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Controversy on the role of iron and a clinical trial with intermittent iron and nutritional supplements in hair loss management

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ABSTRACT

Background: Reports dating 1932, (86 years prior) emphasise the role of iron deficiency in hair loss. However, blood tests sometimes show normal iron levels in these patients. Should we still include iron in our treatment or conclude that iron has no role in hair loss management? In an attempt to review the dilemma we have come across studies recommending intermittent iron therapy, which as a low dose supplement, can be utilized even in the absence of overt deficiencies. A clinical comparison of hair loss patients having normal haemoglobin is presented with standard 2% minoxidil treatment versus intermittent iron therapy once in three days and comprehensive iron therapy along with intermittent once in three days, inclusion of other hair nutrients, antioxidants, vitamins, calcium, aminoacids and omega 3.

Objective: Review the role of iron in hair loss management. Understand why hair loss patients sometimes present with normal iron reports. Evaluate if intermittent iron therapy can help in hair loss management. Evaluate if by the same analogy, inclusion of other intermittent hair nutrients along with iron therapy can deliver better hair growth in addition to controlling hair loss.

Method: Sixty women volunteers having hair loss despite normal haemoglobin, were enlisted for this prospective study. Three groups of twenty women each were created. Treatment group I, received standard hair loss treatment with 2% minoxidil. Iron therapy group II, received intermittent iron therapy and the nutrition group III, received intermittent iron with intermittent inclusion of antioxidants, vitamins, calcium, aminoacids and omega 3 which are known to benefit hair loss management.

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Results were evaluated with global photography, trichoscopy counts for hair density and hair calibre.

Observations: Minoxidil 2% group I had reduction in hair fall after 10 weeks. This group at the end of 6 months had 9% improvement in density, with 17% non responders and 3% worsening of the condition. The intermittent iron therapy group II, had reduction of hair fall after 8 weeks and 16% improvement in density over 6 months. The group III, with Intermittent iron plus intermittent antioxidants, vitamins, calcium, aminoacids and omega 3 had the best benefit showing reduction in hair fall after 4 weeks and 21% improvement in density over 6 months. This group also showed 12% improvement in hair calibre over 6 months. There were no non responders or worsening of condition in group II & III.

Conclusion: Iron is an integral part of hair loss management program. Compensation of low iron levels by autophagy or arrest of hair growth make iron available to maintain normal levels in circulation which may mislead to us believe that there is no iron deficiency. Other nutrients antioxidants, vitamins, calcium, aminoacids and omega 3 are required to ensure complete utilization of iron and also support active hair growth. We present clinical evidence that intermittent iron therapy once in three days along with comprehensive inclusion of other nutrients once in three days consistently results in control of hair loss along with new hair growth. The comprehensive intermittent therapy, can be a considered for management of hair loss without waiting for the evidence of detecting low nutrient levels through laboratory tests.

Introduction:

In our clinical experience iron supplementation has controlled hair loss and improved hair growth in our patients. However some research workers have found normal iron levels in hair loss patients and have also concluded that iron has no significant role in hair loss management (1,2,3). Here we review and analyse the control of hair growth in iron deficiency states and try to understand, why sometimes the iron levels may appear to be normal in hair loss patients. We report the observations of a three group comparative clinical trial with standard 2% minoxidil versus intermittent iron therapy and intermittent iron with intermittent inclusion of other hair nutrients as well.

The comparative clinical trial:

The trial consists of the observations and data from sixty women having normal haemoglobin levels not lower than 11g/dL, with persistent hair loss for more than six months. The sixty women were divided into three groups of twenty each. Group I the treatment group, received hair loss treatment with 2% minoxidil application 1 ml twice a day, morning and evening. Group II, the iron therapy group, received intermittent ferrous sulphate equivalent of elemental iron 100 mg once in three days. Group III was the nutrition group, which received intermittent iron along with intermittent inclusion of antioxidants, vitamins, calcium, aminoacids and omega 3 which are

known to benefit on hair loss management. The cyclical nutrition therapy regimen used is described in table 1. The regimen has been previously published by the author (4,5). Group II and group III did not receive minoxidil or any other scalp application.

Progress of the groups was recorded on day one and thereafter every two months for a period of six months. The parameters evaluated were global photography, trichoscopy hair density counts per centimetre square, hair calibre in microns and patient's personal evaluation score. The haemoglobin levels for group II and group III were monitored every two months till the completion of 6 months.

Global Photography:

Patients from all three groups had photographs taken in five views at a designated, fixed place with the same camera, same lighting, same flash and same settings. The standardized five views were vertex or mid scalp on bending forward, occipital whorl area from back of the scalp, front hairline, right side and left side to show the temporal angles. Photographs were taken at day-1, then every 2 months for next two visits at 4 months and 6 months. Independent evaluation of the photographs was done by three different persons who were blinded about the status of the patient and the group. The photographs, were graded for hair density, hair quality, visible changes in the size of the area of thinning or hair loss and any appearance of new hair growth. Under each of these criteria the improvement was graded from lowest grade 0 (zero) to highest grade V. Grade V - very good, grade IV - good, grade III - noticeable improvement, grade II - marginal or barely noticeable change, grade I - no change at all and grade 0 was considered for deterioration or worsening beyond the initial status (Table 2).

Haemoglobin levels were recorded on day one and then at 2 months, 4 months and 6 months for groups II and III.

Observations:

Group I, the standard treatment group following 2% minoxidil application 1 ml twice a day, complained of hair loss for 8-10 weeks. The average improvement in density was barely appreciable to the patients, on measuring closely it was 2% at 2 months and 5% at 4 months, which improved to 9% at 6 months. The average improvement in calibre was none at 2 months, slightly noticeable to begin as 2% only after 4 months, which improved marginally to 3% at the end of 6 months. There were 85% non responders in the treatment group at 2 months, 66% non responders at 4 months and 47% non responders even at the end 6 months. While 3% expressed concern that the hair loss and thinning had worsened than before.

Group II, the intermittent iron group following intermittent iron therapy equivalent of elemental iron 100 mg once in three days, reported reduced hair loss within 6-8 weeks. The average improvement in density was 3% at 2 months and 11% at 4 months, which improved to 16% at 6 months. The average improvement in calibre was 2% in 2 months, 6% at 4 months which improved to 8% at the end of 6 months. All patients responded with some improvement within the first 2 months. There were no non responders.

Group III the intermittent iron plus intermittent nutrition group showed an average improvement in density of 7% at 2 months and 16% and at 4 months which improved to 21% at 6 months. While the average improvement in calibre in the nutrition study group at 2 months was 4% and at 4 months was 9% which improved to 12% at the end of 6 months. Hair loss was controlled in all the patients in group III, within 3-4 weeks. All the twenty women in the study group responded with varying amount of improvement within 2 months of starting the iron plus intermittent nutritional therapy.

Global photography scores in group I varied between grade 0-I in 86% patients and grade II in the remaining 14% patients by the end of 6 months. Photography scores in group II were between I-II in 90% patients and grade III in

10% patients. Group III had 97% patients scoring between grades III and 3% could be rated as grade IV, though none could be rated as grade V.

Figure 1a, 1b show improvement after four months of low dose once in three days, cyclical nutritional correction in a case of grade III hair loss in a patient which has reversed to grade II, with four months of intermittent iron plus nutritional therapy, without the use of minoxidil or finasteride. While figure 2a, 2b show a result of similar therapy for four months demonstrating improved hair quality and hair regrowth in a male patient over the mid scalp.

Haemoglobin levels were checked for group II and group III. There was no change in the blood haemoglobin at 2 months in group II, which improved by 1 g/dL at 4 months and 2 g/dL at 6 months. Group III showed initial correction of 1 g/dL at 2 months and then significant rise of 3 g/dL at 4 months which maintained well at 6 months.

Discussion:

A duration of 6 months was selected for the trial to have average cover for one telogen phase lasting four months. We expected the telogen follicles to return into anagen. The duration of 6 months also provide adequate duration of treatment for minoxidil response which most studies consider to be 6 months (6), for effective clinical improvement. Complain of hair loss for 8-10 weeks in the minoxidil group can be due to initial increased shedding known to happen with minoxidil during the phasing period (6). The shedding creates a lack of confidence among patients who then insist that the hair loss is severe and unremitted for a longer duration. Minoxidil only extends the growth phase of the hair which would not translate to hair growth without the provision of adequate support of ingredients or raw material required for rapid cell division and mitosis of the growing follicle. Hence results seen were less and slow, including some non responders, in the standard treatment group.

Group II having no minoxidil application and intermittent iron once in 3 days showed early response beginning at 2 months followed by steady progress at 4 months and 6 months. Scientifically it indicates that there are hidden, covert iron deficiencies in patients who are on the lower side of the normal range which when even minimally supported can lead to clinical changes in hair growth and control of hair fall.

Group III using no minoxidil with intermittent iron once in 3 days plus other nutrients also once in 3 days (table 1), showed the best results. The approach provided correction of iron and ensures better utilization of iron along with provision of similar other hidden nutrient deficiencies in early stages of hair loss.

We have come across two studies of 2% minoxidil in females, by Whiting, Jacobson 1992 (7) and Jacobs, Szpunar, Warner 1993 (8). The duration of these studies was 32 weeks compared to the present study being 6 months or 24 weeks. The average improvement in minoxidil group in both the studies at the end of 32 weeks was 14% and 15% better than placebo. The observation compares with our findings of 9% improvement at 6 months, a longer duration may have probably resulted in 14% improvement. The two studies by Whiting, Jacobson 1992 and Jacobs, Szpunar, Warner 1993, had 40% and 56% non responders which also is similar to our findings of 47% non responders at the end of 6 months.

Group II with intermittent iron therapy had 16% improvement within 6 months which was better than the results in minoxidil studies. It is also noted that improvement started within 2 months and there were no non responders which suggests efficacy better than 2% minoxidil in female hair loss.

Group III with intermittent iron plus intermittent nutrition at 24 weeks or 6 months, had 16% improvement which would be slightly better than 14% and 15% recorded with 2% minoxidil at 32 weeks. Again there were no non responders.

Table 1: Cyclical Nutrient Therapy two supplement per day which repeat in 3 – day Cycles	
Monday & Thursday	Antioxidant, Calcium, Vitamin D3
Tuesday & Friday	Iron, Folic Acid, Vitamin C, Omega 3
Wednesday & Saturday	Essential Aminoacids, B-Complex, Biotin
Sunday – no medicines	Detox on Sunday OR add extra a dose of another nutrient as per individual status if required
Provides ten different nutrient combinations that are synergistic with each other over three days preventing overdose and inter nutrient interaction.	

Table 2: Global Photograph Grades in each group		
Grade	Criteria	Improvement in 6 months
Grade 0	Worse than before	
Grade I	No change	86% of only Minoxidil Group
Grade II	Marginal	14% of Minoxidil Group 90% of only Iron Group
Grade III	Noticeable	10% of only Iron Group
Grade IV	Good	97% of Iron & nutrition Group
Grade V	Very good	3% of Iron & nutrition Group



Figure 1a: Grade III hair loss in a female patient with normal haemoglobin



Figure 1b: Improved hair quality and hair regrowth after four months of intermittent iron plus nutritional correction no minoxidil no finasteride



Figure 2a: Grade IV hair loss over mid scalp in a male patient with normal haemoglobin



Figure 2b: Improved hair quality and hair regrowth after four months of intermittent iron plus nutritional correction no minoxidil no finasteride

Group II and group III both received intermittent iron supplements but group III that received intermittent nutrition as well showed better improvement in haemoglobin levels. We shall try to understand the scientific basis of iron intermittent iron supplementation better in the following discussion.

Alleyne, Horne and Miller reviewed iron dosage. They note that adults have 45mg/kg of total iron in their body, sometimes a bit lower in females. The storage forms ferritin and hemosiderin comprise one third of the total while the remaining active two thirds the heme iron present as haemoglobin in the red blood cells, the erythrocytes (9). Recycled iron from senescent red blood cells provide a regular source of 20 mg iron per day. Replacement of iron lost through stools, dead cells, urine, sweat etc calls for an additional requirement of 1-2 mg per day, through the diet (9).

Approximately 10% of oral iron is absorbed. A supplement providing 150-200 mg elemental iron per day in a dose divided three times a day would raise haemoglobin by 2-3 g /dL in 4 weeks (9,10). several more months of continued therapy would be necessary to replenish the iron stores in the body (9,11). The approach however fails as 20% patients develop nausea, epigastric discomfort, constipation and have to stop oral iron. Another 30% stop the therapy on their own (9,12). Reducing the dosage, having iron after food, increasing interval between doses, delivering the total dose in cycles, is recommended (9,13). Absorption of iron decreases with correction of the deficiency, hence gradual correction divided as once in 3 day cycles would not abruptly correct the deficiency and provide better absorption over an extended period achieving better efficiency with lower dosage.

Rise in haemoglobin was slower in group II because a definite number of doses are required for the response (9), which was thus expected to be slow with once in 3 days iron supplements. Though rise in haemoglobin was

not very significant, better levels reached within 2 months in group III may be due to contribution of the comprehensive nutrients added on different days to prevent interaction but improve biological value of the supplement program.

Overall the nutritional support neutralizes free radicals, provides low dose catalysts, cofactors, for metabolism as it includes, zinc, magnesium, selenium, vitamin A, D, C, amino acids, anti inflammatory omega 3. It creates a favourable internal environment and availability of building blocks for creating new cells ensuring effective cellular metabolism, that results in better hair growth. A review of the previous scientific research can explain and provide an insight into the unique thought behind these successful clinical implementations.

Previous research:

As early as 1932 Cunningham concluded from his experiments that iron deficiency can lead to hair loss (14). Hard in 1963 studied and confirmed the association of iron deficiency in the aetiology of diffuse hair loss in non anaemic, iron deficient women (15). Rushton evaluated serum ferritin levels in healthy women who complained of unremitted hair loss for more than six months. Among these women 96% had serum ferritin levels below 40 mg (lowest of normal) and 99% had serum ferritin below 70 mg (14). In a placebo controlled clinic trial, Rushton documented that a supplement of iron and L-lysine for 6 months, decreased telogen hair count in women and reduced hair loss by 31% whereas the hair loss increased by 9% in the placebo group (17,18). Kantor, Kessler et.al confirmed the role of iron in preventing hair loss and highlighted that iron was part of a desaturase, of stearyl-coenzyme A and a cofactor for ribonucleotide reductase responsible for the rate limiting step in DNA synthesis (19). Trost, Bergfeld, have proposed that hair follicles having rapidly dividing cells need more of free biological iron for utilization rather than ferritin which is the storage form. Hence hair follicles tend to be sensitive to minor variations in iron levels (20). Abdel, Hamed

et.al., Rushton et.al. and Ohyama have suggested that iron deficiency in absence of anaemia can lead to telogen phase (21,22,23).

Rebora and Guarrera, described the empty follicle stage of kenogen and had a new perspective describing telogen as a physiological resting stage of the follicle to be saved and preserved for regeneration (24,25). Increasingly more repeated episodes of telogen followed by extended period of kenogen begin to generate bald areas (24,25). Hair follicle may adapt to telogen state under non physiological disruptions or discontinue growth due to unfavourable unsuitable cellular environment for hair growth. Such prolonged adaptation over a period creates lack of growth and baldness.

Hair growth is optional:

Rapid cell division is required in the hair follicle to commence anagen after the telogen resting stage and continue to achieve hair growth throughout the anagen phase. The follicle demands a steady supply of vitamins, minerals, amino acids to ensure cell division and growth. Body first decides if the resources are available and then makes a choice for the hair follicles to remain in resting phase or commence the growth phase. Hair does not form an integral part of any vital body systems. Hair growth can be conveniently shut off to be resumed later under more favourable conditions. Body prefers to use the nutrients thus spared, for better purposeful applications. The reasoning is supported by the discovery of an intracellular regulating process called autophagy.

The mechanism of autophagy:

Yoshinori Oshumi of Japan received the 2016 Nobel Prize for Medicine for the autophagy research work. Autophagy is a programmed biological disintegration of intracellular organelles during states of deficiency, like calorie restriction, starvation, or malnutrition. The staged breakdown is carried out systematically to retrieve and recycle the nutrients which are then redirected to maintain

other vital functions in the body (26). The nutrients retrieved by autophagy during deficiency states ensure that low nutrient levels in the circulation are now restored to normal (26,27). Hence the nutrient deficiencies are not clinically detected and body systems continue to function as normal.

The process of autophagy is also utilized to disintegrate aggregated, deranged proteins, damaged cell organelles, peroxisomes, endoplasmic reticulum, mitochondria and intracellular pathogens (28). The process of autophagy prevents apoptosis and helps in regenerating worn out cells and cell organelles. Autophagy has a key role in preventing degenerative disease, autoimmune disorders, infections and cancer (26,27,28). Autophagy is an adaptive mechanism deployed by the hair follicles to survive under conditions of stress. Experiments show that hair follicles cannot grow under stress, if the autophagy is controlled and down regulated (29).

Paradoxical iron status:

Deshwali et.al. regarded the hair follicles as storage sites for ferritin, which can be utilized in case of deficiency by arresting or compromising the hair growth while maintaining more important functions of the blood, red blood cells and bone marrow cells (30). Which means that the iron deficiency in circulation will get corrected to normal levels, but there will be concomitant hair loss with contradictory lab tests depicting normal iron levels. The iron deficiency therefore is not clinically detectable, creating a paradoxical illusion that there is no correlation between iron deficiency and hair loss. The compensatory processes like autophagy, arrest of hair growth in telogen, followed by kenogen are responsible for providing nutrients and creating the misinterpretation with lack of direct correlation between blood levels despite the presence of nutrient deficiencies.

Park, Na, et.al. reviewed the role of iron deficiency and found it had a significant role in hair loss (31). Research by Ruston et.al.,

Moeinvaziri et al., Kantor, Kessler et.al and Deloche, Bastien et.al have found correlation between iron deficiency and hair loss (32,33,34). Whereas Sinclair, Bregy, Trueb et.al and Olsen, who studied serum Ferritin as the representative of iron stores in the body, have found no relation between iron deficiency and hair loss (35,36,37). The contrasting findings were criticized by Ruston, Bergfeld et.al. (38) It is important to understand nutrient interactions to decipher the controversial findings. Iron deficiency would be masked as hair growth is arrested, follicles are shifted to telogen and ferritin stores in the follicle or the ferritin intended to be used for hair growth is redirected and utilized to compensate the low ferritin levels in circulation (30). Thus clinically, serum ferritin levels continue to appear as normal in presence of hair fall.

At times the available, normal serum ferritin may not be biologically utilized due to other coexisting deficiencies. In addition to normal iron levels, Kelkitli, Ozturk and Aslan, emphasised the importance of zinc for erythropoiesis (39). According to the research of two separate teams, Semba, Bloem et.al, (40) and Suharno, West et.al. (41) mobilization of stored iron to the sites of formation of haemoglobin and the sites of generation of red blood cells (RBC) cannot be accomplished without vitamin A. Beta carotene and vitamin A, also help in iron absorption as noted by Mejia, Chew and García-Casal et.al. (42,43). Similarly as reported by Thakachan et.al. and Diaz et.al. vitamin C has a role in the absorption and the utilization of iron (44,45). Deshwali et.al. draw attention to the role of copper in the formation of haemoglobin and providing the oxygen carrying capacity to the RBCs (30). There is close interrelation between nutrients. Lynch has emphasised the same as we realised, that a balance of numerous other vitamins and micronutrients is required for the effective utilization of iron (46). There could be deficiencies of vitamin A, vitamin C, zinc or copper, in the patients, leading to poor

incorporation of iron into RBC or reduced oxygen carrying capacity, resulting in hair loss, despite normal iron ferritin levels, misleading us conclude that there is no relation between iron and hair loss. Single nutrient assessment cannot represent the complete status of the internal cellular environment in the body.

Iron absorption is better in iron deficient states:

Studies by McCance, Widdowson in 1938, Garnick in 1954 and a review by Conrad ME Jr, Crosby 1963, showed that iron absorption through the intestines itself is regulated to maintain the iron balance in the body (47,48,49). Hahn, Bale et.al. in 1943, demonstrated that iron absorption is better under conditions of in anaemia and anoxia (50). Mucosal iron receptor apoferritin when saturated with internal iron prevents the intestinal mucosa from accepting dietary iron. Intravenous iron was also seen to reach the mucosal cells and block any further iron absorption (50). Recent studies by Du, She et.al. demonstrate that liver-derived protein Hcpidin, controlled by the hcp gene and regulated by transmembrane serine protease 6 gene *Tmprss6* restricts enteric iron absorption and is the key regulator of iron absorption from the diet regulating the body iron content (51).

The iron absorption study of Van Hoek and Conrad in 1961, used radioactive iron and a whole body scintillation counter. They studied normal versus iron deficient human volunteers, to confirm that iron is absorbed better in deficiency states till it reaches an equilibrium with the circulation (52). Iron deficient group showed a quick absorption of 29% of the oral dose and excreted unabsorbed iron for 3-6 days till they reached the equilibrium. While normal group absorbed only 10% of the oral dose at a slower pace and excreted unabsorbed iron over 6-15 days before reaching the equilibrium. The observation indicate faster and better absorption by intestinal mucosa in deficiency states. (52). Brown, Dubach et.al in 1958 studied iron

transport mechanism and confirmed mucosal block from large doses. (53). Morgan and Oates in 2002 (54), recorded that enterocytes in the crypts of Lieburkuhn take up iron from plasma transferrin by receptor-mediated endocytosis, which in turn controls the expression of divalent metal transporter 1 (DMT1) determining the iron absorption by intestinal villus enterocytes. DMT1 was found to display greater expression in iron deficient states. DMT1 as a quick resetting control. Levels of DMT1 and related mediators, begin to reduced within an hour of increasing iron load in the diet or increased parenteral iron in circulation, reaching their lowest in seven hours (54). Frazer, Wilkins et.al in 2003 studied iron absorption in further details to confirm that reduced duodenal expression of divalent metal transporter 1 (DMT1) and duodenal cytochrome b, (Dcytb) but not Ireg1 or hephaestin explains the mucosal block phenomenon of iron absorption (55). The mucosal cells need to renew and regain their ability for iron transport with a three day gap.

Iron is administered better with intermittent dosage:

A double blind randomized trial by Schultink, Gross et.al. in 1995, conducted a randomized, double blind trial of daily iron compared with iron twice weekly, supplements. Both regimens worked equally well, regardless of the severity of anaemia (56). Viteri, Ali et.al. in 1996 conducted a controlled clinical trial where once a week and daily dose of iron were equally effective (54). In a study by Sing, Fong et.al 6% patients did not tolerate daily iron, 30% developed gastrointestinal problems and 30% had poor compliance (57). Chew, Torun et.al. reported six to eight times more side effects in patients who had daily iron as compared to weekly dosage. Intermittent, weekly iron supplements were well tolerated and showed the same benefits as daily dosage (58). Since iron is one of the oldest recognised nutrients causing deficiency disease, a lot of work has been done with iron dosage in pregnant women

and among growing school children to show equal benefit from daily or intermittent dosage. All these studies and previous research lead us to consider intermittent iron therapy is better absorbed and efficient with acceptable tolerance and lower side effects.

High doses of iron are not beneficial:

Food and Nutrition Board, Washington DC, 1993 guidelines on iron deficiency anaemia warn against high doses of iron (59). Centers for Disease Control and Prevention, 1998 CDC report on recommendations for prevention and control of iron deficiency warns that higher doses of iron do not provide higher benefit in the correction of anaemia (60). Thomas, Mackey et.al in 2009 have explored the relation of Fenton reaction and iron in generating hydroxyl free radicals under submitochondrial oxidative stress (61). A study by Gutteridge and John in 1996 also noted that iron in excess is a participant of the Fenton reaction resulting in production of free radicals and contributing to the oxidative damage in the cells (62). Halliwell (63) and Salganik (64) warn that high doses of iron can become pro oxidant. Superoxides in the body are converted to less reactive hydrogen peroxide, by superoxide dismutase (SOD). A person having regular iron and multimineral supplements triggers Fenton reaction between metallic iron or copper ions with the reduced form, hydrogen peroxide, generating more reactive hydroxyl ions and reversing the benefit from conversion of superoxides and peroxides generating a pro oxidant effect. (60,61). Therefore a once in three days iron supplement regimen is preferred for better tolerance, better compliance, lesser side effects, reducing the risk of oxidative damage and creating a cost effective therapy.

The comprehensive low dose nutrient therapy:

We have used once in three days or twice a week intermittent iron therapy for treating hair loss. We extended the same logic to other nutrients as well. Mucosal cells, enzymes, catalysts, cofactors, binding proteins, transporting systems need a 3 day gap to

recharge and reorganize for optimum function once again after every dose. The metabolic systems have a rate limiting capability of utilizing the nutrients. For example, body is unable to utilise folic acid in higher doses due to limited processing ability for conversion of folic acid to its active form by methylation (65). absorption of vitamin C declines markedly with higher doses, giving no further rise in plasma levels and the biological action reverses to become pro oxidant instead of antioxidant (66,67). Multivitamin pills containing calcium, phosphorus, magnesium along with iron, reduce iron absorption, such combinations are best avoided in iron supplementation (68,69).

In order to avoid incomplete absorption, partial bioavailability, reversing the benefits from daily use or high doses of supplements, we were lead into creating a low dose once in three days comprehensive nutritional program for hair loss management. Iron was administered once in 3 days. On the other days we included, antioxidants, amino acids, B-complex, biotin, calcium, vitamin D, omega 3, and vitamin C. Table 1 enlists how ten nutrients were administered over three days rotating in a three day cycle. The approach also avoids possibility of overdose and can be followed for a longer period of time. Hair loss under a variety of indications and causes has been treated with this cyclical nutrition therapy (70,71,72,73,74,75).

Conclusion:

Research workers over past 80 years have strived to convince that intermittent iron therapy is more effective than daily dosage. Iron is an integral part of hair loss management program. Compensation of low iron levels by autophagy or arrest of hair growth make iron available to maintain normal levels in circulation which may mislead to believe there is no iron deficiency. Other nutrients antioxidants, vitamins, calcium, aminoacids and omega 3 are required to ensure complete utilization of iron and also support hair growth. We present clinical evidence that intermittent iron therapy once in

three days along with comprehensive inclusion of other nutrients once in three days consistently results in control of hair loss along with new hair growth. The comprehensive intermittent therapy, can be a considered for management of hair loss without waiting for the evidence of detecting low nutrient levels through laboratory tests.

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