

MAKING SENSE OF THE HAIR ZINC LITERATURE: WHERE DO WE GO FROM HERE?

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SUMMARY

The authors make a critical review on the hair zinc literature, discussing the main contributions in this field. Certain explanations, as well as some solutions aimed to put an end to the confusion which exists on this matter are suggested.

As a first step, it is recommended that only endogenous zinc in hair be reliably measured. Therefore, the zinc metabolic status should be operationally defined in function of the zinc detected in hair. Each one of the variables should thus be identified, quantified and controlled. It must be added that these variables would have to include differences in zinc metabolism. Only then would it be possible to see the real baseline reference value of hair zinc.

At present researchers should begin looking for a functional relation and not just a statistical significant association between hair zinc concentration and zinc metabolic status. At the same time, it would be necessary to ratify and prove findings of the great number of studies reported in the paper, through the replication of studies with experimental animals.

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INTRODUCTION

In 1966, a study by Strain *et al.* (1) indicated that zinc supplementation increased the mean zinc content of hair in a group of Egyptian dwarfs already clinically diagnosed as suffering from a zinc deficiency syndrome (2). Let it not be understood that the two mean zinc levels compared were measured from the same group of dwarfs before and after a therapeutic intervention. There were actually an untreated group of 10 individuals, and a treated group of eight individuals, and these two groups had four individuals in common. With such a small number of cases, where a series of individual curves might have shown some functional relation between increase in zinc content of hair and amount of zinc supplementation, group statistical analysis was used. The very highly significant, non-chance result spurred a great interest in the use of hair zinc as a measure of systemic zinc deficiency.

Authors have found evidence to support (3-12) and to question the use of hair mineral data as an indicator of zinc nutritional status (13-19). No consensus has been reached after 20 years of research. This paper aims to highlight some principal contributions to the field, and to suggest some reasons for and solutions to the confusion which exists.

OCCURRENCE OF ZINC IN HAIR

One of the reasons researchers are so interested in hair zinc is the ready availability of samples. No special training is necessary to collect hair samples, there is no risk and the subject feels no pain. Samples can be cheaply and easily preserved. What are some of the characteristics of zinc occurrence in hair?

The origin of zinc in hair is complex, arising from endogenous and exogenous sources. According to Hopps (20), endogenous sources include the hair matrix, sebum, epidermis and secretions from eccrine and apocrine glands. Zinc, more concentrated in subcutaneous tissues, occurs in relatively large amounts in keratins (21) and keratin-like structure where it is intrinsic to the development of -S-S- linked substances (22). Accumulation of zinc from endogenous sources is irregular (23), and although the zinc originated from hair follicle is firmly bound (24, 25), some of the endogenous zinc can be lost (26, 27).

Zinc is absorbed into hair from several exogenous sources including aqueous solutions, shampoos, cosmetics and external medications (28-33). Acting as a strongly basic anion exchanger, hair's sorption capacity seems to be higher for zinc than for other elements (34), and appears to be more related to its surface than to its matrix (35). Although zinc is distributed evenly across the hair shaft (36-38), it is more concentrated towards the extremity away from the root (28-31). While this seems to mean that longer exposure leads to continuous accumulation of exogenous zinc, others have not found such differences in hair of normal (33) or zinc-deficient individuals (39, 40).

Since only endogenous zinc could reflect zinc nutrition, considerable interest has been shown in anagen hair fibers (41), root analysis (42), specific root bulb (43), i.e., initial and later stages of hair formation, standardization of analyses (44) and washing procedures to remove exogenous zinc from hair (45-50). Unfortunately, it is impossible to remove exogenous zinc without also reducing zinc from endogenous sources (26, 27).

Hair zinc is some of what is left over after the body has used the zinc it needs. Individual needs vary and are determined by multiple factors. Nevertheless, unless this intervening process is somehow able to be quantified, the relation between hair zinc and zinc nutrition will probably remain obscure.

WHAT IS ZINC NUTRITIONAL STATUS IN RELATION TO HAIR ZINC?

The hope of most investigators has been to demonstrate that hair zinc is a valid indicator of zinc nutritional status. Individuals suffering from certain pathological conditions whose symptoms abate with zinc therapy do seem to have lower hair zinc values than healthy people (39, 51-55). Hair zinc in these cases, however, is an unnecessary diagnostic tool, as the clinical symptoms will characterize the syndromes in question. The real goal must then be to use hair zinc to identify those cases of individuals who are not sick but who would be even better off if they had more (or less?) zinc.

How can we operationally define zinc nutritional status in these people? What is hair zinc supposed to indicate anyway? Will hair zinc tell us if a person has ingested regularly the minimum daily requirement of zinc? It seems unlikely since dietary zinc has had no association with hair zinc in infants (56, 57), children (58), adults (59), the elderly (60, 61), vegetarian women (62) nor in people consuming high-zinc food (63). The only exception was the study of McDonald, Gibson and Miler (64). Experimental studies have further shown that dietary zinc does not exert any marked effects on radio-zinc in hair (65). Also enterally taken extra zinc and iron in blood transfusions which significantly increase iron in dermal and epidermal tissues (precursors of hair follicle) failed to show any alteration in zinc levels (66).

Will hair zinc tell us if the zinc content of other body tissues is within normal limits? Most studies in humans have shown no association between hair zinc and zinc in other organs (67), body fluids and secretions (31, 40, 59, 62, 63, 67-81). Even the comparison of different types of hair in the same individual has not produced consistently positive correlations (82-85). Moreover, the amount of hair zinc in newborns could not be predicted from maternal hair zinc (86, 87).

Since severe zinc deficiency is characterized by stunted growth, it might seem logical to conclude that a kind of relation might exist between hair zinc and physical growth. Indeed numerous

investigators have sought out this correlation. No association between growth and hair zinc was found in some instances (77, 88-90). In other cases (53, 91, 92) positive associations were revealed. Chen Xue-Cum *et al.* (53) reported a very significant ($r = 0.227$; $p < 0.002$) positive correlation between hair zinc and height for age in Chinese children. Although this relation was significant, that is, there was only a very small probability of it having occurred by chance, hair zinc explains less than 5% of the variance in growth among these children.

Two other studies claim that hair zinc explains a much greater part of the variance in growth (91, 92). Gentile, Tetralange and Coleman (92) computed a multiple r of 0.895 for hair zinc regressed on height, weight and age in female children. It is not clear whether the absolute heights and weights were used, in which case they would certainly be confounded with age (range 2 to 20 years) in this very small group. Buzina *et al.* (91) found a positive correlation of $r = 0.952$ between hair zinc and relative height for age in 103 children. This finding is striking, since when we consider the multitude of variables which could contribute to growth in height, we find that a single hair mineral explains 90%.

Has experimentally manipulating zinc intake been shown to alter hair zinc? For ethical reasons only animal studies of experimentally induced zinc deficiency have been performed. Among the species studied - including rats (93-99), cattle (100), monkeys (101-103) and birds (104) - a decrease in hair and feather zinc was observed. Experimentally increasing zinc intake in humans has increased hair zinc in healthy subjects of various ages (56, 105-108) as well as in cases of acrodermatitis enteropathica (51), suspected zinc deficiency (39, 52, 53, 55) and in children recovering from malnutrition (54). No dose-response gradient was observed; however, hair zinc increments seemed to be higher (32-100%) in cases of suspected zinc deficiency than in normal children and adults (23-44%). Some other studies, also involving healthy people (108-111), uremics (112), and patients with acrodermatitis enteropathica (113, 114) did not confirm increments of hair zinc after zinc supplementation.

CONFOUNDING VARIABLES

A myriad of factors have been associated with the amount of zinc in hair. These include exposure to zinc in the environment (37, 63, 115-118), changes in seasons (1, 58 75), geographical location (40, 83, 116-129), hair color (130), age (17, 131), sex (see Table 1), undernutrition, reproductive status, and several pathological conditions (see Table 2). Variability in diet, including independent effects of vitamins (68), and other metals (56, 131), also alter the amount of zinc in hair.

TABLE 1

BACKGROUND INFORMATION ON CHANGES IN HAIF ZINC, COMPARING SEXES

Sex (Male)	Increase	No change	Decrease	References
Children		X		Klevay, 1970 (135)
"		X		Baumslag <i>et al.</i> , 1974 (82)
"			X	Creason & Svendsgaard, 1975 (84)
"	X			Gershoff <i>et al.</i> , 1977 (68)
"		X		Erten <i>et al.</i> , 1978 (73)
"			X	Heinersdorf & Taylor 1979 (136)
"			X	Hambidge <i>et al.</i> , 1979 (58)
"		X		Terai <i>et al.</i> , 1979 (137)
"		X		Gibson & DeWolfe, 1979 (138)
"		X		Gibson & DeWolfe, 1979 (139)
"			X	Gibson & DeWolfe, 1980 (140)
"			X	O'Leary <i>et al.</i> , 1980 (102)
"			X	McDonald <i>et al.</i> , 1982 (64)
"	X			Padron, Herrera <i>et al.</i> , 1983 (102)
"		X		Kauf <i>et al.</i> , 1984 (142)
Adults			X	Coleman <i>et al.</i> , 1966 (143)
"		X		Reinhold <i>et al.</i> , 1966 (123)
"		X		Shroeder & Nason, 1969 (144)
"		X		Klevay, 1970 (135)
"		X		Petering <i>et al.</i> , 1971 (145)
"		X		Creason <i>et al.</i> , 1975 (37)
"	X			Baumslag & Petering, 1976 (146)
"	X			McKenzie <i>et al.</i> , 1978 (147)
"	X			Ohtsuka & Suzuki, 1978 (148)
"			X	Deeming & Weber, 1978 (59)
"			X	Ryan <i>et al.</i> , 1978 (47)
"		X		McKenzie, 1979 (63)
"			X	Reilly & Harrison, 1979 (149)
"			X	Burke <i>et al.</i> , 1981 (150)
Adults		X		Anke & Schneider, 1962 (151)
Elderly		X		Greger & Sciscoe, 1977 (60)
"		X		Wagner <i>et al.</i> , 1980 (152)

TABLE 2
BACKGROUND INFORMATION ON CHANGES IN HAIR ZINC
COMPARING CONTROL WITH CONDITIONS ASSOCIATED WITH
ZINC METABOLISM IN MAN

Condition	No Increase change Decrease	Reference
<i>Reproductive status of women</i>		
Pregnancy	X	Klevay, 1970 (135)
"		X Briggs <i>et al.</i> , 1972 (153)
"		X Hambidge & Droegmuller, 1974 (154)
"		X Bergmann, <i>et al.</i> , 1980 (87)
"	X	Vir <i>et al.</i> , 1981 (155)
Lactation		X Baumslag & Petering, 1976 (146)
Multiparous		X Baumslag <i>et al.</i> , 1974 (82)
"	X	Anderson <i>et al.</i> , 1981 (62)
Children of	X	Gibson & DeWolfe, 1979 (139)
----- <i>Undernutrition</i>		
Undernutrition		X Briggs <i>et al.</i> , 1972 (153)
"	X	Amador <i>et al.</i> , 1975 (156)
"		X Amador <i>et al.</i> , 1976 (157)
"	X	Erten <i>et al.</i> , 1981 (73)
"	X	Dorea <i>et al.</i> , 1982 (103)
"		X Dorea <i>et al.</i> , 1982 (104)
"		X Dorea <i>et al.</i> , 1983 (158)
"		X Bencomo <i>et al.</i> , 1983 (54)
"		X Rodríguez <i>et al.</i> , 1985 (159)
"		X Xue-Cun <i>et al.</i> , 1985 (53)
Undernutrition recovery	X	Bradfield <i>et al.</i> , 1969 (160)
"	X	Bradfield <i>et al.</i> , 1980 (161)
"		X Hambidge <i>et al.</i> , 1974 (122)
"	X	Burger & Hogewind, 1974 (162)
----- <i>Growth failure</i>		
Short stature		X Solomons <i>et al.</i> , 1976 (163)
Achondroplasia		X Collip <i>et al.</i> , 1979 (164)
Small-for-age	X	Moser <i>et al.</i> , 1982 (165)
Poor growth		X Xue-Cun <i>et al.</i> , 1985 (53)

TABLE 2. Continued

Condition	Increase	No. change	Decrease	Reference
<i>Debilitating diseases</i>				
Renal failure		X		Condon & Freeman, 1970 (69)
"		X		Mahler <i>et al.</i> , 1970 (166)
"			X	Mahajan <i>et al.</i> , 1979 (167)
"		X		Blendis <i>et al.</i> , 1981 (78)
"			X	Siegler <i>et al.</i> , 1981 (168)
Nondialyzed			X	Mountokalakis <i>et al.</i> , 1979 (169)
Dialyzed			X	Mountokalakis <i>et al.</i> , 1979 (169)
Cancer		X		Addink & Frank, 1962 (170)
"		X		Shneider & Anke, 1966 (171)
"			X	Lin <i>et al.</i> , 1977 (172)
Celiac disease			X	Amador <i>et al.</i> , 1977 (173)
"			X	Rodriguez <i>et al.</i> , 1985 (159)
Achrodermatitis enteropathica			X	Amador <i>et al.</i> , 1975 (156)
Cystic fibrosis			X	Jacob <i>et al.</i> , 1978 (174)
"		X		Mitchell <i>et al.</i> , 1980 (76)
Diabetes			X	Amador <i>et al.</i> , 1975 (175)
Liver cirrhosis			X	Prasad <i>et al.</i> , 1970 (176)
Indian childhood cirrhosis			X	Gupta <i>et al.</i> , 1978 (177)
Sickle cell disease			X	Prasad <i>et al.</i> , 1976 (178)
Systemic illness			X	Eminians <i>et al.</i> , 1967 (40)
<i>Organ-Mental Diseases</i>				
Mental retardation		X		Pihl & Parkes, 1977 (179)
Multiple sclerosis		X		Ryan <i>et al.</i> , 1978 (47)
"		X		Holzbecher & Ryan, 1982 (180)
Down's syndrome		X		Barlow <i>et al.</i> , 1981, 1985 (181,182)
"		X		Barlow, 1983 (183)
Functionally delayed		X		Moser <i>et al.</i> , 1982 (165)
Autistic children		X		Shearer <i>et al.</i> , 1982 (184)
"		X		Wecker <i>et al.</i> , 1965 (185)
Alzheimer-type Dementia		X		Shore <i>et al.</i> , 1984 (186)
Dyslexic		X		Capel <i>et al.</i> , 1985 (187)
<i>Drugs</i>				
Insulin	X			Schneider & Anke, 1966 (171)

TABLE 2. Continued

Condition	No.		Reference
	Increase	Decrease	
<i>Drugs</i>			
Insulin	X		Amador <i>et al.</i> , 1975 (175)
Antimalarials		X	Briggs <i>et al.</i> , 1972 (153)
Oral contraceptives		X	Briggs <i>et al.</i> , 1972 (153)
"			Deeming & Weber, 1978 (59)
"		X	Vir & Love, 1981 (80)
"			Vir <i>et al.</i> , 1981 (155)
Hypertension-controlling		X	Greger, 1977 (61)
Methyltestosterone	X		Castro-Magaña <i>et al.</i> , 1981 (188)
Growth hormone	X		Cheruvanky <i>et al.</i> , 1982 (189)
Anticonvulsants		X	Ikeda <i>et al.</i> , 1983 (190)
Deferoxamine		X	Rea <i>et al.</i> , 1984 (191)
<i>Other Conditions</i>			
Thermal burns		X	Pories <i>et al.</i> , 1966 (192)
Hyperglycemic coma		X	Shneider & Anke, 1966 (171)
Hyperthyreosis		X	Shneider & Anke, 1966 (171)
Beta-Thalassemia		X	Dogru <i>et al.</i> , 1979 (193)
"		X	Rea <i>et al.</i> , 1984 (191)
Hypertension	X		Medeiros & Pellum, 1984 (194)
Premenstrual tension syndromes		X	Hanson <i>et al.</i> , 1985 (195)
Spina bifida	X		Fehily <i>et al.</i> , 1984 (196)
"		X	Fehily <i>et al.</i> , 1984 (196)
Diaper rash		X	Collip <i>et al.</i> , 1985 (197)
Friedreich's disease	X		Barbeau <i>et al.</i> , 1985 (198)
Aspartylglycosaminuria		X	Van Langevelde <i>et al.</i> , 1985 (199)

Another confounding factor has been the morphological changes in hair-root formation due to malnutrition (132) and the slow rate of protein synthesis shown to occur specifically in the protein of skin and hair during zinc deficiency in rats (133) and man (18, 134).

Tables 1 and 2 summarize the results of the principle. Careful scrutiny of these conflicting results confuses one but at the same time serves to illuminate the basic research question: how to quantify and control for all these effects in order to see any real association between hair zinc and some operationally defined measure of zinc nutritional status?

The problem of interspecies research with hair zinc further illustrates this question. There have been inconsistent results regarding the relation of zinc in skin appendages with zinc in other organs (93-99, 101, 102). It could be alleged that differences in hair growth (20, 200-202) and in the incorporation of metals during anagen and telogen phases are responsible for a lack of generality in findings. This would not be so once the differences between species have been identified, quantified and controlled for. The more consistent results of studies with rats compared to humans are more likely due to greater control over confounding variables in rat experiments than, for example, a result of greater variability in hair zinc *per se* in humans (30).

CONCLUSIONS

To be coherent and meaningful, what directions could future research take? A good first step would be to reliably measure only endogenous zinc in hair. Next, zinc nutritional status should be operationally defined; in other words, what is hair zinc supposed to indicate. Then, one by one confounding variables should be identified, quantified and controlled. These would have to include differences in zinc metabolism. It would then be possible to see the real baseline value of hair zinc.

At this point, investigators could begin looking for a functional relation and not just a statistically significant, or non-chance, association between hair zinc and zinc nutritional status. The generality of findings would be shown through the replication of studies within and between species.

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RESUMEN

ANALISIS DE LA LITERATURA SOBRE EL ZINC EN EL CABELLO ¿CUAL ES EL PROXIMO PASO?

Los autores hacen una revisión crítica de la literatura sobre los estudios del zinc encontrado en el cabello, anotando las principales contribuciones al respecto. Sugieren ciertas explicaciones, así como algunas soluciones con miras a terminar con la confusión existente a este particular.

Se recomienda que el primer paso es medir con confiabilidad solamente el zinc

de origen endógeno. Por consiguiente, el estado metabólico del zinc debe ser operacionalmente definido en función del zinc detectado en el cabello. De esta forma, cada una de las variables tendría que ser identificada, cuantificada y controlada. Esas variables, cabe agregar, deberían incluir las diferencias en el metabolismo del zinc. Solamente así podrá obtenerse el valor referencial básico del zinc encontrado en el cabello.

En la actualidad, los investigadores deberían buscar la relación funcional y no solamente el significado estadístico entre la concentración del zinc en el cabello y el estado metabólico del mismo. A la vez, habría que ratificar y comprobar los hallazgos del gran número de estudios de que se da cuenta en este trabajo, mediante la repetición de estudios de experimentación en animales.

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