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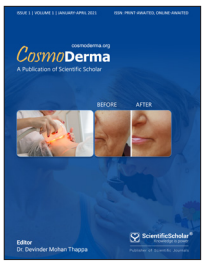

Perspective

Controversies of micronutrients supplementation in hair loss

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ABSTRACT

Hair loss is a common problem causing significant psychosocial impact in the affected individuals. Supplementation of micronutrients in various combinations is commonly practiced by dermatologists for hair loss. Even though the micronutrients are essential for hair growth, their exact role in the pathogenesis of hair loss is controversial. Therefore, in the absence of documented deficiency, the role of supplementing these micronutrients is debatable. It may rather lead to toxicities and unintentional medical consequences. Due to inadequate evidence supporting the role of micronutrients in hair loss, further research is recommended to bridge the gaps in our knowledge. This perspective discusses the role and controversies in using various micronutrients in hair loss.

Keywords: Micronutrient, Hair loss, Supplements

INTRODUCTION

Micronutrients are vitamins and minerals required in small quantities by the body, but their deficiency can cause a significant impact on our health. Hair follicles being a high turnover structure require a good supply of nutrition for proliferation. Although micronutrients help in hair growth, their exact role in hair follicle function is poorly understood. Patients with hair loss are often prescribed hair supplements by physicians and dermatologists. As hair loss is a distressing condition, patients often self-medicate themselves.[1,2] Unsupervised use of certain micronutrients can cause toxicity. Thus, in this perspective, we shall discuss the role and controversies in the use of micronutrient supplementation in hair loss. The review will cover the following headings:

1. Physiology/pathomechanism of micronutrients in hair growth
2. Existing evidence of micronutrients use in hair loss
3. Screening of micronutrients and interpretation
4. Laboratory interferences in micronutrients
5. Toxicity of micronutrient supplementation
6. Regulations for supplements
7. Treatment.

PHYSIOLOGY/PATHOMECHANISM OF MICRONUTRIENTS IN HAIR GROWTH

Vitamins

Fat-soluble vitamins

The role of vitamin D in the hair cycle has been demonstrated in animal studies. Murine hair follicle cells in the anagen stage have the highest activity of vitamin D receptor (VDR). Knockout mice, homozygous for a VDR mutation, developed hair loss three months after birth. Vitamin D also plays a role in immune regulation and anti-inflammation. Due to its immunomodulatory action, its role in alopecia areata (AA) is of particular interest.[3] Vitamin A deficiency causes telogen effluvium (TE) and hair fragility. Retinoic acid receptor dimerizes with VDR and has a role in the hair cycle. It is important for anagen initiation.[2] Vitamin E being an antioxidant has a theoretical role in the management of hair loss, which is supported by oxidant-antioxidant imbalance in the pathogenesis of AA.[4]

Water-soluble vitamins

Among vitamin B complex, riboflavin, biotin, niacin, folate, and B12 deficiencies are related to hair loss. Vitamin B2 (Riboflavin), as a component of coenzymes flavin mononucleotide and flavin adenonucleotide, plays a role in cellular function. The B12 and folate are essential for nucleic acid production and thus play a role in highly proliferative cells of hair follicles. Biotin as a cofactor of carboxylase enzyme plays a role in cell signaling and gene regulation.[4] Vitamin C enhances intestinal iron absorption. Animal studies show the role of vitamin C in the hair follicle cycle by increasing insulin-like growth factor-1 in dermal papilla promoting hair shaft elongation.[2]

Minerals

Iron deficiency impairs the proliferation of hair matrix cells due to high ferritin demand. Some studies indicate that various hair follicle genes are regulated by iron.[2] Zinc plays a role in the hedgehog signaling pathway, which is essential for hair morphogenesis. Selenium is a cofactor of glutathione peroxidase, which is a potent antioxidant. Animal studies have revealed hair loss in rats deficient of selenium and knockout mice lacking a protein for selenium cofactor demonstrated hair loss.[5]

Fatty acids

Unsaturated fatty acids may modulate androgen action by inhibition of 5α-reductase, similar to the drug finasteride. Omega-6 fatty acid promotes hair growth by enhancing follicle proliferation.[1]

EXISTING EVIDENCE OF MICRONUTRIENTS USE IN HAIR LOSS

*Levels of Evidence and Grades of recommendation are taken from "Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009)." The link is given below

https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009

Vitamins

Vitamin D

In a systematic review and meta-analysis conducted by Lee *et al*.,[6] mean serum vitamin D level was significantly lower in cases of AA compared to healthy controls (Level 3a). The role of topical vitamin D analogs in the management of AA was promising but inconsistent. Studies correlating the association of vitamin D levels and female pattern hair loss (FPHL) or TE were small and provided contradictory results. Large randomized controlled trials are needed in non-scarring alopecia before making recommendations.[3,4]

Vitamin E

One study has shown tocotrienol supplementation improved hair loss compared to the placebo group (Level 2b). There were conflicting results in studies evaluating serum vitamin E levels in AA. One study showed decreased serum vitamin E levels in cases compared to controls whereas the other study showed no such association. Hence, there is little or no evidence supporting vitamin E supplementation in hair loss in the absence of deficiency.[7]

Biotin

In a review of biotin supplementation for hair loss, only 18 case reports were found, and all these cases had either inherited or acquired causes of biotin deficiency, which was controlled with supplementation (Level 5). The efficacy of biotin supplementation in the absence of deficiency in the management of hair loss was not demonstrated.[8]

Folate and B12

Two case–control studies conducted in Turkey reported no significant differences in serum folate and B12 levels between AA cases and healthy controls (Level 3b).[9] In a cross-sectional study, only 2.6% of the subjects with TE had B12 deficiency and none had folate deficiency.[10] However, a study done in New York showed significantly lower levels of vitamin B12 in TE patients with dysesthesia (TED) compared to patients with only TE. The TED patients had hair growth after vitamin B12 supplementation (Level 3b).[11] Hence, there is inadequate evidence in support of these vitamins' supplements in patients with only hair loss.

Table 1: Existing evidence on iron supplementation in alopecia.

Trost *et al*., and Pierre *et al*.[12] - Review	Iron deficiency may be related to TE, AGA, and AA All these studies were conducted in women and in non-scarring alopecia Improvement in hair growth will be seen if the patient's serum ferritin is maintained above 70 ng/mL.
Olsen *et al*.[13]	Iron deficiency is common in females but not increased in patients with FPHL and CTE compared with controls (Level 3b)
Gowda *et al*.[14]	Higher proportion of patients with TE had iron deficiency than in FPHL or MPHL but not significant (P=0.069). Iron deficiency was significantly associated with female gender rather than the type of alopecia
Deo *et al*.[15] in India	Neither low hemoglobulin nor low serum ferritin level were significantly associated with TE or FPHL
Case-control studies conducted in Iran[16]	No difference in iron status in AA patients compared to controls (Level 3b)

TE: Telogen effluvium, AGA: Androgenetic alopecia, AA: Alopecia areata, CTE: Chronic telogen effluvium, FPHL: Female pattern hair loss, MPHL: Male pattern hair loss,

Minerals

Iron

The evidence of iron supplementation in hair loss is depicted in Table 1.

Zinc

A cross-sectional study found 9.6% of subjects with TE had zinc deficiency.[10] In a case-control study comparing zinc levels in patients with AA, androgenetic alopecia (AGA), and TE, low zinc levels were seen in AA and TE.[17] In another case–control study, no difference in zinc level was found between CTE cases and controls.[18] Hence, there is conflicting evidence in support of zinc deficiency and hair loss.

Selenium

Two studies demonstrated alopecia and hair depigmentation in patients receiving total parenteral nutrition due to selenium deficiency, which was reversed after many months of selenium supplementation.[19,20] In a single case–control study in ovarian cancer patients receiving chemotherapy, selenium supplementation along with other micronutrients decreased hair loss and gastrointestinal symptoms (Level 2b).[21]

SCREENING OF MICRONUTRIENTS AND INTERPRETATION

Routine screening is not required for patients presenting with hair loss if there are no risk factors. The screening tests and their interpretation in patients with risk factors are shown in Table 2.[2]

LABORATORY INTERFERENCES IN MICRONUTRIENTS

Biotin supplements interfere with certain immunoassays utilizing biotin-streptavidin technology [Table 3]. Hence,

Table 2: Screening of micronutrients in high-risk patients and their interpretation.

Tests	Risk factors	Interpretation
Serum ferritin	• Premenopausal women • Malabsorption • Achlorhydria • Vegans • Vegetarians	• The cutoff value of serum ferritin for detecting iron deficiency varies widely in the literature. • Optimal ferritin level for hair regrowth ranges from 40 ng/L to 70 ng/L
Serum-25 (OH) vitamin D2	Less sun exposure, dark skin	Optimal level – 30 ng/mL and deficiency below 20 ng/mL
Serum zinc	• Malabsorption • Malignancy • Alcoholism, Valproic acid drug intake • Vegetarians	• Lower normal limit – 10.7 mmol/L • Functional effects of deficiency may be observed before serum levels decrease below normal
Biotin	• Ingestion of raw egg whites • Prolonged antibiotic usage	• Plasma biotin level is not a reliable marker of biotin deficiency • Measuring urinary excretion of biotin and estimating biotinylated carboxylates in lymphocytes is recommended
Serum selenium	• Areas with low selenium soil content • Long-term hemodialysis • HIV • Malabsorption	A serum level of 120–160 μg/L of selenium represents the normal range

Table 3: Micronutrients causing laboratory interferences.

Micronutrient	Mechanism of laboratory interference	Deranged laboratory assay
Biotin	Serum biotin competes with biotinylated reagents for the binding sites on streptavidin reagents in Biotin-streptavidin based immunoassays creating false-positive or false-negative results	• TSH, FT3, FT4, testosterone, progesterone, vitamin B12, prostate specific antigen, LH, and FSH • FDA released safety alert in 2017, after a patient's death due to heart attack after falsely low troponin levels due to biotin interference. • Recently, some HCG devices are prone to biotin interference and false negative results
Ferritin	Elevated in systemic inflammation/infection as acute phase reactant	To rule-out false-negative results, ESR and CRP levels can be tested

TSH: Thyroid-stimulating hormone, FSH: Follicle-stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine, LH: Luteinizing hormone, HCG: Human chorionic gonadotropin, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, FDA: Food and Drug Administration

Table 4: Manifestations of micronutrient toxicity.

Micronutrient	Manifestations of toxicity
Vitamin A	Pruritus, scaling, fissuring of lips, sore tongue, brittle nails, diffuse alopecia, liver failure, and increased intracranial pressure
Vitamin E	Mucosal bleeding and reduced thyroid hormone production
Selenium	Massive hair loss, skin blistering, and gastrointestinal problems
Zinc	Abdominal pain, diarrhea, vomiting, interaction with iron, and reduced immune function

detailed history taking should be done before ordering such assays. Interpreting serum ferritin also needs attention, as the levels can be elevated in inflammation, infection, and malignancy masking iron deficiency.[2,4]

TOXICITY OF MICRONUTRIENT SUPPLEMENTATION

Unsupervised micronutrients intake can sometimes lead to toxicity especially fat-soluble vitamins [Table 4]. Vitamin A intake more than 10,000 IU/day can cause vitamin A toxicity and hair loss.[4] Apart from fat-soluble vitamins, excess consumption of trace elements can also lead to toxicity. Selenium toxicity (>400 mcg/day) will also result in massive hair loss. Acute adverse effects of excess zinc intake are pain, vomiting, and diarrhea. Chronic effects include interaction with iron and reduced immune function. Even continuous iron supplements can also lead to toxicity if unmonitored.[2,4]

REGULATIONS FOR SUPPLEMENTS

Many popular branded hair supplements declare their product as "not for medicinal use" in their product label. There are no regulations for monitoring their products (including Food and Drug Administration). Unregulated companies can take advantage of the vulnerable population.

Table 5: Treatment recommendations in various micronutrient deficiencies.

Iron	• In iron deficiency – Elemental iron 100–200 mg/day • Continue treatment three to six months after correction of iron deficiency • Concomitant treatment with ascorbic acid 500–1000 mg/day/L-lysine 1000 mg/day may improve the iron absorption • Dietary sources – Lean meat, seafoods, beans, lentils, spinach, and dark chocolate
Vitamin C	Vitamin C supplementation plays a role in hair loss secondary to iron deficiency. Dose: 500 mg–1 g/day
Vitamin D	• In deficiency – 60,000 IU of cholecalciferol (D3) weekly for one to three months • Maintained with 500–1000 IU of oral vitamin D to prevent recurrent deficiency • Dietary sources – Fatty fish, fish liver oil, egg yolk, mushrooms, and fortified dairy products
Biotin	Not recommended for hair loss patients except in case of inherited or acquired deficiency
Vitamin A	2,00,000 IU single dose every four to six months
Zinc	Elemental zinc 2–3 mg/kg/day

Hence, the onus is on the treating dermatologists to carefully prescribe these supplements.

TREATMENT

Treatment should be given to the patients only with documented nutritional deficiency. The following table summarizes dosing regimen for micronutrient deficiency [Table 5].[2]

SUMMARY

- Supplemental iron, vitamin C (to improve iron absorption), and vitamin D in patients with AGA, AA, and TE with documented deficiency of iron and vitamin D (Grade D recommendation).
- There is inadequate data to recommend supplementation of folic acid, riboflavin, zinc, and vitamin B12.

- Biotin supplementation is not recommended in the management of TE, AA or AGA (Grade D recommendation).
- In the absence of documented deficiency, the role of supplementing these micronutrients is debatable. It may rather lead to toxicities and unintentional medical consequences.

CONCLUSION

It is unclear regarding ideal range of micronutrient levels to prevent or correct hair loss. More research needed on the role of each micronutrient in normal hair follicle cycle. Controlled trials and meta-analysis are needed to make recommendations for screening of deficiency and supplementation of these micronutrients in non-scarring alopecia. Our advice is to eat healthy diet, have good sleep hygiene, and manage stress to prevent micronutrient deficiency as prevention is always better than cure.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Guo EL, Katta R. Diet and hair loss: Effects of nutrient deficiency and supplement use. Dermatol Pract Concept 2017;7:1-10.
2. Ruiz-Tagle SA, Figueira MM, Vial V, Espinoza-Benavides L, Miteva M. Micronutrients in hair loss. Our Dermatol Online 2018;9:320-8.
3. Thompson JM, Mirza MA, Park MK, Qureshi AA, Cho E. The role of micronutrients in alopecia areata: A review. Am J Clin Dermatol 2017;18:663-79.
4. Almohanna HM, Ahmed AA, Tsatalis JP, Tosti A. The role of vitamins and minerals in hair loss: A review. Dermatol Ther (Heidelb) 2019;9:51-70.
5. Goldberg LJ, Lenzy Y. Nutrition and hair. Clin Dermatol 2010;28:412-9.
6. Lee S, Kim BJ, Lee CH, Lee WS. Increased prevalence of vitamin D deficiency in patients with alopecia areata: A systematic review and meta-analysis. J Eur Acad Dermatol Venereol 2018;32:1214-21.
7. Beoy LA, Woei WJ, Hay YK. Effects of tocotrienol supplementation on hair growth in human volunteers. Trop Life Sci Res 2010;21:91-9.
8. Patel DP, Swink SM, Castelo-Soccio L. A review of the use of biotin for hair loss. Skin Appendage Disord 2017;3:166-9.
9. Gonul M, Cakmak SK, Soylu S, Kilic A, Gul U. Serum vitamin B12, folate, ferritin, and iron levels in Turkish patients with alopecia areata. Indian J Dermatol Venereol Leprol 2009;75:552.
10. Cheung EJ, Sink JR, English Iii JC. Vitamin and mineral deficiencies in patients with Telogen Effluvium: A retrospective cross-sectional study. J Drugs Dermatol 2016;15:1235-7.
11. Daly T, Daly K. Telogen effluvium with dysesthesia (TED) has lower B12 levels and may respond to B12 supplementation. J Drugs Dermatol 2018;17:1236-40.
12. Trost LB, Bergfeld WF, Calogeras E. The diagnosis and treatment of iron deficiency and its potential relationship to hair loss. J Am Acad Dermatol 2006;54:824-44.
13. Olsen EA, Reed KB, Cacchio PB, Caudill L. Iron deficiency in female pattern hair loss, chronic telogen effluvium, and control groups. J Am Acad Dermatol 2010;63:991-9.
14. Gowda D, Premalatha V, Imtiyaz DB. Prevalence of nutritional deficiencies in hair loss among Indian participants: Results of a cross-sectional Study. Int J Trichol 2017;9:101-4.
15. Deo K, Sharma YK, Wadhokar M, Tyagi N. Clinico epidemiological observational study of acquired alopecias in females correlating with anemia and thyroid function. Dermatol Res Pract 2016;2016:6279108.
16. Esfandiarpour I, Farajzadeh S, Abbaszadeh M. Evaluation of serum iron and ferritin levels in alopecia areata. Dermatol Online J 2008;14:21.
17. Kil MS, Kim CW, Kim SS. Analysis of serum zinc and copper concentrations in hair loss. Ann Dermatol 2013;25:405-9.
18. Yavuz IH, Yavuz GO, Bilgili SG, Demir H, Demir C. Assessment of heavy metal and trace element levels in patients with telogen effluvium. Indian J Dermatol 2018;63:246-50.
19. Vinton NE, Dahlstrom KA, Strobel CT, Ament ME. Macrocytosis and pseudoalbinism: Manifestations of selenium deficiency. J Pediatr 1987;111:711-7.
20. Masumoto K, Nagata K, Higashi M, Nakatsuji T, Uesugi T, Takahashi Y, *et al*. Clinical features of selenium deficiency in infants receiving long-term nutritional support. Nutrition 2007;23:782-7.
21. Petru E, Petru C, Benedicic C. Re: Selenium as an element in the treatment of ovarian cancer in women receiving chemotherapy. Gynecol Oncol 2005;96:559; author reply 559-60.

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