

RUDZIŃSKI, Gracjan, KUSAK, Natalia, BRZUSZKIEWICZ, Kinga, ŁOZOWSKI, Borys, GRUNWALD, Arkadiusz & DALMATA, Weronika. Hair loss following COVID-19 infection - the state of current knowledge and treatment approaches. *Journal of Education, Health and Sport*. 2023;13(1):251-258. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2023.13.01.037>
<https://apcz.umk.pl/JEHS/article/view/40988>
<https://zenodo.org/record/7401665>

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences). Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przynależność dyscypliny naukowej: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). © The Authors 2022; This article is published with open access at License Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper. Received: 04.11.2022. Revised: 21.11.2022. Accepted: 05.12.2022.

Hair loss following COVID-19 infection - the state of current knowledge and treatment approaches

Wypadanie włosów w następstwie infekcji COVID-19 - stan wiedzy na rok 2022 i metody leczenia

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DOI: <https://doi.org/10.12775/JEHS.2023.13.01.037>

Keywords: SARS-CoV-2, hair, Nutrition, drug treatment

Abstract

Introduction: Telogen effluvium is a non-scarring hair loss that can occur after COVID-19 infection. It usually occurs after about 3 months, causes diffused hair loss and lasts up to 6 months. The purpose of this narrative review is to collect and summarize the effects of potential methods to promote hair regrowth in patients after COVID-19 infection.

Material and method: The article reviews available in PubMed and ResearchGate databases, studies on telogen effluvium and SARS-CoV-2. Due to the limited literature, articles on telogenetic hair loss progressing independently of COVID-19 were also included in the review.

Results: Hair loss after COVID-19 infection occurs in almost 30% of patients. This is likely related to pro-inflammatory cytokines released during infection and the pro-thrombotic effect of the virus. Telogen effluvium is the most common type of alopecia occurring after COVID-19 infection - about 86% of all cases. It affects women more often than men. It seems that its severity may correlate with the severity of the infection. Other than female gender and a history of chronic disease, it is unlikely to find any other contributing factors. Effective

treatments seem to include the use of oral supplements such as vitamin D, polyunsaturated fatty acids and zinc. In addition, topical application of minoxidil and high-platelet plasma treatments have shown good outcomes. Conclusions: Given the fairly common occurrence of hair loss after COVID-19 infection, it seems reasonable to seek the most effective strategies for its treatment. At present, it appears that the best results are obtained by combining different treatment approaches.

Introduction

Telogen effluvium (TE) is an abnormal hair turnover resulting in excessive loss of telogen hair. This is probably the most frequent underlying cause of shedding in children (1). A few prevalent causes of these are acute severe illness, chronic diseases, iron deficiency anemia, thyroid disease, surgery, malnutrition, and medications such as oral contraceptives or lithium (2). Telogen effluvium (TE) is generally characterized by scattered loss of hair 2-3 months after the onset of a stressor (3). The event that triggers this type of alopecia causes the anagen phase to end prematurely, followed by the transition to the catagen and telogen phases. Such a sequence of events causes hair loss. It is usually a non-scarring type of alopecia, usually self-limiting and in its acute form resolving within 6 months (4). When the body reacts to infection with SARS-CoV-2, by creating a pro-inflammatory response that results in damage to tissues and other repercussions. Pro-inflammatory cytokines are unleashed and anticoagulant mechanisms are disrupted, potentially triggering TE via a microthrombosis and/or inflammatory response in hair follicles(5). It has already been confirmed that elevated levels of interferons are connected to acute TE (6). Damage to matrix cells can occur through a storm of cytokines which results in telogen effluvium (7). Some dermal manifestations of COVID-19 such as urticaria, livedoid vasculopathy, a rash resembling chicken pox or COVID toes (8), which can be explained among patients with SARS-CoV-2 infection, are that an increase in pro-inflammatory cytokines has been observed: interleukin 1b, interleukin 6, tumor necrosis factor α , and interferon types 1 and 2 (9).

During the COVID-19 pandemic, the most prevalent form of hair loss observed was telogen effluvium (10). There are articles reporting an association between hair loss and COVID-19. Moreno-Arrones et al. assessed 191 patients with acute TE who had previous infection with SARS-CoV-2. The mean age of individuals was 47.4 years. Seventy-eight percent of them were women (11). According to a large-scale study (538 cases) examining the clinical implications of COVID-19, the incidence of alopecia was found in 28.6% of affected individuals (12). Khalifa E Sharquie et al. studied 39 patients who developed intense hair loss 2-3 months after SARS-CoV-2 infection. Of the subjects, 36 (92.3%) were women and 3 (7.69%) were men (10).

Up to a quarter of COVID-19 patient experience acute classical telogen effluvium within the first two to three months, with women at higher risk than men (13). Michela Starace et al. collected data from 128 patients. The intensity of post-viral hair loss observed in patients with a prior history of COVID-19 infection is likely to relate with the severity of COVID-19 infection (14).

Rahaf A. Abdulwahab et al. studied 343 patients who visited to a dermatology clinic between 2020 and 2022. Their analysis showed that telogen effluvium (TE) was the most frequently presented type (156, 86.7%), then alopecia areata (15, 8.3%) and androgenetic alopecia (9, 5.0%) as post COVID-19 manifestation. Hair loss after infection was present among 28.4% of male patients in comparison to 60.2% of female patients. Similarly, 61.1% of participants with chronic health problems experienced hair loss after COVID-19 infection compared to 51% of others without medical history. All other factors were nonsignificant correlated with hair loss after being infected (15).

Nutrition

Losing hair patients often ask if nutritional supplements would be able to restore hair growth or prevent further loss. The links between hair growth and nutrition, are complex. Nevertheless, hair follicles are among the most metabolically active. The growth of hair can be affected by caloric and protein malnutrition, as well as a deficiency of micronutrients (16). The effect of reduced protein intake or sudden weight loss on acute telogen effluvium is well known (17). Quite commonly reported symptoms in COVID-19 are loss of taste and smell, which can result in appetite decrease causing nutritional deficiencies and eventually exacerbate hair loss (18).

Supplementation and treatment strategies

Multivitamins

Vitamin A

This vitamin plays many roles in the body: it is essential for vision, is engaged in immunological function and is needed for differentiation and cell growth (19). In general, a well-balanced diet will provide a reasonable healthy

amount of vitamin A (20). However, it is worth bearing in mind that excessive vitamin A supplementation can cause loss of hair (21).

Vitamin E

Vitamin E is known to be involved in oxidation-antioxidant balance and assists in reducing damage triggered by free radicals (22). Researchers have shown that vitamin E, through its ability to reduce oxidative stress on hair follicles and inhibit lipid peroxidation, can enhance hair growth (23). There are few studies demonstrating the pathophysiology of post-COVID-19 syndrome, but much evidence suggests that it is a multifactorial and complex syndrome. Depending on the virus type, it specifically affects immune function, inflammation and oxidative stress (24).

Vitamin D

Vitamin D has become widely popular for boosting patients' immunity while undergoing COVID-19 infection (25). Supplementation with vitamin D at 10-25 µg per day has a reasonable preventive effect against variety of acute respiratory infections (26). Receptors for vitamin D are found to be expressed in the cells of hair follicles and have the capacity to modulate the proliferation of keratinocytes and the cycle of hair (27). Research data showed a link between a poor serum vitamin D levels and telogen effluvium (28). Recent studies report that for female pattern baldness, the use of oral vitamin D together with topical minoxidil has better results than applying minoxidil alone (29).

Biotin

Although it has become popular among consumers, biotin has not been shown to be effective in healthy individuals for nail and hair growth. There is no evidence to support the benefits of biotin supplementation beyond known cases of deficiency (30). While a deficiency of biotin causes hair loss, there is no proof-based data showing that supplementation with biotin stimulates hair growth (20).

Folic acid/ Vitamin B12

Data are not sufficient to advocate for screening and supplementation in cases of telogen effluvium (20).

Polyunsaturated fatty acids

The growth of hair is controlled by the cell interaction between the dermal papilla cells (DPCs) as well as other cells found within the hair follicle. Jung-Il Kang et al. demonstrated the mechanism and effect of fermented fish oil (FFO) extract obtained from mackerel and its ingredient docosahexaenoic acid (DHA) in regulating hair growth. Fermented fish oil extract caused induction of cell cycle progression and activation of extracellular signal-regulated kinase (ERK), p38 and Akt. Also, the fermented fish oil extract also induced nuclear translocation of β-catenin, a stimulator of the anagen phase, by upregulating phosphoglycogen synthase kinase3β (GSK3β). These findings demonstrate that FFO extract and DHA have been shown to foster growth of hair via anagen-activating pathways in dermal papilla cells (31).

The effect of a 6-month supplementation of omega 3&6 acids and antioxidants was studied in 120 women with female pattern baldness. It was shown to enhance hair density and decrease the percentage of telogen and the percentage of miniaturized anagen hair(32).

Micronutrients

Iron

Patients with hair loss after COVID-19 treatment should have their serum ferritin levels assessed. When ferritin serum levels are below the reference level oral iron supplementation may improve hair regrowth (33,34). It should be added that vitamin C supplementation is essential in patients who experience hair loss associated with iron deficiency (20).

Zinc

Zinc is an essential trace element, meaning that the the organism is unable to produce it on its own (20). A retrospective cross-sectional examination of one hundred and fifteen individuals diagnosed with telogen effluvium (acute and chronic) revealed that 9.6% were zinc deficient (35). Zinc is a powerful promoter of recovery of follicles (36). Evidence shows that in women experiencing hair loss, zinc supplementation has been shown to enhance hair density (37). If the initial zinc concentration is low, zinc supplementation is advised for patients suffering from hair loss after COVID-19, due in part to its popularity as an immune booster (34).

Selenium

Consumption of selenium in excess of 400 µg per day may cause toxicity (20). Interestingly, the occurrence of selenium toxicity as a result of using a liquid dietary supplement that contained 200 times the recommended concentration of selenium induced hair loss in a significant number of patients (38).

Table 1 Nutrition standards for the Polish population 2020 - vitamins and minerals (39):

Micronutrient	Adult males (≥19 years)		Adult women (≥19 years)	
	AI	RDA	AI	RDA
Vitamin A		900 µg		770 µg
Vitamin E	10 mg		8-11 mg	
Vitamin D	5-15 µg		5-15 µg	
Biotin	30 µg		30-35µg	
Folic acid/ Vitamin B12		400 µg		400-600 µg
Iron		10 mg		10-27 mg
Zinc		11 mg		8-13 mg
Selenium		55 µg		55-70 µg

(AI - Adequate Intake) / (RDA - Recommended Dietary Allowance)

The impact of exercise

Yumeng Jiang studied the effects of exercise on androgenetic alopecia (AGA). Overall, 592 patients with AGA were qualified. Out of them, 377 were women (63.68%) and 215 were men (36.32%). Changes in pre- and post-exercise status are associated with frequency of exercise and type of exercise. However, they are not related to family history nor gender. The improvement rate in AGA patients performing exercises lasting more than 60 minutes was 3.106 times better than in those who performed any type of exercise but with a duration of less than 30 minutes. And those who did aerobic exercise showed, 5,416 times better improvement rate. Performing aerobic exercise or any exercise lasting >60 minutes may help postpone the progression of AGA and reduce the severity of AGA (40). Unfortunately, there is no data showing the effect of exercise on hair loss following COVID-19, but it seems that leading a healthy lifestyle can positively affect hair regrowth.

Therapeutic treatments

Mesotherapy

Mesotherapy is a minimally invasive technique for medical or cosmetic purposes. It involves limited intradermal injection of pharmaceutical and/or non-pharmaceutical substances (41). The penetration depth of the needle should not exceed 4 mm in order to be effective (42). It is possible to use pharmaceuticals, plant extracts, vitamins and other bioactive substances, but alcohol- or oil-based substances for mesotherapy should not be used due to the risk of skin necrosis (43). By bypassing the epidermal layer, which significantly reduces the drugs applied topically to the deeper layers of the skin, better nutrition of the hair follicles is achieved. In addition, better stimulation of the anagen phase is achieved through the trauma caused by repeated injections (44). However, the effectiveness of using mesotherapy for hair loss-related conditions still needs to be tested in scientific studies(34).

Fathia M. Khattab et al. conducted a study to examine the effectiveness of single-session botulinum toxin A injection compared to repeated sessions of multivitamin mesotherapy in treating telogenetic hair loss. Botulinum toxin A as well as multivitamin mesotherapy have been shown to be effective in managing telogen effluvium, as demonstrated by improvements in hair parameters such as terminal hair and multiple follicular units. Those two treatments have very minimal and generally well-tolerated side effects. While both treatments have comparable success rates, a single session of botulinum toxin A is a preferable choice to multiple sessions of mesotherapy (45).

Topical minoxidil

Minoxidil known to open the ATP-sensitive potassium channel (KATP), was initially formulated and used as an agent for the hypertension treatment (46). However, it also turned out to be useful in treating hair loss (47). Not only does minoxidil use its vasodilatory effects to promote and increase the circulation of blood in the hair follicle, but it also has the capacity to activate an enzyme prostaglandin synthase-1 with the ability to promote the growth of hair (48). Minoxidil is known not only for its potential to prolong the duration of the follicle growth phase, but also has the ability to stimulate the transition from the loss phase (telogen) to the growth phase (anagen) (49). The anti-inflammatory effect of minoxidil has also been demonstrated in experiments with cell cultures. It works by inhibiting prostacyclin and interleukin-1a, which are mediators of inflammation(50,51).

When using minoxidil topically (foam and solution), during the first few weeks hair loss can be observed, confirming the effectiveness of the medication, paradoxically. The shedding is likely to be triggered by the rapid transition of the hair cycle from telogen to anagen(21).

Post-COVID hair loss, is distinguished by gradual remission. And it is at this moment that the use of mixodil may prove to be an effective inducer of both hair regrowth and hair preservation (34).

It is worth noting that the efficacy of minoxidil solution itself may not be associated with higher concentrations. According to a randomized controlled trial, a 5% minoxidil solution was more effective than a 10% (24).

Topically administered minoxidil has been considered to be safe, but some patients suffered from adverse effects following its application. The most frequent adverse effect of minoxidil is contact dermatitis with common symptoms in the form of scaly skin and pruritus. The incidence is higher at a concentration of 5% than at 2% (52).

Platelet-Rich Plasma (PRP)

Platelet-rich plasma (PRP) is an autologous serum with high concentrations of platelets and growth factors. PRP growth factors are known to foster regrowth of hair by inducing differentiation of hair follicle stem cells, as well as inducing and extending the proliferative anagen phase of hair follicles. They also activate anti-apoptotic pathways and augment angiogenesis to boost dermal papilla vascularization to enhance the dermal papilla fibroblast survival (53). These autologous growth factors can be directly injected into the intended tissue, which allows the delivery of more growth factors than the volumes than normal blood circulation alone is able to deliver to the affected areas (54). Only a handful of peer-reviewed trials have investigated the efficacy of using PRP to manage TE, and their findings are conflicting (34).

Akif İşlek et al. conducted a study on 9 patients, following COVID-19, who developed accelerated hair loss with androgenetic alopecia (AGA). These patients received for 4 sessions of platelet-rich plasma (PRP) injections. PRP injections proved effective, with 5 patients describing the treatment as "very effective" (55). To achieve the best results, Dr. Stacy Chimento advises three to four treatments a month apart, as well as an additional session after six months, and then a last session after a year (56).

Low Level Light Therapy (LLLT)

Red or near-infrared laser light has been known for a relatively long time to foster regeneration and tissue repair and low-level laser therapy (LLLT)-low-intensity light boosts cellular activity (57). Low level laser therapy's biological effects encompass anti-inflammatory action, relief of pain, healing of wounds, anti-swelling, immunity, as well as localized blood circulation improvement. And, most importantly, increasing hair regrowth (58). Stimulation of epidermal stem cells within the hair follicles and shifting the follicles to the anagen phase are regarded as the main among the diverse mechanisms (2). Mohamed Amer et al. conducted a study in which 20 female patients including seven with telogenetic alopecia and 13 with female pattern baldness underwent 32 LLLT treatments over 16 consecutive weeks. Application of LLLT to the scalp with a wavelength of 655 nm showed that the women with female pattern baldness had an increase in hair count. However, there is no significant difference in the group of TE patients (59). LLLT apparently seems to be safe and successful in treating hair loss in theory. However, there is a strong need for further clinical and in vitro evaluation (60).

COVID-19 vaccines

Some of the side effects of the COVID-19 vaccine may be underpinned by molecular mimicry and the production of pathological autoantibodies, causing for example hair loss (61).

The Oxford/AstraZeneca vaccine has been proved as safe and effective method used against COVID-19 symptoms, but one case report indicates its possible role in causing alopecia areata in genetically preconditioned individuals via mechanisms of immunity (40).

Alfredo Ross et al. describe 3 cases of patients who experienced a relapse of alopecia areata after a single dose of the vaccine. This occurred 2-3 weeks after vaccination; the patients had previously been in full remission(62).

After COVID-19 vaccination, a total of 18 patients were described who developed AA. The following vaccines were used: in 3 patients AstraZeneca, in 4 Moderna and in 11 after Pfizer/BioNTech vaccination. The beginning of post-vaccination symptoms in the majority of cases varied from a few days to 3 weeks. About 50% of the affected individuals (9) had a personal history of AA, and there were only 5 patients who did not have a previous personal or family history of AA as well as any other autoimmune conditions. Majority of sufferers experience AA restricted to the head skin (63).

However, the reason for hair loss in those cases is still unclear, as no information is known about the health and immune status of the recipients of the vaccine before vaccination. Co-infections that can occur in vaccinated individuals following immunization may be perceived as an effect of the vaccine (64).

Hence, the benefits of administering the COVID-19 vaccine far exceed the risks of aggravating the disease, and authors strongly recommend its use in all qualifying patients with alopecia areata (62).

Conclusions

Given the fairly common occurrence of hair loss after COVID-19 infection, it seems reasonable to seek the most effective strategies for its treatment. At present, it appears that the best results are obtained by combining different treatment methods such as a complete diet providing the full daily requirement of vitamins (A, D, E), micronutrients (zinc, iron) and polyunsaturated fatty acids involved in the process of hair regrowth. In some cases, topical minoxidil and platelet-rich plasma treatments are also worth considering.

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