e.southern.edu/senior_research/61?utm_source=knowledge.e.southern.edu%2Fsenior_research%2F61&utm_medium=PDF&utm_campaign=PDFCoverPages)

This Article is brought to you for free and open access by the Southern Scholars at KnowledgeExchange@Southern. It has been accepted for inclusion in Senior Research Projects by an authorized administrator of KnowledgeExchange@Southern. For more information, please contact [jspears@southern.edu.](mailto:jspears@southern.edu)

Running Head: HEADACHE

Concentrations of Hair Minerals Determined by

Inductively Coupled Plasma-Mass Spectrometry

in People with Headaches

by

Joel R. Mundall

Southern Adventist University

ABSTRACT

Calculations were made to determine what relationships exist between headaches and hair mineral levels of 1,995 hair tissue mineral analyses by inductively coupled plasma-mass spectrometry. Of the 1,995 samples (1,089 females, 906 males), 163 (100 females, 63 males) were taken from patients who had been diagnosed with headaches. Above average hair levels of bismuth and the earth metals were found among the both the males and females of the headache group. An age correlation analyses showed highest headache incidence in teens and early forties. A direct correlation was also found between calcium and magnesium levels, which peaked in the late twenties. Further study should be done to determine why these levels are elevated and what can be done to keep them balanced.

INTRODUCTION

According to the National Headache Foundation (NHF), more than 45 million Americans get chronic recurring headaches. This results in about 50 billion dollars of loss to industries from absenteeism and medical expenses each year (NHF, 2001). The quality of life of each person who gets headaches is affected and headaches are the ninth most common reason for a patient to consult a physician (Blanda, 2001). Unfortunately, even the medical profession is still looking for answers to the problem of headaches. The question of the fundamental causes of headaches remains to be answered.

There are about 150 categorizations ofheadaches, but the main headache syndromes as established by the International Headache Society in 1988 are the following: migraine, tensiontype headache, cluster, sinus, rebound, and menstrual (Evans, Fitzgerald, Morain, & Silberstein, 1998). About 90% of headaches reported to a physician are classified as either tension-type headaches (the most common type) or migraines. Tension-type headaches are so named because of the prior supposition that they were caused by tense muscles in the cranium. Because no research supports muscle contraction as always being the etiologic cause, the old names for this type of headache — muscular contraction headache and tension headache — have been replaced by the name ''tension-type headache" (Blanda, 2001).

There is still more to be discovered about the etiology of headaches. One such area of research deals with the role mineral imbalances may play in the pathogenesis of headaches. Some research has explored the role of ionized magnesium (Mg^{2+}) in headaches. The review by Paul Mason (1999) presents studies that have shown low magnesium (Mg) concentrations are present in people who get migraines or tension-type headaches. Those people also experience headache relief when given IMg^{2+} intravenously. The role of intracellular calcium (Ca) levels and

involvement of calcium-magnesium pumps in cells has also been investigated. One study has proposed some concern about the cases where Ca levels are high and the Mg levels are low (Marcus, Altura, & Altura, 2001). However, a high Ca^{2+}/Mg^{2+} ratio has not been found to be present among the tension-type headache group of another study (Mauskop, Altura, Altura & Cracco, 1996). Still, IMg^{2+} levels for each of the three main headache types are important, and especially for cluster headaches (Mauskop, et al., 1996).

Although the role of Ca and Mg in headache formation is not totally clear, the Ca channels appear to be involved. Because Ca is considered a second messenger, understanding of this role is essential to understanding how Ca channels play into headache formation. Mathews, Van Holde & Ahem (2000) described this role of Ca as a second messenger. In muscle and nerve cells, cAMP bears the signal for Ca to be let into the cytoplasm. In muscle cells, this release of calcium triggers muscle contraction. In nerves, influx of Ca through the presynaptic membrane triggers synaptic transmission. Because of the role of Ca as a second messenger to stimulate a cellular response, Ca channel blockers are used to reduce the pain signals being sent to the brain. Interestingly, Mg, which was given to some of the aforementioned headache patients, also functions as a Ca channel blocker through competitive inhibition (Swenson, 1996). These complexities make the earth metals great targets for study in order to better understand the biochemical level of headache formation.

There are many ways to examine the mineral levels in the body, including blood, urine, and hair analysis. Hair analysis has the advantage of showing the mineral condition of the body over a longer period of time than blood levels, which may fluctuate daily (depending upon dietary intake and the mineral involved) or may be so tightly regulated in the blood that serum tests show

almost no fluctuation (Markus, 1999). For identifying etiologic agents of a chronic ailment, getting data from a broader time window is helpful.

This study sought to obtain a better understanding of body mineral levels associated with headaches through identifying hair level anomalies. Because the prime use of hair mineral analysis is identifying body burdens of toxic elements, the concentrations of toxic elements (mainly, AI, Sb, As, Bi, Cd, Pb, Hg, U, Ni, Ag and Sn) were analyzed. Identification of gender, age and mineral-mineral relationships, in addition to headache to non-headache relationships, was also done in order to find any relevant information from those areas.

MATERIALS & METHODS

Population

All subjects of this study were patients of Connell Medical Center, located in Connell, Washington. Under the direction of Dr. Jon Mundall, hair samples were sent to Doctor's Data Inc. (DDI) for testing. All results from 1995 to 2001 were collected and compiled into a database along with some personal data like age, gender, diagnoses given at time of sampling, etc. The database contained the results of 1,995 hair analyses in which the average age was 47.8 years, with a standard deviation of 21.6 years. There were 906 male and 1,089 female entries in the complete data set. Of the 1,995 patients, 163 had been diagnosed with headaches. Of these 163 people, there were 63 males (average age: 39.2 yrs., standard deviation: 20.0 yrs.) and 100 females (average age: 40.3 yrs., standard deviation: 17.4 yrs.).

Hair Analysis

All of the hair samples of this study were sent to DDI, which uses microwave digestion followed by inductively coupled-mass spectrometry (ICP-MS) as described by staff of DDI (1998). DDI's reference ranges for normal and safe concentrations of hair minerals were established, according to the protocol published by NCCLS, using its patient data as well as an American healthy population study (DDI, 2001) and were used for comparison.

Calculations

Average, median, and standard deviation values were calculated for each mineral tested of each of nine groups – the entire set of data, those with headaches, those without headaches, all males, all females, headache males, headache females, non-headache males, and non-headache females. Outlying values, those values which were more than 1 ,000 times above the average or) 1 00 times above the next highest value, were removed from the data in order to remove suspected contaminations from environmental sources and improve the accuracy of the average values of some minerals. All data values below detection limits as well as outlying values were computed as being zero in the "AverageA" and "StDevA" functions, but were ignored in calculating the "Average" (see Appendix A). The "AverageA" calculation was used primarily and, except for in Appendix A, is the calculation being referred to when the "average" is mentioned. The coefficient of correlation was calculated to determine age-mineral and mineral-mineral correlations.

RESULTS

Toxic Elements

Except for bismuth (Bi), all of the concentrations of toxic elements of those with headaches were the same as or below the averages of the non-headache group (Table 1). Only Bi showed any considerable elevation with a median value of 0.0345 ppm, 1.28 times the median of the non-headache group. The median value of Bi among the headache group, although elevated, lay within the reference range established by DDI for Bi (< 0.06 ppm). The average, however, was 0.113 ppm, which exceeded the limit. This variation which caused this median-average difference was even more pronounced in the standard deviation, which was very large -0.252 ppm.

Gender Ratios

Due to gender differences, the mineral ratios were analyzed within each gender (Figures 3 and 4). The headache to non-headache ratios within each gender showed elevated earth metal concentrations among the headache group (about 10% higher) (Table 2). This was similar to the gender inclusive comparisons (Figures 1 and 2). However, women had much higher levels (almost double) of the earth metals and lower levels of the alkali metals as compared with men. Some other comparisons within each gender also yielded interesting fmdings. In the overall data set, the men had more than twice as high levels of antimony (Sb), boron (B), cadmium (Cd) and lead (Pb) (Table 3). Women, on the other hand, had much higher Bi levels. These gender ratios of Sb, B, Cd, Pb and Bi were similar in the headache and non-headache subsets

Age

An age analysis of the headache and non-headache groups showed a non-linear correlation between age and mineral levels (Figures 5 to 10). The incidence of headaches (the number of people with headaches divided by the total number of people) was also found to be non-linearly

associated with age when this calculation was performed for each five-year age range (Figures 5 and 6). Headaches occur most frequently among those of ages 10-14 years and 40-44 years. The maxima for Ca and Mg levels were directly between the ages of the peaks of headache incidence. Ca and Mg levels showed a similar pattern as headache incidence (Figures 5 and 6) and were higher in those with headaches (Figures 9 and 10).

Outside of Reference Ranges

Deviations from the reference ranges established by DDI were present in a few places. Only one element, germanium, was below its reference range of 0.045 to 0.065 ppm, with an average of 0.021 ppm. The average and median values of chromium (Cr), vanadium (V), and Mg of the females with headaches were above the top end ofDDI's reference range (Table 4). Ca of headache females, zinc (Zn) of all females, antimony (Sb) of all males and cadmium (Cd) of all males had average concentrations above the top of the reference range, yet had median values within the range.

Mineral-Mineral Correlations

)

A test for correlation between Ca and Mg yielded a correlation value of 0.765 for the headache group and 0.755 overall, and shows direct correlation (Table 5). The high levels of correlation that were found among the elements within each of the Group I and Group II families are also shown in Table 5. These correlations can also be seen in Figures 7 and 8.

DISCUSSION

It was expected that there would not be any one toxic element in high concentrations in the headache group because it is such a large group and headaches can be caused by a variety of conditions. However, the lack of any toxic element being greatly elevated above the reference

range or the non-headache group can be interpreted several ways. Either toxic elements are not involved, or if they are involved, they do not show up noticeably in the hair for one of three reasons. First, if toxicity were an etiologic factor, perhaps the toxin varies from person to person so that a single toxin does not show up as being elevated among the whole group. A second way that toxicity could be implicated although not seen in the results is by having a toxic cause that for some reason is not adequately represented in hair tissue. Elemental mercury (Hg) is exemplifies this possibility. Although its organic counterparts can be reliably measured in the hair, Hg concentrations in the hair do not accurately reflect the body burden of elemental Hg (Yamaguchi, 1975). Thirdly, toxic elements could still be involved through an oversight if the reference range is set too high or because the whole study group has elevated levels of that element which makes it appear "normal" to have hair levels in that range. Despite the large study group, a disproportional representation of the population is still possible, especially since the people in this study probably were tested because they had some form of chronic medical condition.

For similar reasons as those used to determine that toxin levels testing within normal ranges do not necessarily settle the issue that toxic elements are not involved, false positives cannot be ruled out either. In this study, Bi concentration was found to be elevated among women and those with headaches. However, the possibility of a false-positive cannot be rejected because it is difficult to know why the Bi levels are elevated. Further study should be done to determine the relevance of an elevated Bi concentration in the hair.

Elevated hair levels of earth metals, most importantly Ca and Mg, can be explained several ways. First, they may just indicate some form of metabolic stress. Though stress may not be the ultimate source of headaches, it is a trigger for their onset (Evans, et al., 1998). This explanation is rather broad, but it fits well with the broad range of possible headache causes. According to the

American Council for Headache Education (2001), research has shown that headaches are caused by an "electrical and chemical instability" in key brain centers that regulate blood flow in the head and neck and the flow pain messages to the brain. As far as the molecular pathogenesis of headaches, the results of this study coincide with other studies in that it points to the involvement ofCa and Mg levels, which are important in maintaining electrical and chemical stability.

Second, high Ca and Mg levels in the hair may not indicate high tissue levels. They could be blocked from entering cells, or be excessively pumped out of cells. Either way, the extracellular levels of these minerals would be elevated and lead to an increased amount being excreted in the hair. If this were toxin related, perhaps the blockage of the pathways of these minerals is caused by a toxic element. A second possible way that toxins could be implicated is through alteration of homeostatic equilibria (for example interfering with hormonal regulation). This could cause elevated hair levels, which possibly is at the expense of other body sources of these minerals. If either of these is the case, it is not hard to see how Ca and Mg levels could be elevated in the hair. It will require further study to test these possibilities.

The difference between the levels of earth metals and alkali metals between men and women demonstrates the differences in body chemistry that exist. Many gender differences are hormonally related, which perhaps would explain this difference as well. The elevated levels of Sb, B, Cd, and Pb among the men may have many implications. The reason for the elevation of these minerals in men should be investigated further, but perhaps it is just something simple. For example, men probably do more work in industries where they are exposed to these elements.

Deviations from the reference ranges could have multiple causes. The reference ranges could be erroneous. Stephen Markus (1999) suggested that hair Ca levels should be between 340 and 850 ppm. If this range were used, the median Ca level for females with headaches would lie

within the reference range. These phenomoma could also be caused if the subjects of this study were not adequate representatives of the overall population. Although the size of this study group is quite large, it is still possible because this group of people probably contains an overly high proportion of patients with chronic ailments.

Even when excluding the outlying values, the large standard deviation for most elements prevents direct clinical application in making diagnosis (Austin, 1999). Due to this problem, there is a big difference between the use of hair analysis for research and its use for clinical diagnosis of disease. Hair analysis is mainly effective for detecting heavy metal toxicity and is still quite limited for other diagnostic usage. This is partly due to a lack of research in this area, but mostly due to the widely overlapping results which limit its clinical use. Still, studies such as this may provide a better understanding of what can be learned from the analysis results, so the healthcare provider can work more knowledgeably. Despite the large standard deviations that make direct clinical application difficult, the fmdings of this study still have value.

The comparisons between age and mineral levels as well as between age and headache incidence showed some similarity. The peaks in the incidence of headaches did not exactly correlate with Ca and Mg levels. Perhaps they would be more closely correlated if there were more data for some of the age ranges. The results from the headache groups of ages 0-4, 5-9, 25- 29,30-34,55-59, and 60-64 should be considered as preliminary because there were fewer than ten people in each of those groups. Despite there not being a more clear correlation between Ca and Mg levels, the peaks in headache incidence did seem to be associated with periods of large hormonal changes (teens and early forties). These phenomena might also be related to something that happens in the teen years and has repercussions thirty years later. More research should be done to determine the cause of this age-mineral relationship. It is also interesting to note how this

data describes the aging process. There is the most Ca and Mg in the third or fourth decade of life, and then these levels descend throughout the remaining portion of life.

The mineral-mineral relationships, on the other hand, have been studied extensively. Being methodically arranged on the periodic table, one would expect the elements of a given group to have similar properties. This was indeed the case for the Group I and Group II elements in this study. From this perspective, a high Ca to magnesium ratio does not appear to be a problem. However, it is difficult to know what oxidation state the minerals are in before becoming built into the growing hair. If only ionic serum levels are relevant in headache formation, these hair data may be describing a condition that is distinct from the easy assumption that the body has too little or too much of a certain element. In other words, they could just be in a different oxidation state or be bonded to something else (methylated, for example). These mineral level deviations from normal homeostasis may reflect an altered homeostatic balance, possibly from hormone dysfunction. Here again, the Ca and Mg levels fluctuate together because the homeostatic balances are interconnected.

Ca and Mg levels are elevated, especially during the late twenties, among those who have tension-type headaches. The elevation might be due to a homeostatic unbalance, a problem of the parathyroid gland or of the body's ability to sense Ca concentrations. These mineral differences found in hair analysis still have limited clinical application until they can be explained by further research. The age and mineral maxima show a correlation with age and seem to be hormonally related. If these earth metals make a difference in headache formation, more research should be done to determine why they behave the way they do and what can be done to keep them balanced.

		Sb As			Bi Cd Pb Hg U Ni Ag Sn	
Average 0.934 0.811 0.767 1.484 0.724 0.713 0.804 0.901 1.187 0.475 0.492						
Median 0.854 0.766 0.783 1.300 0.847 0.813 0.752 0.972 0.923 1.000 0.923						

Table 1 Headache to Non-Headache Ratios of Toxic Elements. Only bismuth is elevated.

Table 2 There were elevated levels of Group II elements and lower levels of Group I elements among the headache group. The female to male ratios of those elements are similar to the headache to non-headache ratios.

Table 3 Except for Bi, males had much higher levels of most of these elements. The mineral level differences between the genders are quite noticeable for these elements.

Table 4 These elements exhibited averages that were outside of DDI's reference ranges.

١.

j.

Table 5 Coefficients of correlation of Group I and II elements showed high correlation among the members of each of these two families of elements.

Figure 1 Slightly low alkali earth metals among those with headaches.

Figure 2 There were elevated earth metals among those with headaches.

Figure 3 The female to male ratios of Group I elements shows that females had lower concentrations of these elements. This also exhibits a periodic trend.

Figure 4 The female to male ratios of Group II elements shows that females had higher concentrations of these elements.

y

Figure 5 The headache incidence was calculated by dividing the number of people with headaches by the total number of people in the database of the given age range. Headache incidence and Ca levels both peaked in the middle ages.

Figure 6 Both the percentage of people with headaches (headache incidence) and magnesium were nonlinearly associated with age and peaked in the middle ages. Mg levels and headache incidence trends are similar, especially above age 40.

Figure 7 This shows the earth metal concentrations throughout life of everyone in the database. Although there are some peaks, these levels remain fairly constant throughout life. In addition, this demonstrates the Ca-Mg correlation.

Figure 8 The earth metal concentrations throughout life of those with headaches are highest during the late twenties. These levels are much higher than average in the twenties and forties. This also shows the Ca-Mg correlation.

Figure 9 This shows the elevation of calcium among the headache group because both the headache and non-headache groups are plotted on the same scale.

Figure 10 This makes the elevation of magnesium among the headache group clear because the two groups are plotted on the same scale.

LITERATURE CITED

- Alberti, A., Gallai, V., Mazzotta, G., & Sarchielli, P. (1996). Electromyographical ischemic test and intracellular and extracellular magnesium concentration in migraine and tension-type headache patients. *Headache, 36,* 357-61.
- American Council for Headache Education. (2001, January 9). Retrieved April 22, 2002, from http://www .achenet.org/understanding/causes. php
- Austin, S., & Soloway, N. (1999). Hair mineral analysis. In M. T. Murray, & J. E. Pizzomo (Eds.), Textbook of Natural Medicine. 2nd ed. (pp. 159-164). New York: Churchill Livingstone.
- Blanda, M. (2001). Headache, Tension. eMedicine Journal, 2(7). Retrieved April 14, 2002, from http://www.emedicine.com/emerg/topic231.htm
- Doctor's Data, Inc. "Preparation of Hair for Measurement of Elements by Inductively Coupled-Mass Spectrometry (ICP-MS)", Biological Trace Element Research, Vol. 62, 1998
- Doctor's Data, Inc. *Review of JAMA Article on Hair Analysis.* (2001, January 08). Retrieved March 03, 2002, from http://www.doctorsdata.com/RESPONSE.HTM
- Evans, R. M., Fitzgerald, P., Morain, C., & Silberstein, S.D. (Eds.). (1998, October). JAMA Migraine Information Center. Retrieved April 14, 2002, from http://www.ama-assn.org/speciallmigraine/support/educate/types.htm
- Ferrari, M.D. (1998). Migraine. *Lancet,* 351(9108): 1043-51.
- Frompovich, C. J. (1982). *Understanding Body Chemistry and Hair Mineral Analysis.* Coopersburg, PA: C J Frompovich Publications.
- Gilliss, D., Kreutzer, R., McNeel, S., Seidel, S., & Smith, D. (2001). Assessment of Commercial Laboratories Performing Hair Mineral Analysis. *Journal of the American Medical Association, 285,* 67-72.
- Kaplan-Machlis, B., & Swain, R. (1999). Magnesium for the Next Millennium. *Southern Medical Journal, 92,* 1040-1047.
- Markus, S. (1999). Mineral status evaluation. In M. T. Murray, & J. E. Pizzomo (Eds.), Textbook of Natural Medicine. 2nd ed. (pp. 211-215). New York: Churchill Livingstone.
- Marcus, J. C., B.T. Altura, and B.M. Altura. (2001). Serum ionized magnesium in post-traumatic headaches. *Journal of Pediatrics,* 139(3):459-62.
- Mason, P. (Comp.). The Magnesium Web Site. (1999, February 19). Retrieved April 11, 2002, from http://www.execpc.com/~magnesum/migraine.html
- Mathews, C. K., van Holde, K. E., & Ahem, K. G. (2000). Biochemistry (3rd ed.). San Francisco: Benjamin/Cummings.
- Mauskop, A., Altura, B. M., Altura, B. T., & Cracco, R. Q. (1996). Intravenous magnesium sulfate rapidly alleviates headaches of various types. *Headache, 36,* 154-60.
- National Headache Foundation. Retrieved April 14, 2002, from http://www.headaches.org/presskit/NHFFactSheet.htm

Y

- Steindel, S. J. (2001). The Uncertainty of Hair Analysis for Trace Metals. *Journal of the American Medical Association, 285,* 83-85.
- Swenson, R. S. (1996). Is magnesium important in headache? JNMS: Journal of the Neuromusculoskeletal System, 4(3), 94-101.
- Yamaguchi, S., H. Matsumoto, S. Kaku, M. Tateishi, & M. Shiramizu. (1975). Factors Affecting the Amount of Mercury in Human Scalp Hair. *American Journal of Public Health,* 65(5), 484-488.

Appendix A

 \backslash

 $\big)$

Appendix A, part 2

 $\bigg)$

ÿ.

Appendix A, part 3

 $\bar{\lambda}$

 $\bar{\mathcal{J}}$

characteristics that make this ".^{4"} quality work.

 $\hat{\boldsymbol{\epsilon}}$

ğ,