3-1981

A study of hair zinc levels and intraocular pressure

Karen Fern
Pacific University

Debra Stoenner
Pacific University

A study of hair zinc levels and intraocular pressure

Abstract

Zinc is present in the metalloenzyme carbonic anhydrase which is found in the ciliary body and is involved in the production of aqueous humor. It is known that a reduction in carbonic anhydrase, via carbonic anhydrase inhibitors, lowers intraocular pressure. This paper investigates the possibility that chronic subnormal zinc nutriture may also decrease carbonic anhydrase activity and thus lower intraocular pressure. Ten subjects each having intraocular pressures < 10mm Hg, as measured by Goldmann tonometry, were selected from a normal clinical population. Ten control subjects, having intraocular pressures from 12-l?mm, were matched to the experimental group for sex and age. Hair zinc and other mineral levels were assessed for all subjects at the Parmae Laboratory in Dallas, Texas. Results indicate that there is no significant difference (at the .01 level) in hair zinc and other mineral levels for the experimental and control groups.

Degree Type

Thesis

Degree Name

Master of Science in Vision Science

Committee Chair

Diane P. Yolton

Subject Categories

Optometry

A STUDY OF HAIR ZINC LEVELS AND INTRAOCULAR PRESSURE

by
Karen Fern
Debra Stoenner

Advisor: Diane P. Yolton, Ph.D.

A Thesis Presented to the Faculty
of Pacific University in Partial Fulfillment of
the Requirement for the Degree
Doctor of Optometry

March, 1981

THESIS SUBMITTED BY

Karen Fern
Karen Fern

Debra Stoenner
Debra Stoenner

ACCEPTED BY

Diane P Yolton
Diane P. Yolton, Ph.D.

ACKNOWLEDGMENTS

The authors would like to extend appreciation and gratitude to Dr. Diane Yolton for her guidance, encouragement, and assistance in the conception and completion of this thesis.

We would like to thank Beta Sigma Kappa and the Oregon Optometric Association for their support and funding of this research project.

We would also like to thank Dr. Robert Yolton for his suggestions and assistance, especially in the "formative" stages of proposals and grant applications.

Special thanks to Marlys Gustafson, for her help with release forms, letters, etc. , and to Laurel Gregory for her assistance in the library.

ABSTRACT

Zinc is present in the metalloenzyme carbonic anhydrase which is found in the ciliary body and is involved in the production of aqueous humor. It is known that a reduction in carbonic anhydrase, via carbonic anhydrase inhibitors, lowers intraocular pressure. This paper investigates the possibility that chronic subnormal zinc nutriture may also decrease carbonic anhydrase activity and thus lower intraocular pressure. Ten subjects each having intraocular pressures ≤ 10mm Hg, as measured by Goldmann tonometry, were selected from a normal clinical population. Ten control subjects, having intraocular pressures from 12-17mm, were matched to the experimental group for sex and age. Hair zinc and other mineral levels were assessed for all subjects at the Parmae Laboratory in Dallas, Texas. Results indicate that there is no significant difference (at the .01 level) in hair zinc and other mineral levels for the experimental and control groups.

INTRODUCTION

The presence of zinc in living organisms and its role as an essential nutrient for plants and animals has long been recognized. However, its ubiquity in food makes it seem unlikely that sufficient zinc deprivation would occur to result in significant problems in human nutrition or clinical medicine. This attitude has now changed. Zinc deficiency in man was established in 1963 when Praasad and his co-workers reported on the causative relationship of this mineral to the occurrence of dwarfism and hypogonadism in boys in parts of the Middle East.[1]

In the past decade, zinc deficiency has been recognized in children in the United States.[2] The children were identified by very low concentrations of zinc found during a survey of mineral concentration in hair. These low hair zinc levels, in what were considered to be normal children, were associated with impaired taste acuity, poor appetite and low growth percentiles.

Zinc is an integral part of several metalloenzymes including carbonic anhydrase, alkaline phosphatase, lactic, malic, and glutamic dehydrogenases, and carboxypeptidase.[3] In addition, zinc acts as a cofactor in a variety of enzyme systems including DNA dependent - RNA polymerase, arginase, enolase, several peptidases, oxalactic decarboxylase and carnosinase.[3] It has become apparent that zinc is involved in a wide range of cellular activities and is vitally involved in fundamental

processes of RNA and protein synthesis and metabolism.

Recent attention has emphasized the importance of zinc for visual function.[4] The eye has some of the highest concentrations of zinc in the entire body, with the retina, choroid, and ciliary body having especially high concentration.[5,6] The high levels of zinc in these tissues are thought to be related to the activity of zinc dependent enzymes.[5] Underlying almost all the work on zinc metabolism is the concept that zinc deficiency results in decreased activity of a zinc related enzyme[7] which in turn may lead to clinical signs and symptoms.

For example, retinal dehydrogenase is a zinc dependent enzyme found in the retina; this enzyme converts retinol (vitamin A) to retinal (vitamin A aldehyde), which is necessary for rhodopsin formation. Rats fed a diet deficient in zinc were shown to have a decreased zinc concentration in the retina and a significant reduction of retinol dehydrogenase activity.[8] Humans with night blindness and documented zinc deficiency showed a return to normal dark adaptation threshold levels after treatment with zinc and vitamin A. Treatment with vitamin A alone resulted in no change.[9,10] Thus zinc deficiency can decrease the activity of a critical enzyme in the retina, with consequent manifestation of the clinical symptom of night blindness.

Another zinc-dependent enzyme that is found in red blood cells, gastrointestinal mucosa, kidney tubules and the ciliary body epithelium is carbonic anhydrase. Friedenwold, in 1949, first suggested that the carbonic anhydrase found in the ciliary body of the eye was involved in the formation of aqueous humor.[11] Wistrand and Garg maintain that the

processes of RNA and protein synthesis and metabolism.

Recent attention has emphasized the importance of zinc for visual function.[4] The eye has some of the highest concentrations of zinc in the entire body, with the retina, choroid, and ciliary body having especially high concentration.[5,6] The high levels of zinc in these tissues are thought to be related to the activity of zinc dependent enzymes.[5] Underlying almost all the work on zinc metabolism is the concept that zinc deficiency results in decreased activity of a zinc related enzyme[7] which in turn may lead to clinical signs and symptoms.

For example, retinal dehydrogenase is a zinc dependent enzyme found in the retina; this enzyme converts retinol (vitamin A) to retinal (vitamin A aldehyde), which is necessary for rhodopsin formation. Rats fed a diet deficient in zinc were shown to have a decreased zinc concentration in the retina and a significant reduction of retinol dehydrogenase activity.[8] Humans with night blindness and documented zinc deficiency showed a return to normal dark adaptation threshold levels after treatment with zinc and vitamin A. Treatment with vitamin A alone resulted in no change.[9,10] Thus zinc deficiency can decrease the activity of a critical enzyme in the retina, with consequent manifestation of the clinical symptom of night blindness.

Another zinc-dependent enzyme that is found in red blood cells, gastrointestinal mucosa, kidney tubules and the ciliary body epithelium is carbonic anhydrase. Friedenwold, in 1949, first suggested that the carbonic anhydrase found in the ciliary body of the eye was involved in the formation of aqueous humor.[11] Wistrand and Garg maintain that the

physiological role of carbonic anhydrase in the ciliary body of human eyes is to catalyze the hydration of CO_2 to ensure the rapid primary formation of bicarbonate ions.[11] Some authors then suggest that the primary event in the secretory process of aqueous production depends on the formation of these bicarbonate ions.[12] The work on carbonic anhydrase inhibitors such as acetazolamide further suggests that the formation and transfer of bicarbonate ions by carbonic anhydrase is important for aqueous production and maintenance of intraocular pressure. It is well known that acetazolamide (Diamox) causes a decrease in the rate of the formation of aqueous in glaucomatous and normal eyes by reducing the activity of carbonic anhydrase. This reduction in the rate of formation of aqueous leads to a lowering of intraocular pressure.[13] The presence of acetazolamide has been shown to decrease the rate of transfer of bicarbonate ions from the ciliary processes to aqueous. As a consequence, the rate of entry of water into the aqueous is diminished and the intraocular pressure is reduced.[12]

Research by Galin, Nano, and Hall has shown that when acetazolamide is given systemically, the ocular zinc concentration is unaltered in the ciliary body, where acetazolamide is known to exert a physiological effect.[5] However, the availability of the zinc for the protein moiety of the enzyme may be altered so that the enzyme activity is reduced even though the tissue content of zinc remains the same. It is also known that acetazolamide inhibition is reversable,

therefore one would not expect a quantitative change in zinc concentration, but rather a change in activity caused by an alteration in substrate site availability, polarity, or other factors. The carbonic anhydrase found on human erythrocytes is inhibited by a number of agents known to form complexes with metal ions; these agents are thought to act by combining with zinc.[14]

Carbonic anhydrase is a zinc dependent enzyme whose inhibition by acetazolamide results in a lowering of intraocular pressure. Chronic suboptimum zinc nutriture may cause a similar lowering of intraocular pressure through a decreased carbonic anhydrase activity due to a change in zinc availability.

Serum levels and hair analysis are two of the most frequently used techniques to determine zinc defiency. Hair analysis gives average mineral levels for a period of several months as opposed to blood chemical analysis which gives information related to a specific period in time. For the diagnosis of a chronic state of metabolic deficiency hair analysis is more informative. The second advantage of hair analysis is that hair mineral levels seem to reflect the intracellular concentrations while serum levels indicate extracellular levels.[15] Since most minerals are involved in intracellular functions, hair levels would be better suited to assess the levels of the minerals to determine if an excess or deficiency is occuring within the cells. This study attempts to evaluate the possible effects of chronic

sub-optimum zinc nutriture in the cells of the ciliary body; therefore hair analysis was selected as the diagnostic test. Thus to determine if low intraocular pressure is a result of low zinc nutriture, we measured the level of hair zinc in patients with low intraocular pressure found routinely in a normal clinical population and in patients with normal intraocular pressure. The analysis used to determine hair zinc levels in these patients also assessed the levels of other minerals found in the hair; these will also be reported.

METHODS

Subject Selection

The experimental group consisted of ten subjects with intraocular pressures of ≤10 mm Hg as measured by Goldmann tonometry. These subjects were selected from patients who had undergone complete visual exams at Pacific University Optometry Clinic, who exhibited intraocular pressures at or below 10 mm Hg, and who exhibited no ocular or systemic pathology. Testing consisted of confirming that the patients fulfilled the pressure criterion with remeasurement of intraocular pressure by Goldmann tonometry. After the low pressure criterion was confirmed, the patient's case history was updated to assure that the subjects were free of systemic disease and were not undergoing any nutritional supplementation for metabolic deficiencies. Direct opthalmoscopy and visual field testing were performed to help establish the absence of ocular pathology. A control gourp of 10 subjects consisting of patients and students at Pacific University College of Optometry, with normal pressures ranging from 12 to 17 mm Hg were matched to the experimental group for age and sex. Control subjects were screened for health and dietary supplementation in the same fashion as the experimental group.

Hair Analysis

Hair samples were obtained from all subjects using the

following technique. Approximately 3 grams of recent hair growth (within 2 inches of the scalp) were obtained from the sub-occipital region of the head. A pubic hair sample was obtained from one subject who had recently had a permanent. (Permanents may alter the results of hair analysis.) The hair samples were analyzed for zinc and other minerals using atomic absorbtion spectrophotometry by Parmae Laboratory, Dallas, Texas.

Several factors alter zinc levels in the hair. These include sex, age, hair color, distance of hair sample from the scalp, and bleaching, dyeing and permanent waving of the hair.[16,17,18,19,20] Schroeder and Nason found variations in zinc levels of different hair colors; blond hair was found to have relatively low concentration.[17] Attempts were made to minimize these variables by matching for sex and age, screening for bleaching, dyeing, and permanent waving, and using a standard technique for obtaining hair samples.

Data Analysis

Results from the low intraocular pressure and normal intraocular pressure groups were compared using a paired two-tailed t-test. A p value of .01 was used to determine significance.

RESULTS

The 12 female and 8 male subjects ranged in age from 22 to 36. The range of intraocular pressure in the test group was 7 to 10 mm Hg and the range in the control group was 12 to 17 mm Hg.

The results of analysis of the hair minerals is shown in Table 1. The mean zinc value for the low intraocular pressure group was 20 ± 7 mg%. The mean zinc value for the control group was 24 ± 13 mg%. There was no significant difference between the two groups at the .01 level. Comparison of hair levels of other minerals also showed no significant differences between the low intraocular pressure group and the normal intraocular pressure group.

DISCUSSION

Our results indicate that there is no significant difference between hair zinc levels in subjects with low intraocular pressure and with normal intraocular pressure. Several factors which may have influenced the results of this study warrant consideration and further investigation.

Perhaps only a very slight concentration change of zinc in the ciliary body is sufficient to alter enzyme activity; this change may not be reflected in hair levels. Several studies indicate that hair analysis is useful in the diagnosis of clinical zinc deficiencies or to evaluate dietary intake, but cannot be used to define the state of zinc metabolism or critical levels of intracellular zinc.[17,21,22] Deeming and Weber found that subtle zinc deficiencies in the diet of rats were not quantified in hair levels.[21]

Another consideration which may have contributed to the results is the regulation of carbonic anhydrase activity. Perhaps the concentration of zinc in the ciliary body is not the critical factor for carbonic anhydrase activity; alterations of zinc availability or "usefulness" to the enzyme, in the presence of adequate zinc concentration, may affect activity. It is also possible that other factors, unrelated to zinc, may be critical in regulating carbonic anhydrase activity. In either case, the zinc levels in the low intraocular pressure

group and the normal intraocular pressure group could be the same, but differential enzyme activity would result.

Other factors in the regulation of intraocular pressure may be reflected in the results of this study. The role of carbonic anhydrase activity in regulating aqueous humor production and affecting intraocular pressure has been documented. The fact that aqueous humor production is the critical regulating process in subjects with low intraocular pressure is another question. Structural variations which increase the efficiency and rate of aqueous outflow, such as larger pore size in trabecular meshwork, or greater surface area of the drainage network, may be responsible for the difference in intraocular pressure between the two groups.

A review of recent literature provides little information concerning trace elements and intraocular pressure. A study by Lane indicated that low hair chromium levels are significantly related to the level of elevation of intraocular pressure seen during sustained accommodative closework.[23] Results of our study show no significant difference in hair chromium levels between subjects with low intraocular pressure and those with normal intraocular pressure; however no attempt was made to control the accommodative response of the subjects during intraocular pressure measurement.

In summary, there was no significant difference in the hair levels of zinc and other minerals between subjects with low intraocular pressure and those with normal intraocular

pressure. Perhaps a more appropriate and informative test for zinc would be to assay the activity of serum alkaline phosphatase, a zinc requiring enzyme whose activity might be affected by small changes of intracellular zinc.[24] Further work is needed to determine if zinc and other minerals are critically involved in the production of aqueous humor and the maintenance of intraocular pressure.

REFERENCES

1. Sandstead HH, Prasad AS, Schulert AR, Farid Z, Maile A, Bassilly S, and Darby WJ: Human Zinc Deficiency, Endocrine Manifestations and Response to Treatment. Am J Clin Nutr 20: 422, 1967.

2. Hambridge KM, Hambridge C, Jacobs M, and Baum JD: Low Levels of Zinc in Hair, Anorexia, Poor Growth, and Hypogeusia in Children. Pediat Res 6: 868-874, 1972.

3. Underwood EJ: Trace Elements in Human and Animal Nutrition. New York, Academic Press, 1971, p 209.

4. Wong EK, Leopold IH: Zinc Deficiency and Visual Dysfunction. Metab Pediat Ophthal 3: 1-4, 1979.

5. Galin MA, Nano HD, and Hall T: Ocular Zinc Concentration. Investigative Ophthalmology 1: 142-148, 1962.

6. Racz P, Orgdon M: Determination of Zinc in Human Eye Tissues by Anode Stripping Voltammetry. Analytica Chemica Acta 75: 250-252, 1975.

7. Burch RE, Sullivan JF: Clinical and Nutritional Aspects of Zinc Deficiency and Excess. Medical Clinics of North America 60: 675-685, 1976.

8. Huber AM, Gershoff SN: Effects of Zinc Deficiency on the Oxidation of Retinol and Ethanol in Rats. J Nutr 105: 1486-1490, 1975.

9. McClain CJ, Van Thiel DH, Parker S, Badzin LK, and Gilbert H: Alterations in Zinc, Vitamin A, and Retinol-Binding Protein in Chronic Alcoholics: A Possible Mechanism for Night Blindness and Hypogonadism. Alcohol Clin Exp Res 3: 135-141, 1979.

10. Morrison SA, Russell RM, Carney EA, and Oaks EV: Zinc Deficiency: A Cause of Abnormal Dark Adaptation in Cirrhotics. Am J Clin Nutr 31: 276-281, 1978.

11. Wistrand PJ, Garg LC: Evidence of a High Activity C-type of Carbonic Anhydrase in Human Ciliary Processes. Invest Ophthalmol Visual Sci 18: 867-870, 1979.

12. Moses RA,ed.: Adler's Physiology of the Eye. St. Louis, CV Mosby Company, 1975, pp 219-220.

13. Becker B: Carbonic Anhydrase and the Formation of Aqueous Humor. Am J Ophthal 47: 342, 1959.

14. Vallee B: Biochemistry, Physiology and Pathology of Zinc. Physiological Review 39: 449, 1959.

15. Bland J: Hair Tissue Mineral Analysis: An Emergent Diagnostic Technique. Northwest Diagnostics, 1980.

16. McBean LD, Mohsen MS, Mahloudji M, Reinhold JG, and Halstead, JA: Correlation of Zinc Concentrations in Human Plasma and Hair. Am J Clin Nutr 24: 506-509, 1971.

17. Schroeder HA, Nason AP: Trace Metals in Human Hair. J Invest Derm 53: 79-83, 1969.

18. Deeming SB, Weber CW: Hair analysis of Trace Minerals in Human Subjects as Influenced by Age, Sex, and Contraceptive Drugs. Am J Clin Nutr 13:1175, 1978.

19. Briggs MH, Briggs M, and Wakatama A: Trace Elements in Human Hair. Experientia 28: 406, 1972.

20. McKenzie, JM: Alteration of Zinc and Copper Concentration of Hair. Am J Clin Nutr 31:470, 1978.

21. Deeming SB, Weber CW: Evaluation of Hair Analysis for Determination of Zinc Status Using Rats. Am J Clin Nutr 30: 2047, 1977.

22. Reinhold J, Kfoury G, and Arslanian M: Relation of Zinc and Calcium Concentrations in Hair to Zinc Nutrition in Rats. J Nutr 96: 519, 1968.

23. Lane, BC: Deficit Nutriture, Accommocative Stimulus and Ocular Hypertension. Presented at the American Academy of Optometry Annual Meeting. Dec 1980.

24. Kasarskis EJ, Schuna A: Serum Alkaline Phosphatase after Treatment of Zinc Deficiency in Humans. Am J Clin Nutr 33: 2609, 1980.

TABLE I: HAIR MINERAL LEVELS IN SUBJECTS WITH LOW IOP AND NORMAL IOP

	Mineral	Normal Range[1]	Subjects With Low IOP Mean ± SD	Subjects With Normal IOP Mean ± SD
Essential Minerals	Zinc	13 - 21 (M) 15 - 21 (F)	20 ± 7	24 ± 13
	Calcium	32 - 72 (M) 40 - 87 (F)	111 ± 118	183 ± 192
	Magnesium	3.2 - 7.2 (M) 6.0 - 10.0 (F)	12.9 ± 15.2	13.7 ± 14.9
	Sodium	19 - 62	15 ± 7	16 ± 4
	Potassium	16 - 46	8 ± 4	8 ± 4
	Copper	1.2 - 3.2	2.7 ± 2.4	1.6 ± 1.2
	Phosphorus	9 - 15	12 ± 3	12 ± 2
	Iron	1.8 + 4.5 (M) 2.7 - 5.5 (F)	1.8 ± .4	1.4 ± .9
	Manganese	.07 - .23	.25 ± .07	.17 ± .05
	Chromium	.04 - .08	.06 ± .02	.04 ± .02
	Nickel	.15 - .45	.23 ± .06	.33 ± .13
	Selenium[4]	.04 - .12	.03 ± .01	.03 ± .01
Toxic Minerals	Arsenic[4]	.01 - .03	.01 ± .003	.01 ± .00
	Mercury[4]	.01 - .20	.08 ± .04	.10 ± .04
	Cadmium	.01 - .15	.09 ± .05	.06 ± .02
	Lead	.1 - 2	.5 ± .3	.4 ± .1
Other Minerals[5]	Aluminum	.01 - 2.0	.63 ± .24	.71 ± .28
	Silicon	.08 - .25	.15 ± .11	.13 ± .04
	Cobalt	.04 - .16	.08 ± .04	.09 ± .04
	Lithium	.01 - .03	.01 ± .003	.01 ± .00

1. As determined by Parmae Laboratory, Dallas, TX.
2. All levels in mg %.
3. M - Males; F - Females.
4. Nine pairs - data not available for one subject.
5. Essentiality - toxicity not well documented.