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# Red LED light therapy for telogen effluvium in the course of long COVID in patients with and without androgenetic alopecia

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## Abstract

**Introduction and Objective**. Photobiomodulation with the use of light-emitting diodes (LEDs) seems to be a promising option for long COVID. This retrospective study evaluates the efficiency of LED irradiation in the treatment of TE in the course of long COVID in patients with and without androgenetic alopecia.

**Materials and methods.** A retrospective single-centre chart review of patients with post-COVID hair loss was performed. 140 patients enrolled to the study were divided into four groups depending on the type of alopecia and treatment: 1) telogen effluvium with LED therapy (TE LED+), 2) telogen effluvium without LED therapy (TE LED-), 3) telogen effluvium and androgenetic alopecia with LED therapy (TE+AGA LED+), and 4) telogen effluvium and androgenetic alopecia without LED therapy (TE+AGA LED-). Clinical and trichoscopic parameters were compared.

**Results**. After 12 weeks, cessation of hair loss and a negative hair pull test were more common in TE LED+ and TE+AGA LED+ in comparison to the patients without LED therapy ($p<0.001$, $p=0.035$, respectively). An increased number of thick hairs and an increased number of hairs within follicular units were more common in patients treated with LED irradiation, regardless of the type of alopecia, compared to the patients without LED therapy.

**Conclusions**. The study revealed that LED therapy is safe, well tolerated and seems to be a promising therapeutic option for TE in patients with long COVID. It can be used as adjuvant therapy leading to faster reduction of hair loss, enhancing hair regrowth as well as hair shaft thickness and density.

## Key words

light-emitting diodes, long COVID, alopecia

## INTRODUCTION

The COVID-19 pandemic has become an important problem for public health worldwide. It is estimated that 80% of survivors will experience long-term medical complications after initial recovery [1, 2]. Such symptoms are defined as long COVID if they develop during or after COVID-19, persist for ≥ 12 weeks and cannot be explained by another diagnosis [2]. According to the meta-analysis performed by Lopez-Leon et al., hair loss is one of the five most common long-term symptoms [2]. So far, associations between COVID-19 and various types of alopecia, including telogen effluvium (TE), androgenetic alopecia (AGA), alopecia areata (AA), anagen effluvium (AE) and pressure-induced alopecia (PA) have been reported. However, out of all these conditions, TE occurs the most often [3, 4]. Diffuse hair loss usually begins within weeks or up to three months after infection [5–7], and its onset occurs sooner in comparison to TE caused by other factors [5, 7]. A meta-analysis performed by Nguyen et al. revealed that patients with post-COVID TE did not have a pre-existing diagnosis of TE [3]. Therefore, it is understandable that such increasing and sudden hair shedding negatively affected patients' quality of life, and caused anxiety [8]. Unlike TE, androgenetic alopecia (AGA) in the majority of patients was diagnosed before the onset of COVID-19; however, data considering its course following COVID-19 are lacking [3, 9].

It has been suggested that a cytokine storm in the blood of patients with COVID-19 may initiate alterations in the hair follicle cycle, leading to exacerbation of AGA and rapid development of TE [3, 5, 9, 10]. Currently, there is no standardized treatment for post-COVID hair loss [4, 9]. Promising therapeutic option targeting inflammation

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associated with COVID-19 seems to be photobiomodulation. Photobiomodulation, also known as low-level light therapy (LLLT), is based on the application of light in the red or infrared spectrum produced from light-emitting diodes (LEDs) or laser to modulate cell metabolism. Typically in photobiomodulation, light with relatively low intensity in the range of 0.04–50 J/cm$^2$ and low power density < 100 mW/cm$^2$ is used [11–13]. Marashian et al. demonstrated that photobiomodulation using red LED light reduced levels of pro-inflammatory cytokines: IL-6, IL-8 and TNF-alpha, and inhibited cytokine storm in mildly to moderately ill patients with COVID-19, compared to the placebo group in which no such effect was observed [13]. Infrared LED photobiomodulation was demonstrated to improve cardiopulmonary function in COVID-19 patients [14], whereas whole-body or transcranial photobiomodulation was shown to be beneficial in the treatment of long COVID brain fog [15]. Among a broad range of dermatological indications, LEDs have been used to treat hair loss. LED irradiation was safe and well-tolerated as monotherapy or combined with standard therapies, both in scarring and non-scarring alopecia [12]. Considering potential therapeutic targets, photobiomodulation might be promising option for post-COVID hair loss [11, 16–19] (Fig. 1). To the best of the authors' knowledge, so far there is only one study evaluating LLLT therapy in combination with microneedling in 10 patients with hair loss related to COVID-19 [10].

## OBJECTIVE

The aim of this retrospective study was to investigate whether LED irradiation might be beneficial in the treatment of telogen effluvium in the course of long COVID in patients with and without androgenetic alopecia.

## MATERIALS AND METHODS

***Sample of patients and data collection.*** A retrospective single-center chart review was performed of all adult patients admitted to the dermatology outpatient clinic from 1 January 2021 – 31 April 2023 due to hair loss following COVID-19. All collected data were part of routine diagnosis and treatment and included age, gender, type of alopecia, comorbidities, results of hair pull test and trichoscopy, laboratory results and previous treatment.

***Inclusion criteria.*** Age >18 years, non-scarring hair loss following COVID-19, SARS-CoV-2 infection, confirmed by a positive PCR test and reported in medical history, persistent hair shedding despite stable treatment for a minimum of two months, two trichoscopic examinations performed during the first visit and control visit after 12 weeks.

***Exclusion criteria.*** Previously diagnosed scarring or non-scaring alopecia excluding androgenetic alopecia, pregnancy, breastfeeding, lack of stable previous treatment of hair loss, lack of control trichoscopic examination, intensive hair shedding before COVID-19, thyroid dysfunction, anemia, vitamin D, B12 and iron deficiency, use of regenerative therapies for hair loss within three months before baseline.

Before enrolment to the study, written informed consent was obtained from all patients to use their medical records The study was approved by the Local Ethics Committee (Approval No. KE-0254/121/04/2023).

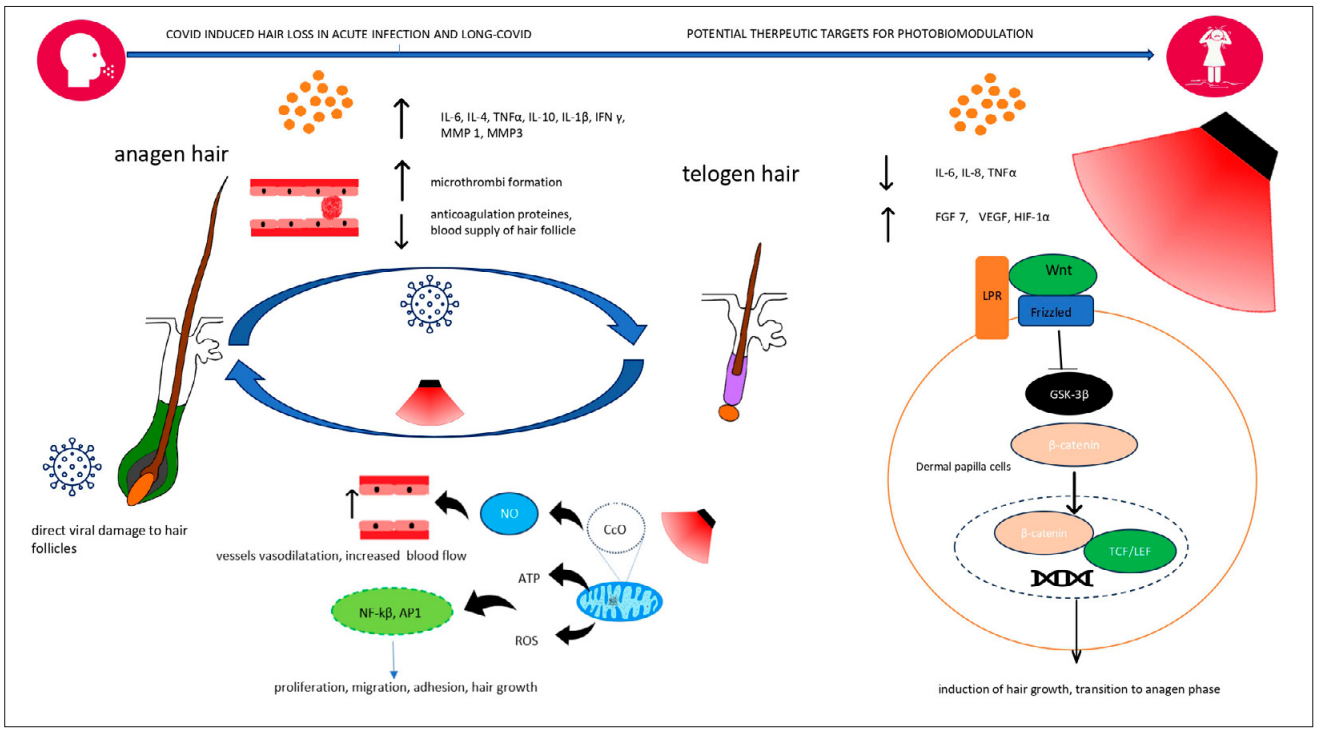


**Figure 1.** Potential therapeutic targets for photobiomodulation in hair loss among patients with long- Covid [11, 16–19]
IL-6 – interleukin-6; IL-4 – interleukin-4; TNFα – tumour necrosis factor alpha; IL-10 – interleukin-10;, IL-1β – interleukin-1beta; IFN γ – interferon gamma; MMP 1 – matrix metalloproteinase 1;MMP3 – matrix metalloproteinase 3; FGF7 – fibroblast growth factor 7; VEGF – vascular endothelial growth factor; HIF-1α – hypoxia-inducible factor 1; LPR – low-density lipoprotein-related protein; GSK3β – glycogen synthase kinase-3; TCF – T-cell factor; LEF – lymphoid enhancer factor; CcO – cytochrome c oxidase; NO – nitric oxide), ROS; reactive oxygen species; AP1 – activator protein1; NF-kβ – (nuclear factor- kβ

The medical records of 167 patients were identified, among whom 140 met the inclusion criteria. The patient selection flow chart is presented in Figure 2.

Patients were divided into four groups:

1) telogen effluvium with LED therapy (TE LED$^+$) (53 patients);
2) telogen effluvium without LED therapy (TE LED$^-$) (27 patients);
3) telogen effluvium and androgenetic alopecia with LED therapy (TE+AGA LED$^+$) (47 patients);
4) telogen effluvium and androgenetic alopecia without LED therapy (TE+AGA LED$^-$) (13 patients).

In the LED$^-$ group, LED therapy was not applied due to contraindication, such as epilepsy, light-induced severe headaches or problems with access to the hospital due to pandemic restrictions. In all groups, patients continued previous topical or systemic treatment for hair loss.

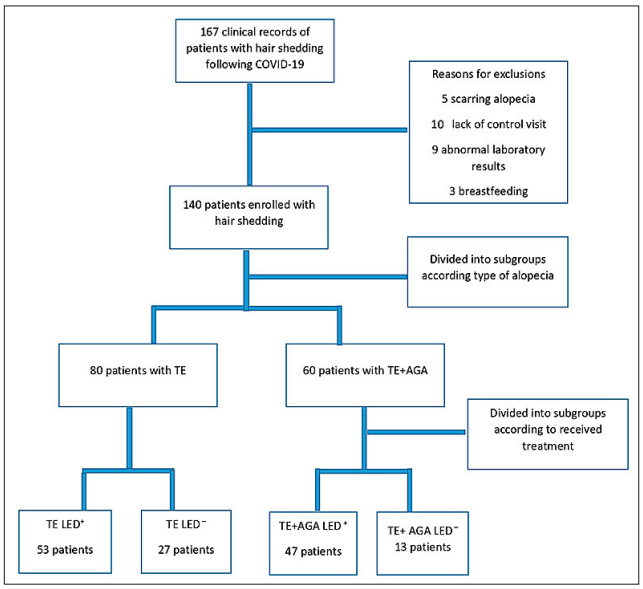


**Figure 2.** Patient selection flow chart
TE – telogen effluvium; AGA – androgenetic alopecia; TE+AGA – telogen effluvium and androgenetic alopecia; TE LED$^+$ – telogen effluvium with LED therapy; TE LED$^-$ –:telogen effluvium without LED therapy; TE+AGA LED$^+$ – telogen effluvium and androgenetic alopecia with LED therapy; TE+AGA LED$^-$ – telogen effluvium and androgenetic alopecia without LED therapy

In all patients from the LED$^+$ group, the LED irradiations were performed using a source of light based on the LED matrix illuminator: Red Beam pro+, Model APRO (MedLight GmbH), which provides red light operating at 630±5 nm with a maximum power density of 100–120 mW/cm$^2$. The dose per session – 37 J/cm$^2$, light power density – 68 mW/cm$^2$, time – 9 minutes 39 seconds, distance from the scalp – 15 cm. During treatment, patients' eyes were protected by goggles. Irradiations were performed once a week for a period of 10 weeks.

***Assessment of LED effectiveness.*** To determine the effect of LED therapy on post-COVID hair loss, the results of the hair pull test and trichoscopic examinations performed in patients from the LED$^+$ and LED$^-$ group before (baseline visit) and after 12 weeks (control visit, the time corresponded to two weeks after the last irradiation in the LED$^+$ group) were compared. Trichoscopy was performed according to standard procedure using a FotoFinder Dermoscope (FotoFinder Systems GmBH). The type of alopecia was established based on trichoscopic criteria, along with the result of the hair pull test and, if available, trichogram results [20]. In the case of the presence of: hair shaft heterogeneity, vellus hair, predominance of follicular units with one hair shaft in the frontal area, yellow dots and/or presence of upright regrowing hair together with a positive hair pull test, coexistence of TE with AGA was diagnosed [20]. The proportion of thick hairs >0.05 mm, mid-thick hairs 0.03–0.05 mm and thin hairs <0.03 mm, as well as the proportion of follicular units with 1–3 hairs and presence of upright regrowing hair in the frontal, occipital and temporal areas at baseline and after 12 weeks was compared. The primary endpoint was resolution of hair shedding reported by the patient, confirmed by a negative hair pull test and change in the proportion of hair according to the size and proportion of follicular units with 1–3 hairs before and after twelve weeks. The secondary endpoint was assessment of subjective symptoms such as trichodynia or scalp itching.

***Statistical analysis.*** The data were statistically analyzed using STATISTICA 13 software. Mean (M) and standard deviation (SD) were estimated for numerical variables, as well as absolute numbers (n) and percentages (%) of the occurrence of items for categorical variables. Student t test for unpaired data was used to compare the age of patients and disease duration between the two groups, Student t test for paired data was used to compare numerical trichoscopic parameters between baseline and control visit, and the Fisher exact test was used to compare categorical clinical parameters between baseline and control visit. The significance level was assumed at 0.05.

## RESULTS

***Characteristics of TE LED$^+$ and TE LED$^-$ groups.*** Gender, age and duration of hair shedding did not significantly differ between the LED$^+$ and LED$^-$ groups. The majority of participants were females: 52/53 and 26/27 in the LED$^+$ and LED$^-$ groups, respectively. The LED$^+$ group included 53 patients aged 38.3±15.0 years, on average, and the LED$^-$ group included 27 patients aged 44.4±13.2 years, on average (p=0.082). Duration of hair shedding before the baseline visit was 5.7± 1.8 months vs. 6.3 ±1.5 months, on average, in the LED$^+$ vs. LED$^-$ group, respectively (p=0.147).

During the baseline visit, all patients from both groups had a positive pull test. In both groups, patients continued previous treatment for hair loss, including topical minoxidil or topical steroid: in LED$^+$ 50.9% and 69.8% and in LED$^-$ 92.6% and 62.9%, respectively. The majority of patients had a mild or asymptomatic course of COVID that did not require hospitalization: 84.9% /92.6% in the LED$^+$ / LED$^-$group, respectively. The most common symptoms of long COVID in both groups were fatigue and memory loss: LED$^+$ 71.1%, 64.1% and LED$^-$ 44.4% and 48.1%, respectively (Tab. 1).

***Characteristics TE+AGA LED$^+$ and TE +AGA LED$^-$ groups.*** The majority of participants were females: 45/47 and 12/13 in the LED$^+$ and LED$^-$ group, respectively. The LED$^+$ group included 47 patients aged 52.2±16.7 years, on average, and the LED$^-$ group included 13 patients aged 59.8±18.1 years, on average (p=0.162).

In all patients from both groups, AGA was diagnosed before COVID-19 onset and patients used a stable treatment for AGA. Severity of AGA was evaluated using the Norwood-Hamilton scale in men and Ludwig classification in women. In both groups, the majority of females had grade I or II, whereas two male patients had stage IV and one had stage III. In both groups, all patients had a positive hair pull test and continued the previous treatment. In the $LED^+$ group, patients received topical minoxidil or steroid or oral finasteride (76.6%, 55.3% and 21.3%, respectively), whereas in the $LED^-$ group, topical minoxidil was used by 84.6% of patients, finasteride by 23.1% and topical steroid by 61.5%. Duration of hair loss before the baseline visit was 6.3± 2.1 months vs. 5.3 ±1.6 months, on average, in the $LED^+$ vs. $LED^-$ group, respectively (p=0.429). A severe course of COVID-19 was observed in 29.8% patients from the $LED^+$ and in 7.7% from the $LED^-$ group. The most common symptoms of long COVID in both groups were fatigue and memory loss: $LED^+$ 70.2%, 74.5% and $LED^-$ 61.5% and 61.5%, respectively (Tab. 1).

***Comparison of clinical parameters between baseline and control visit.*** The improvement of clinical parameters was analyzed, i.e. hair pull test, trichodynia, itch, regrowing hairs in the patients who presented such symptoms on the baseline visit (Tab. 2).

Among patients with positive hair pull test on baseline visit in the TE $LED^+$ group, hair loss stopped and the pull test was negative in a significantly higher percentage of patients compared to the TE $LED^-$ group (86.8% vs. 48.1% of patients, respectively; p <0.001). Trichodynia was reported by 25 patients from the $LED^+$ group and 24 patients from the $LED^-$ group at baseline. After 12 weeks, resolution of trichodynia was observed in 21 out of 25 (84%) patients in the TE $LED^+$ group and 14 out of 24 (58.3) patients in the TE $LED^-$ group (p=0.062). Regrowing hairs were observed more commonly in patients from the $LED^+$ group, compared to the $LED^-$ group in the frontal, occipital and temporal areas (p=0.001; p=0.001; p<0.001, respectively).

In the TE+AGA $LED^+$ group hair loss stopped and the pull test was negative in a significantly higher percentage

**Table 1.** Characteristic of the study group

| PARAMETER | TE | | TE+AGA | |
|---|---|---|---|---|
| | $LED^+$(n=53) | $LED^-$(n=27) | $LED^+$(n=47) | $LED^-$(n=13) |
| Gender: Female/Male | 52/1 | 26/1 | 45/2 | 12/1 |
| Age (years), M±SD | 38.3±15.0 | 44.4±13.2 | 52.2±16.7 | 59.8±18.1 |
| | p=0.082 | | p=0.162 | |
| Duration of hair shedding before baseline visit (months), M±SD | 5.7±1.8 | 6.3±1.5 | 6.3±2.1 | 5.8±1.6 |
| | p=0.147 | | p=0.429 | |
| 1–3 months, n (%) | 7 (13.2) | 1 (3.7) | 2 (4.2) | 2 (15.4) |
| 4–5 months, n (%) | 19 (35.8) | 4 (14.8) | 17 (36.2) | 2 (15.4) |
| ≥6 months, n (%) | 27 (51.0) | 22 (81.5) | 28 (59.6) | 9 (69.2) |
| Onset of hair shedding after COVID-19 recovery | | | | |
| 1–3 months, n (%) | 44 (83.0) | 26 (96.3) | 41 (87.2) | 13 (100) |
| 4–5 months, n (%) | 9 (17.0) | 1 (3.7) | 6 (12.8) | 0 (0.0) |
| ≥6 months, n (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Treatment for hair loss before baseline visit | | | | |
| topical minoxidil, n (%) | 27(50.9) | 25 (92.6) | 36 (76.6) | 11 (84.6) |
| topical steroid, n (%) | 37 (69.8) | 17 (62.9) | 26 (55.3) | 8 (61.5) |
| Finasteride, n (%) | 0 (0.0) | 0 (0.0) | 10 (21.3) | 3 (23.1) |
| Severity of AGA | | | | |
| Ludwig grade I/II/III (n) | - | - | 21/26/6 | 5/6/2 |
| Norwood-Hamilton grade III/IV (n) | - | - | 1/1 | 0/1 |
| Comorbidities, n (%) | | | | |
| Hypertension | 5 (9.4) | 4 (14.8) | 7 (14.8) | 2 (15.4) |
| Depression | 7 (13.2) | 3 (11.1) | 8 (17.0) | 0 (0.0) |
| Obesity | 3 (5.3) | 1 (3.7) | 2 (4.25) | 0 (0.0) |
| Multiple sclerosis | 1 (1,9) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Symptoms of long COVID, n (%) | | | | |
| Brain fog | 11 (20.7) | 6 (22.2) | 7 (14.9) | 4 (30.7) |
| Memory loss | 34 (64.1) | 13 (48.1) | 35 (74.5) | 8 (61.5) |
| Vertigo | 8 (15.0) | 1 (3.7) | 5 (10.6) | 0 (0.0) |
| Fatigue | 38 (71.7) | 12 (44.4) | 33 (70.2) | 8 (61.5) |
| Severe course of COVID-19, n (%) | 8 (15.1) | 2 (7.4) | 14 (29.8) | 1 (7.7) |
| Vaccination, n (%) | 28 (52.8) | 19 (70.4) | 27 (57.5) | 6 (46.2) |

TE – telogen effluvium); AGA – androgenetic alopecia; $LED^+$ – with LED therapy; $LED^-$ – without LED therapy); n – number.

**Table 2.** Comparison of clinical parameters between baseline and control visit in patients who presented negative symptoms

| Improvement / clinical symptoms | TE | | | TE+AGA | | | TE vs TE+AGA | |
|---|---|---|---|---|---|---|---|---|
| | $LED^+$N2/N1 (%) | $LED^-$N2/N1 (%) | p | $LED^+$N2/N1 (%) | $LED^-$N2/N1 (%) | p | $LED^+$(p) | $LED^-$(p) |
| Negative hair pull test after treatment / positive hair pull test before treatment | 46 / 53 = 86.8 | 13 / 27 = 48.1 | <0.001 | 37 /47 = 78.7 | 6 / 13 = 46.2 | 0.035 | 0.301 | 1 |
| No trichodynia / trichodynia | 21 / 25 = 84.0 | 14 /24 = 58.3 | 0.062 | 30 / 31 = 96.8 | 9 / 10 = 90.0 | 0.433 | 0.161 | 0.113 |
| No itch / itch | 4 / 7 = 57.1 | 2 / 3 = 66.7 | 1 | 9 / 11 = 81.8 | 3 / 5 = 60.0 | 0.547 | 0.326 | 1 |
| Regrowing hairs / Lack of regrowing hairs | | | | | | | | |
| – frontal area | 35 / 41 = 85.4 | 11 / 25 = 44.0 | 0.001 | 28 / 34 = 82.4 | 1/ 13 = 7.7 | <0.001 | 0.761 | 0.030 |
| – occipital area | 23 / 52 = 44.2 | 2 / 27 = 7.4 | 0.001 | 20 / 46 = 43.5 | 0 / 13 = 0.0 | 0.003 | 1 | 0.550 |
| – temporal area | 35 / 51 = 68.6 | 4 / 24 = 16.7 | <0.001 | 27 / 41 = 65.9 | 2 / 13 = 15.4 | 0.003 | 0.825 | 1 |

N1– number of patients presenting clinical symptoms at baseline visit; N2 – number of patients with improvement at control visit (after 12 weeks from baseline visit); TE – telogen effluvium; TE+AGA – telogen effluvium coexisting with androgenetic alopecia.

of patients compared to the TE+AGA $LED^-$ group (78.7% vs. 46.2% of patients, respectively; p=0.035). Trichodynia was reported by 31 patients from the $LED^+$ group and 10 patients from the $LED^-$ group. After 12 weeks resolution, trichodynia was observed in 30 out of 31 patients (96.8%) from the TE+AGA $LED^+$ group, and in 9 out of 10 patients (81.8%) from TE+AGA $LED^-$ group (p=0.433). Regrowing hairs were observed more commonly in patients from the $LED^+$ group, compared to the $LED^-$ group in the frontal, occipital and temporal area (p<0.001; p=0.003; p=0.003, respectively).

***Comparison of trichoscopic parameters between baseline and control visit.*** In the TE $LED^+$ group the percentage of thick hairs in the frontal, occipital and temporal areas increased significantly (p=0.024; p=0.009; p=0.015, respectively), whereas in the TE $LED^-$ group, the proportions of thick hairs did not change significantly. The percentage of mid-thick hairs in frontal, occipital and temporal area did not differ significantly in both TE $LED^+$ and TE $LED^-$ groups. The percentage of thin hairs decreased significantly in TE $LED^+$ group (p=0.001) and increased in LED- group (p=0.036). In patients from the TE $LED^+$ group, the mean number of hairs per follicular unit increased significantly in the frontal area from 1.67 ± 0.25 to 1.78 ± 0.25 (p<0.001) and in the occipital area from 2.07±0.31 before to 2.17±0.25 after therapy, p<0.001. In the TE $LED^-$ group, the number of hairs per follicular unit in the frontal area decreased from 1.82±0.31 to 1.67±0.36, p=0.028 (Tab. 3, Fig. 3).

In the TE+AGA $LED^+$ group, the percentage of thick hairs in the frontal, occipital and temporal areas increased significantly (p<0.001; p= 0.020; p=0.007, respectively), whereas in the TE+AGA LED- group the hair proportions did not change significantly. In patients from the TE+AGA $LED^+$ group, the mean number of hairs per follicular unit increased significantly in the frontal area from 1.37 ± 0.25 – 1.56 ± 0.25 (p<0.001), and in the occipital area from 1.95±0.33 at baseline to 2.04±0.3 after therapy, p=0.003 (Tab. 3, Fig. 3).

***Comparison between TE $LED^+$ and TE+AGA $LED^+$ groups.*** TE $LED^+$ and TE+AGA $LED^+$ groups did not differ with regard to the reduction of hair shedding confirmed by a negative hair pull test (p=0.301) or trichodynia resolution (p=0.161). The presence of regrowing hairs in all investigated areas did not differ significantly in both groups (Tab. 2).

***Comparison between TE $LED^-$ and TE+AGA $LED^-$ groups.*** The groups did not differ significantly with regard to the cessation of hair loss or trichodynia resolution (p>0.05). Regrowing hairs in the frontal area were observed more commonly in the TE LED- group, compared to the TE+AGA LED- group (44% vs 7.7%; p=0.030) (Tab. 2).

## DISCUSSION

Hair shedding is a distressing consequence of COVID-19, and sudden hair loss may cause fear of being totally bald and consequently lower the patient's quality of life, and have a demoralising effect on self-esteem or self-image [21, 22]. Numerous studies have been carried out demonstrating TE to be one of the most common sequelae of COVID-19 [6, 21, 23]. In the presented study, 80 patients were diagnosed with TE and 60 with TE co-existing with AGA. Pre-existing AGA was reported to be the most common type of concurrent alopecia in patients with post-COVID TE, and was usually diagnosed before COVID-19, which is in agreement with the results of the current study [3, 24]. Similar to other studies, the prevalence of females was observed. It has been suggested that this might result not only from hair length which makes hair loss more obvious, but also from their sense of beauty and a gender-specific predisposition to develop TE [24].

Post-COVID TE has unique features: an earlier onset within 1–3 months after recovery, and shorter duration (2 months, on average, compared to the classic type) [3, 7]. In the current study, in accordance with other reports, hair shedding began within 1–3 months in the majority of patients; however, its duration was longer. Moreover, the tendency was observed of hair shedding persisting for more than 6 months in all groups, which might result from the fact that all patients in the current study were also diagnosed with long COVID. Considering the abundance of studies focusing on acute TE, our study is of special interest because it gives attention to prolonged duration of hair loss in patients with long COVID. So far, only a single study has reported a hair loss duration longer than six months, observed in 32.94% of patients with post-COVID TE [21].

It has been suggested that excessive hair loss after COVID-19 might result from release of proinflammatory cytokines, microthrombi formation leading to insufficient blood supply of hair follicles or direct viral damage to hair follicles [5].

**Table 3.** Comparison of trichoscopic parameters between baseline and control visit

| Parameter | TE | | | | | | TE+AGA | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LED⁺ | | | LED⁻ | | | LED⁺ | | | LED⁻ | | |
| | baseline visit M±SD | control visit M±SD | p | baseline visit M±SD | control visit M±SD | p | baseline visit M±SD | control visit M±SD | p | baseline visit M±SD | control visit M±SD | p |
| Proportion of thick hairs (%) | | | | | | | | | | | | |
| – frontal area | 62.7±14.3 | 65.9±14.5 | 0.024 | 66.4±17.6 | 63.5±14.7 | 0.205 | 41.7±17.2 | 52.0±19.9 | <0.001 | 39.1±17.1 | 43.5±15.1 | 0.270 |
| – occipital area | 67.4±17.0 | 73.7±14.4 | 0.009 | 71.0±21.5 | 73.5±15.4 | 0.561 | 58.0±17.1 | 63.1±16.3 | 0.020 | 63.3±11.4 | 63.5±13.4 | 0.916 |
| – temporal area | 46.0±22.3 | 52.0±22.0 | 0.015 | 54.1±24.7 | 55.4±22.2 | 0.740 | 34.8±25.9 | 43.9±21.6 | 0.007 | 26.7±24.8 | 33.9±22.5 | 0.254 |
| Proportion of mid-thick hairs (%) | | | | | | | | | | | | |
| – frontal area | 30.1±12.5 | 28.7±12.2 | 0.248 | 28.6±16.5 | 30.0±14.9 | 0.492 | 38.1±13.0 | 36.6±14.9 | 0.550 | 45.2±13.3 | 43.0±11.0 | 0.569 |
| – occipital area | 29.7±15.4 | 24.0±13.2 | 0.057 | 27.3±21.3 | 24.6±14.8 | 0.540 | 36.9±16.3 | 33.4±14.4 | 0.086 | 33.1±11.7 | 32.2±11.8 | 0.453 |
| – temporal area | 43.3±20.1 | 39.0±19.5 | 0.096 | 37.3±23.3 | 38.2±20.1 | 0.764 | 46.6±23.1 | 41.7±19.2 | 0.103 | 63.5±24.0 | 53.9±20.0 | 0.123 |
| Proportion of thin hairs (%) | | | | | | | | | | | | |
| – frontal area | 7.2±4.3 | 5.4±4.0 | 0.001 | 5.0±3.9 | 6.5±2.9 | 0.036 | 20.2±11.9 | 11.4±7.2 | <0.001 | 15.7±8.3 | 13.5±7.9 | 0.040 |
| – occipital area | 2.9±3.4 | 2.3±2.9 | 0.119 | 1.7±3.0 | 1.9±3.1 | 0.771 | 5.0±7.0 | 3.5±4.8 | 0.028 | 3.6±4.3 | 4.3±3.5 | 0.681 |
| – temporal area | 10.7±8.5 | 9.0±8.2 | 0.159 | 8.6±8.8 | 6.4±5.4 | 0.329 | 18.7±15.4 | 14.4±13.0 | 0.067 | 9.8±4.9 | 12.2±4.6 | 0.338 |
| Average number of hairs within follicular unit | | | | | | | | | | | | |
| – frontal area | 1.67±0.25 | 1.78±0.25 | <0.001 | 1.82±0.31 | 1.67±0.36 | 0.028 | 1.37±0.25 | 1.56±0.28 | <0.001 | 1.37±0.18 | 1.36±0.20 | 0.825 |
| – occipital area | 2.07±0.31 | 2.17±0.25 | <0.001 | 2.04±0.25 | 2.12±0.27 | 0.058 | 1.95±0.33 | 2.04±0.30 | 0.003 | 1.96±0.21 | 1.95±0.23 | 0.659 |
| – temporal area | 1.60±0.35 | 1.67±0.32 | 0.091 | 1.74±0.36 | 1.78±0.44 | 0.734 | 1.39±0.34 | 1.48±0.29 | 0.054 | 1.36±0.24 | 1.37±0.22 | 0.896 |

TE – telogen effluvium; AGA – androgenetic alopecia; LED⁺ – with LED therapy; LED⁻ – without LED therapy

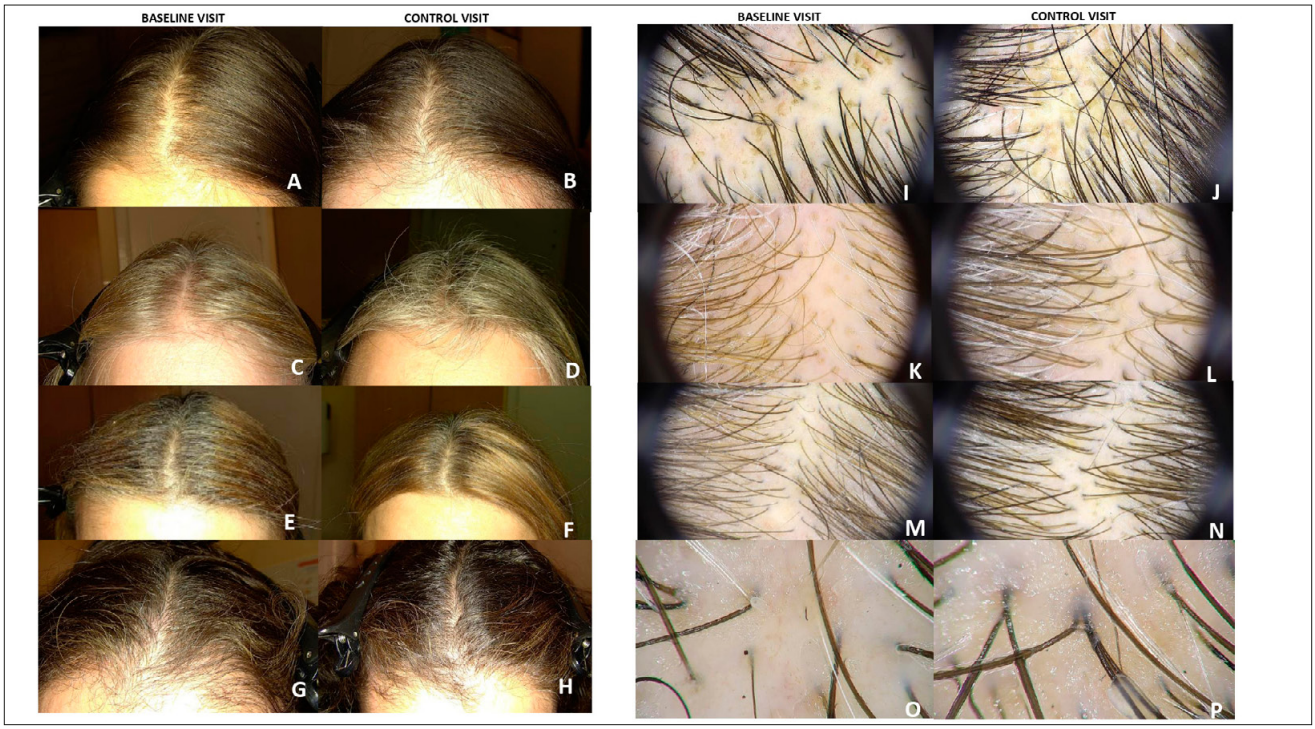


**Figure 3.** Comparison of clinical and trichoscopic images during baseline and control visit in patients with LED therapy. TE + AGA LED⁺ group; B,D, J, L clinically presented regrowing hairs and increased number of thick hairs after 10 LED irradiation, compared to baseline visit (A,C, I, K); TE LED⁺ (F,H,N,P) increased thickness and number compared to baseline visit (E,G,M,O)

Increased secretion of inflammatory cytokines such as interleukin-6, (IL-6), interleukin-4 (IL-4), interleukin-10 (IL-10) and interleukin-1beta (IL-1β), tumor necrosis factor alpha (TNFα) and interferon gamma interferon (IFN γ) has been reported in patients with COVID-19 [13, 25, 26]. Among those cytokines, IL-6, IL-1β, INF γ, TNFα were demonstrated to induce catagen or inhibit anagen in murine and/or human hair follicles [27–29]. Interestingly, IL-4, which is associated with a non-severe course of COVID-19, was also reported to induce apoptosis in cultured human follicular keratinocytes and may regulate catagen formation in the hair follicle [25, 30]. The cytokine storm is important for initiating TE. It has also been proposed that inflammation observed in COVID-19 may greatly accelerate the gradual

process of pattern hair loss progression [9], since similar cytokines, such as IL-6 or TNFα, were demonstrated to be involved in the pathogenesis of AGA [28, 31, 32]. Unlike acute COVID-19, data considering cytokine levels in long COVID are inconclusive. A meta-analysis performed by Yin et al. revealed the presence of increased IL-6 levels in patients with long COVID compared to the healthy group, but lower levels in comparison with acute COVID [33]. In another study, increased levels of interleukin 17 (IL-17), TNF-α and interleukin 2 (IL-2) were reported in long COVID, whereas higher levels of IL-6 were observed only in the acute phase. Interestingly, cytokine levels of INF-y, IL-10 and IL-4 did not show significant differences between the acute and long COVID group. Studies have also reported that immune dysregulation and increased levels of selected cytokines might persist from 8–14 months [34]. Therefore, it cannot be excluded that the observed alteration in cytokine levels in long COVID might be responsible for prolongation of the hair shedding observed in the patients in the current study [35].

A number of treatments have been proposed to control post-COVID TE, including: topical minoxidil, oral hair growth supplements, vitamins, minerals or regenerative strategies, such as adipose-derived mesenchymal cells and platelet-rich plasma [4, 10]. So far, only one study has reported promising results of combined therapy: low-level light therapy (LLLT) with red and blue light together with microneedling in preliminary study including 10 patients with androgenetic alopecia and a positive COVID-19 history [10]. The presented retrospective study reports for the first time the results of LED therapy with the use of red LED light in a large group of patients with post-COVID hair loss either TE or TE coexisting with AGA, compared to 40 patients without LED treatment.

Inhibition of hair loss confirmed by a negative hair pull test was observed more often both in TE and TE+AGA groups after 10 LED irradiations compared to the $LED^-$, in which hair shedding was still observed. TE is considered a self-limiting condition; nevertheless, during the baseline visit, all patients presented a positive hair pull test and did not report reduction in the severity of hair shedding despite its longer duration. Therefore, in the opinion of the authors of the current study, the chance for fast spontaneous improvement was low. The observed earlier cessation of hair loss in $LED^+$ groups compared to $LED^-$ groups might result from a direct immunomodulatory effect of photobiomodulation inducing faster remission. This is of special interest since prolonged hair shedding lasting longer than 6 months might lead to development of chronic TE characterized by a poorer prognosis [36, 37].

A potential therapeutic effect of red LED light was demonstrated in the inflammatory phase of mild to moderate COVID-19, and after 72 hours led to a reduction in the circulating levels of IL-6, interleukin 8 (IL-8) and TNFα [13]. It is likely that reduction of cytokines responsible for anagen termination or catagen induction may lead to reduction of hair shedding. However, it cannot be excluded that the observed cessation of hair loss in the groups treated with LED irradiations resulted not only from modulation of inflammatory processes, but also from a direct effect on hair follicles. In the dermal papilla cells, LLLT therapy was demonstrated to increase Wnt signalling [17], considered to be a key factor in promoting hair growth [10]. Han et al. documented that red light LED irradiation promoted hair growth in an *in vitro* hair follicle organ culture by activating the Wnt/β-catenin signaling pathway [38]. In another study, immunohistochemistry of the dorsal skin in mice treated with LLLT revealed increased β-catenin/Sonic Hedgehog expression similar to the group treated with minoxidil, and an increased proliferation rate of fibroblast growth factor-7 (FGF7) [16], whereas skin biopsies demonstrated an increased number of anagen follicles. According to the authors, this suggests a possible role for photobiomodulation in the hair-promoting activity related to inducing the anagen phase, enhancing hair growth capability and new hair development [16]. In the current study, together with the cessation of hair shedding, a significantly increased percentage of regrowing hair was observed in all assessed areas, both in TE $LED^+$ and TE+AGA $LED^+$ in contrast to both $LED^-$ groups, which might result from the mechanisms described above.

After a treatment course consisting of 10 LED irradiations, a significant increase in the number of hair shafts per follicular unit in the frontal and occipital area in both TE and TE+AGA groups were observed, whereas in TE $LED^-$ a reduction of hair density was noted, possibly resulting from ongoing hair shedding. Trichoscopic examination revealed a significantly increased percentage of thick hairs in the frontal, occipital and temporal areas, both in TE $LED^+$ and TE+AGA $LED^+$, which led to clinical improvement. It is accepted that LLLT irradiation prolongs the duration of the hair growth phase, stimulates anagen reentry in telogen hair, prevents premature catagen induction and increases rates of proliferation in active anagen hair [12, 39, 40]. Taken together, modulation of the hair cycle leads to an increase of hair diameter and density, which is in agreement with the results obtained in the current study. Gentile at al. also reported increased hair density after combined therapy consisting of LLLT microneedling and growth factors [10].

So far, improvement after LLLT therapy has been observed mainly in AGA, whereas TE did not respond to the treatment [12, 41, 42]. In the presented study, a beneficial effect of photobiomodulation was observed both in TE and in TE coexisting with AGA. It cannot be ruled out that the observed improvement in TE groups resulted from a different mechanism leading to development of post-COVID TE, including not only inflammation but also insufficient blood supply of hair follicles due to microthrombi formation. Kato et al. demonstrated that hair follicles are very sensitive to ischemia. A study performed *in vivo* on a mice model and *ex vivo* on organ cultures of human scalp cells and mouse hair follicles demonstrated that anagen hairs exposed to ischemia exhibited a significant decrease in hair growth rate, hair shaft size, and colour. Taken together, a reduced blood supply of hair follicles may contribute to impaired hair growth and hair loss, whereas hyperoxygenation treatment may induce hair fiber growth during anagen and delay onset of catagen [43]. Evidence suggests that one of the molecular mechanisms of action in photobiomodulation is photodyssociation of nitric oxide (NO) from cytochrome c oxidase. An increased level of circulating NO induces vasodilation and improves blood flow, leading to better hair growth [11, 44].

Post-COVID TE may be associated with trichodynia. In the current study, trichodynia was present both in patients with TE and TE+AGA in the $LED^+$ and $LED^-$ group. The resolution of trichodynia was observed in all groups. Starace et al. reported the presence of trichodynia in patients with post-COVID TE [45]. Trichodynia was reported to be associated

with increased substance P expression. This neuropeptide is a key factor in neuroinflammation and is involved in neuropathic pain which occurs in the scalp in association with hair loss [46]. Within hair follicles, substance P was demonstrated to trigger microinflammation by increasing mRNA expression of inflammatory cytokines, such as IL-1β, IL-6, and IL-8, and mRNA expression of hair growth-related factors [47]. Data concerning the effect of photobiomodulation on substance P are inconclusive and difficult to compare, since different light sources with different wavelengths have been used [48–50]. Therefore, further studies are required to evaluate the effect of red LED light on substance P [45]. Considering that trichodynia might also be related to stress, it cannot be excluded that the observed relief of symptoms was associated with cessation of hair loss and clinical improvement observed by the patients. Interestingly, in the current study, no significant differences were observed between the TE LED$^+$/ TE+AGA LED$^+$ groups and between TE LED$^-$ and TE+AGA LED$^-$, regarding cessation of hair loss. However, hair regrowth in the frontal area was observed significantly more often in patients from the TE LED$^-$ group in comparison to TE+AGA LED$^-$, which might result from the younger age of patients in the TE LED$^-$ group.

The majority of enrolled patients did not start the therapy of post-COVID hair loss in the authors department, therefore no comparisons could be made about the efficacy of previous treatments. The patients reported using either topical minoxidil or topical steroids, which did not lead to improvement, since severe hair shedding confirmed by a positive hair pull test was present at the baseline visit. Therefore, it is assumed that the previous therapy was insufficient. In this study, LED irradiations were used as adjuvant therapy according to the standard protocol, including the same distance from the scalp, dose per session and number of irradiations, which ensured the comparability of results. The main indication for finasteride was pre-existing androgenetic alopecia. All patients continued their previous treatment both for post-COVID hair loss and androgenetic alopecia without any modification. Therefore, in the opinion of the authors of this article, a more prominent improvement in LED treated groups, both with TE or TE+AGA, in comparison to LED$^-$ groups might result either from modulation and boosting of the therapeutic effect of used medications, or from direct effects of LED irradiation on hair follicles. Further randomized studies are required to confirm this hypothesis. The observations are in accordance with other studies suggesting that post-COVID hair loss usually does not respond to single interventions and requires complementary therapy [4, 10].

It has been suggested that the severity and shorter duration of post-COVID TE may be related to the individual course of the infection and severity of COVID-19 [7]. In the current study, the majority of patients reported a mild or asymptomatic course of COVID-19. Considering the increased immunity of the general population, a relatively high proportion of people vaccinated against COVID-19 and the presence of new virus variants causing a milder course of illness, this study is of special interest because it shows that patients with mild COVID might also be prone to developing hair loss [51], which might tend to persist longer.

All patients in presented study tolerated the therapy well and reported that the observed gradual reduction of hair shedding reduced their fear of becoming totally bald, and positively affected their well-being. From this point of view, LED therapy seems to be a promising therapeutic option for patients with post-COVID hair loss, because it leads to clinical improvement, shortens hair shedding duration, and thus may reduce unwanted stress [52].

A limitation of this study is its retrospective character, since it included only reports of patients who consulted a dermatologist due to long-lasting and severe hair loss. Another limitation is the diversity of pre-existing treatment that patients received before starting LED therapy.

## CONCLUSIONS

Hair loss is a common and stressful sequel of COVID-19; therefore, there is a need for a safe therapy for patients. Despite the self-limiting nature of hair loss, in some patients the hair shedding may last longer and tend to become chronic. The presented study revealed that LED therapy is safe, well tolerated and seems to be a promising therapeutic option for post-COVID TE in patients suffering from long COVID, with or without androgenetic alopecia. This therapy can be used as an adjuvant treatment leading to faster reduction of hair shedding, enhancing hair regrowth and relieving subjective symptoms, such as trichodynia in prolonging post-COVID hair loss. Apart from the cessation of hair shedding, LED therapy increases the percentage of thick hair and increases hair density, which all together lead to a clinically and cosmetically accepted improvement. Further studies are required to evaluate the long-term effects of such therapy, and to evaluate whether earlier application of LED therapy would prevent or shorten the post-COVID hair loss.

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**Ethical Considerations.** The study was approved by the Local Ethics Committee (Decision No. KE-0254/121/04/2023), and complied with Ethical Guidelines of the 1975 Declaration of Helsinki. Informed Consent Statement. Before enrolment, all patients were acquainted with the objective of the study and provided written informed consent for use of their medical records. Written informed consent was also provided by the patients for the publication of clinical and trichoscopic images included in the study.

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