OCHOŃSKA, Izabela, JAGLARZ, Karolina, KUCA, Maciej, CHOLEWA, Marcin and JASIEWICZ, Maria. Non-pharmacological therapies in the treatment of chemotherapy-induced alopecia – a literature review. Journal of Education, Health and Sport. 2025;77:56966. eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.77.56966
https://apcz.umk.pl/JEHS/article/view/56966

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 13.12.2024. Revised: 08.01.2025. Accepted: 08.01.2025. Published: 08.01.2025.

Non-pharmacological therapies in the treatment of chemotherapy-induced alopecia – a literature review

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Abstract

Introduction and Objective. Every year, 20 million people are diagnosed with cancer, most of whom undergo chemotherapy at some stage of treatment. Chemotherapy is associated with various side effects, with hair loss being one of the most visible and socially stigmatizing. This study aimed to evaluate and summarize existing strategies for preventing chemotherapy-induced hair loss.

Review methods. Data for this paper were gathered using electronic databases like PubMed and Google Scholar, with a focus on papers from the last five years, particularly clinical trials, double-blind randomized studies, meta-analyses, and reviews.

State of Knowledge. Around 65% of chemotherapy patients experience hair loss. Currently, the FDA has approved one method for preventing chemotherapy-induced alopecia (CIA): scalp cooling. This technique induces localized vasoconstriction, reducing the penetration of chemotherapy drugs into hair follicles. Scalp cooling is generally well-tolerated. Other potential methods include scalp injections of autologous platelet-rich plasma, which contains growth factors and anti-inflammatory cytokines, and microneedling, an invasive procedure with uncertain effectiveness, especially as a standalone treatment, that aims to stimulate angiogenesis.

Conclusions. Effective, reliable methods for preventing chemotherapy-induced alopecia (CIA) are still lacking. A holistic approach to oncology care is needed to address the diverse needs of patients. Discovering new preventive methods would greatly improve patients' ability to cope with cancer treatment. However, most current approaches show only moderate efficacy or are still in clinical trials.
Keywords: chemotherapy-induced alopecia; CIA; hair loss; cancer; hair loss treatment; chemotherapy

Introduction and objective

One of the biggest problems facing contemporary medicine is cancer. Globally, around 20 million new instances of cancer were reported in 2022, and 9.7 million people died from the disease. According to estimates, one in five individuals, irrespective of gender, will receive a cancer diagnosis in their lifetime, and around one in nine men and one in twelve women will pass away from the illness [1]. Most of them are eligible for treatment regimens that include chemotherapy. It offers the chance of a permanent remission and a cure, and in many instances, it is the only practical way to fight the illness [2]. Despite encouraging treatment results, it's crucial to remember that chemotherapy includes serious adverse effects that have been well-documented. Although chemotherapy is good at destroying cancer cells, it can also damage healthy cells that divide quickly, such as the keratinocytes in hair follicles. Cytotoxic chemotherapies can cause hair-related issues, including alopecia, hirsutism, hypertrichosis, as well as changes in hair pigmentation and texture [3]. Chemotherapy-induced alopecia (CIA), which affects about 65% of patients, is therefore a typical side effect of chemotherapy that involves significant hair thinning or loss [4]. Hair loss due to chemotherapy in cancer patients is generally transient; however, it can significantly affect emotional well-being, leading some patients to decline additional treatment. Although hair typically regrows following treatment, the duration of this process may extend over several months, potentially exacerbating psychological distress [5]. Given that hair loss is frequently stigmatized in society and considering hair as an important part of many people's identities, this has a detrimental effect on patients' quality of life. Research assessing quality of life in patients prior to and following the commencement of chemotherapy cycles reveals enhanced psychophysical functioning, diminished symptom severity, and an improved overall health status relative to the post-chemotherapy condition [6]. As of right now, there are no set protocols for treating or

preventing chemotherapy-induced alopecia. Even when a variety of tools and drugs are used, the results are frequently disappointing. The U.S. Food and Drug Administration (FDA) has approved only one intervention to prevent CIA: scalp cooling. Minoxidil and bimatoprost can be used to encourage improved hair regrowth once treatment ends, however they are not advised during chemotherapy [7]. Patients undergoing cancer treatment frequently experience severe weariness as a result of the many hospital stays, several chemotherapy cycles, and extended pharmaceutical use. As a result, wherever feasible, many people look for non-pharmacological, alternative ways to manage the side effects of medication. One of the most obvious and emotionally upsetting side effects of chemotherapy is alopecia, which has made it a major focus of research into preventative and treatment strategies [8]. This article reviews non-pharmacological approaches for treating chemotherapy-induced alopecia, assessing their effectiveness and potential emotional benefits for patients undergoing cancer treatment.

Review methods

The electronic databases PubMed and Google Scholar were used to perform the literature review. "Chemotherapy-induced alopecia", "CIA", "hair loss", "cancer", "hair loss treatment", "chemotherapy" and their variants were the key search terms. With special attention to papers from the previous five years, the review concentrated on clinical trials, double-blind randomized controlled trials, meta-analyses, reviews, and systematic reviews that were published between 2018 and 2024. This study does not incorporate case report findings.

State of knowledge

Hair loss is one of the most common side effects of chemotherapy, affecting approximately 65% of patients undergoing treatment [9]. Due to its prevalence, it has become a symbolic representation of cancer. However, the issue extends beyond aesthetic considerations. Alopecia, as a side effect of oncological therapy, presents a particular challenge, especially for women, for whom hair plays a significant role in both gender and social identity. Hair is considered one of the key attributes of femininity, serving not only as a visual element but also as an expression of personality. Alongside clothing, it represents an important means of self-expression. Even temporary loss of this feature can lead to a significant decline in well-being, which may affect the mental resources necessary for effectively coping with cancer. This phenomenon has such profound consequences that 47% of patients have identified hair loss as the most traumatic aspect of chemotherapy [10]. CIA also has significant psychosocial consequences. The characteristic changes in patients' physical appearance resulting from treatment make it difficult,

and often impossible, to conceal health issues from those around them. Furthermore, concerns about disclosing the illness in public spaces are intensified by the social stigma associated with cancer. Patients are reluctant to be seen solely through the lens of their disease or to be defined by its effects. Although this phenomenon may initially appear to be of little significance, it has a considerable impact on patients' decisions regarding therapy. As many as 14% of patients reported discontinuing life-saving treatment due to the fear of hair loss [10]. As medical professionals, we should not underestimate this complex issue. Our goal should be not only to understand the needs of patients but also to implement the best available methods for the prevention and treatment of chemotherapy-induced alopecia, in order to improve patients' quality of life and support their mental resources during oncological treatment. CIA is one of the most common side effects of oncological treatments. It involves both complete and partial hair loss, with a reduction of more than 50% of the original hair volume. This phenomenon is typically transient—hair usually begins to regrow within six months after the completion of treatment. In cases where hair regrowth does not occur, the condition is diagnosed as permanent chemotherapy-induced alopecia (pCIA) [9]. It is important to emphasize that while CIA is a side effect of chemotherapy, it is generally not permanent. However, in the case of pCIA, hair regrowth does not take place, potentially leading to a long-lasting aesthetic and psychological issue. CIA primarily results from the effects of oncological drugs on rapidly dividing cells. Chemotherapy drugs are cytotoxic, meaning they damage cells with high mitotic activity, including hair follicle cells. Hair on the scalp undergoes three growth phases: anagen, catagen, and telogen. The anagen phase is the growth phase, during which there is intense cellular division in the hair matrix, leading to hair elongation. The catagen phase is a transitional phase, in which cellular division ceases and the hair matrix begins to atrophy. The telogen phase is the resting phase, during which hair growth halts, and as the hair follicle deteriorates, the hair falls out [11]. Among the hair on the scalp, the largest proportion consists of hairs in the anagen phase, which can make up as much as 90% of all hairs [9]. It is important to note that this growth phase is the most susceptible to the effects of chemotherapeutic agents, leading to their damage and, consequently, hair loss. Since chemotherapy drugs target rapidly dividing cells, hair cells, which are part of the actively dividing follicular apparatus, become one of the primary targets of these treatments. This explains why hair loss is one of the most common side effects of oncological treatment, particularly in the case of chemotherapy involving highly cytotoxic drugs. Moreover, it is important to note that chemotherapy does not only affect hair follicle cells in the anagen phase. Depending on the type of therapy used, damage can also occur in

other phases of the hair growth cycle, which may lead to various forms and degrees of alopecia, ranging from partial hair loss to complete baldness. Such damage to hair cells affects not only the structure of the hair itself but also the growth cycle, potentially disrupting the balance between the different phases and delaying the regeneration process. The incidence of CIA is closely related to the type of drug used, its concentration, and the administration schedule. Different classes of oncological drugs are associated with varying degrees of risk for hair loss. Topoisomerase inhibitors, particularly those used in the treatment of breast, ovarian, or lung cancer, show the highest incidence of CIA. For these drugs, the risk of hair loss ranges from 60% to 100%, depending on the specific pharmacokinetic properties of the drug as well as individual patient factors, such as sensitivity to the therapy and genotype. Another group of drugs that cause CIA includes microtubule inhibitors, such as paclitaxel, which lead to hair loss in approximately 80% of cases. Alkylating agents, such as cyclophosphamide, are also associated with a risk of hair loss, ranging from 60% and higher. In contrast, drugs from the group of antimetabolites, such as methotrexate, carry the lowest risk of CIA, ranging from 10% to 50%, making them relatively safe in terms of their impact on the patient's appearance [9,13]. It is important to note that the above data refer to monotherapy, where a single drug is used. In the case of combination therapy, in which multiple drugs are administered together, the incidence of CIA may increase significantly. This phenomenon results from the synergistic effects of these substances, which amplify each other's side effects, including their impact on hair follicles. Increasing the dosage of oncological drugs also leads to a higher frequency of CIA, which is particularly evident in the case of docetaxel. Data show that at a dose of 55 mg/m² of docetaxel, alopecia is observed in patients, and raising the dose to 100 mg/m² results in hair loss in 83.8% of patients, highlighting the dose-dependent relationship between the drug and the severity of the side effect [14]. In light of the above data, it is also important to note the significant individual differences among patients. The variability in responses to treatment regarding the occurrence of CIA is influenced by several factors, such as genotype, age, overall health, the presence of comorbidities, and the use of adjunct therapies, such as antiemetics or steroids, which may affect the severity or reduction of hair loss risk. Therefore, a thorough analysis of the risk of CIA should be an integral part of the treatment planning process to tailor the therapy to the patient's individual needs. In summary, the occurrence of CIA is the result of complex interactions between the type of drug, its dose, and the patient's individual characteristics. This phenomenon significantly impacts the quality of life of oncological patients, particularly women, for whom hair is an important element of gender identity.

Prolonged hair loss can lead to a diminished sense of self-worth and, in extreme cases, serious psychological issues. For this reason, the treatment strategy should also address psychosocial aspects, including the potential use of preventive therapies aimed at minimizing the risk of CIA and providing psychological support for patients in whom hair loss is inevitable.

Table 1. The incidence of CIA depending on the group of drugs.

Group of drugs	Example	Incidence of CIA
Topoisomerase Inhibitors	Doxorubicin	60-100%
Antimicrotubule Agents	Paclitaxel	80%
Alkylators	Cyclophosphamide	>60%
Antimetabolities	5-fluorouracil	10-50%

Prevention and therapy methods. Currently, both pharmacological and non-pharmacological methods are available for the treatment of CIA. Pharmacological therapies are based on substances commonly used in the treatment of other types of hair loss, such as androgenetic alopecia. These include minoxidil, 5α-reductase inhibitors, spironolactone, and bimatoprost [9]. In addition, research is ongoing to identify new therapeutic targets, which are being tested in animal models. One of the approaches under investigation is local vasoconstriction. This method involves the topical application of epinephrine or norepinephrine, which aim to reduce blood flow within the hair follicle, potentially inhibiting the hair loss process.

Non-pharmacological methods:

- Scalp cooling

- LLLT (Low-Level Laser Therapy) / PBMT (Photobiomodulation)

- PRP (Platelet-Rich Plasma)

- Microneedling

Scalp cooling. The mechanism of action of the scalp cooling method is based on local vasoconstriction. Lowering the temperature causes a reduction in the diameter of blood vessels within the scalp, leading to decreased blood flow in this area. As a result, the distribution of chemotherapy drugs to the hair follicles is limited, as is their availability for absorption by the

cells. Additionally, the reduced temperature slows down the metabolism of hair cells, which exhibit high mitotic activity. Slowing down their metabolic rate leads to a reduced uptake of the drug, which in turn decreases the exposure of these cells to the chemotherapy agent. These two phenomena result in a reduced amount of the drug reaching the hair cells, ultimately lowering the risk of CIA [17]. The local reduction of chemotherapy drug concentration in the scalp translates into a reduced risk of adverse effects, which are often dose-dependent, while the systemic action of the drug remains unchanged, and its concentration in other parts of the body is unaffected by this therapy.

The first references to scalp cooling, also known as scalp-cooling, appeared in the 1970s [18]. Initially, it was an experimental technique, but over the years it was further developed and refined. Research into the use of scalp cooling to prevent CIA led to the creation of more effective protocols and devices that allow precise control over the temperature and duration of cooling. Contemporary cooling methods are based on two main solutions: cooling caps and cooling machines. Currently, the most commonly used cooling systems are cooling caps, such as Elastogel and Penguin, as well as cooling machines, including the Paxman Scalp Cooling System and DigniCap [17]. Cooling caps, due to their design, offer easy application and can be used in outpatient settings. In contrast, cooling systems such as Paxman and DigniCap employ advanced technology to precisely control temperature and provide more comprehensive protection against hair loss during chemotherapy. In 2015, the DigniCap system received official approval from the U.S. FDA for use in reducing the risk of CIA [19]. DigniCap became the first cooling system to receive such approval in the United States, marking an important step in recognizing this method as an effective and safe form of adjunctive therapy. Two years later, in 2017, the FDA also approved the Paxman Scalp Cooling System, which has also shown high efficacy in preventing CIA [20]. The effectiveness of both systems has been confirmed in numerous clinical trials conducted on diverse patient groups, including preclinical studies and studies involving patients undergoing oncological treatment.

Paxman. In a study conducted on 91 Indian women with breast cancer, the use of the Paxman scalp cooling system demonstrated efficacy in preventing alopecia, defined as a loss of less than 50% of hair, in 81% of patients. The study focused on patients treated with anthracyclines and taxanes, which are commonly used in breast cancer therapy. As part of the treatment protocol, cooling caps were applied 30 minutes before the chemotherapy infusion to lower the scalp temperature to 3°C. Cooling was maintained throughout the infusion, and after its completion,

the caps were left on the scalp for an average of 45–150 minutes. This phase aimed to provide further protection against the spread of toxic chemicals to the hair follicles, potentially reducing the intensity of chemotherapy-induced hair damage [21]. In another study involving 140 Japanese patients, the effectiveness of the Paxman scalp cooling system was evaluated. Among 80 patients who used the cooling system at least once, 45.6% experienced hair loss exceeding 50%. In contrast, in the group of 74 patients who did not use the system, 60.7% had hair loss exceeding 50%. These results suggest that the use of scalp cooling during chemotherapy may significantly reduce the severity of hair loss, particularly when treating with anthracyclines and taxanes [22]. According to the results of both studies, the scalp cooling method was generally well-tolerated by patients. The most commonly reported side effects were headaches and chills, typical for cooling the skin to low temperatures. Although these side effects were common, they did not have a significant impact on the overall acceptance or continued use of the therapy [21,22]. However, in a study conducted among African American women, the effectiveness of the Paxman method was found to be lower compared to other groups. In this case, only 26% of the patients in the study experienced alopecia prevention with less than 50% hair loss. It is important to note that this study involved only 15 patients, which may limit the representativeness of the results. Nonetheless, it underscores the need for further research on the effectiveness of this method in different ethnic and genetic groups [23]. In summary, the use of the Paxman scalp cooling system represents a promising method for preventing CIA, particularly when treating with anthracyclines and taxanes. However, further research is needed to better assess the effectiveness of this method in various patient populations and with different chemotherapy regimens. Additionally, side effects such as headaches and chills should be monitored to optimize patient comfort during treatment.

DigniCap. One study conducted on 163 women in the early stages of breast cancer showed an overall efficacy of the scalp cooling method at 57%. However, it is worth noting the particularly high effectiveness of the method in the context of therapy based on paclitaxel and trastuzumab, where 81% of patients retained more than 50% of their hair. This high result is an important benchmark in evaluating the effectiveness of scalp cooling in the context of a specific treatment regimen. Scalp cooling therapy began 30 minutes before the chemotherapy infusion, and the scalp temperature was maintained at 3°C throughout the infusion. Depending on the chemotherapy drug used, the scalp cooling time (PCT) was adjusted to optimize the cooling effectiveness. For therapy with epirubicin and cyclophosphamide (EC), the cooling time was

120 minutes, whereas for TC regimens (docetaxel and cyclophosphamide) and weekly paclitaxel, the cooling time was shortened to 60 minutes [29]. In another study involving 178 patients treated with various chemotherapy regimens, the overall efficacy of the DigniCap system was 68%. The efficacy varied depending on the treatment regimen. Patients treated with anthracyclines and taxanes achieved an efficacy of 59.5%, indicating a moderate but still significant effect of cooling in reducing hair loss. Therapies including carboplatin were more effective, with a 71.4% success rate in preventing hair loss. Interestingly, patients treated with paclitaxel, though representing only 2.2% of the study group, achieved 100% efficacy in maintaining their hair. On the other hand, for therapy with docetaxel and cyclophosphamide, the efficacy was 87%, underscoring the high effectiveness of the method in treating cancers with these drugs. All studies employed the same cooling protocol: the scalp temperature was maintained between 3°C and 5°C, cooling started 30 minutes before the chemotherapy infusion, and continued for 60–120 minutes after the infusion. This approach aimed to maximize the protection of hair follicles from the harmful effects of chemotherapy drugs, while minimizing the risk of side effects such as hair loss. It is also worth emphasizing that 70.2% of patients expressed satisfaction with using the DigniCap device. The high level of patient acceptance suggests that this scalp cooling method is well tolerated and represents an effective strategy for preventing CIA. Despite certain limitations, such as the need to adjust cooling therapy according to the type of chemotherapy, the results point to the significant role of this technology in treating oncology patients. In conclusion, the DigniCap system demonstrates high efficacy in preventing chemotherapy-induced alopecia, particularly in therapies based on paclitaxel, trastuzumab, and other taxane-based drugs. By appropriately adjusting the cooling parameters, such as scalp temperature and cooling time, it is possible to minimize the risk of hair loss, which is crucial for improving the quality of life of patients undergoing intensive cancer treatments. Further research into optimizing these parameters and expanding the use of the system across a broader patient population is necessary to confirm and expand upon the results obtained to date. Promising therapeutic outcomes are also provided by a meta-analysis conducted by Katherine A. Lambert and her team, which included 31 clinical studies involving 2,179 patients who used three available scalp cooling systems: Paxman, DigniCap, and Penguin. The meta-analysis examined scalp cooling protocols using these systems, which involved various temporal cooling application schemes depending on the device. For both the Paxman and DigniCap systems, scalp cooling began 30 minutes before the chemotherapy infusion, and cooling continued during the infusion and for 90 minutes after its completion. For the Penguin

system, cooling started earlier—50 minutes before chemotherapy administration—and continued throughout the infusion, with the cap being replaced every 30 minutes. Additionally, this system maintained cooling for another 4 hours after the infusion was completed. The analysis of the effectiveness of these different approaches found that the Penguin system showed the highest efficacy in preventing hair loss for patients receiving taxane-based therapies. This system achieved a 72.8% success rate, defined as reducing hair loss to less than 50%. The Paxman system achieved 53.1% efficacy, while the DigniCap system showed 60.8% efficacy. These results indicate a significant difference in scalp cooling efficacy depending on the device used, which may be related to differences in the cooling protocol and the precision of maintaining the scalp temperature. Further analysis of cooling efficacy in relation to the type of chemotherapy showed an overall prevention efficacy of 69.9% for paclitaxel-based therapy, while for docetaxel-based therapy, the efficacy was 60.5%. The variation in results depending on the cooling system and chemotherapy regimen highlights the need for further research to tailor cooling strategies to the individual needs of patients, which could ultimately improve the efficacy of this method in preventing chemotherapy-induced hair loss.

PRP. The process of treatment using platelet-rich plasma (PRP) involves the collection of autologous blood from the patient, which is then processed to obtain a platelet concentrate. After performing the necessary separation procedures and removing unwanted components, a concentrate containing a high concentration of platelets is obtained. These platelets have the ability to synthesize various factors that support regenerative and proliferative processes in the body. Platelet activation occurs primarily through interaction with collagen in the skin and endogenous thrombin, which triggers a cascade of biochemical reactions leading to the release of substances such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), transforming growth factor (TGF), fibroblast growth factor (FGF), connective tissue growth factor (CTGF), insulin-like growth factor-1 (IGF-1), and a range of anti-inflammatory cytokines, including interferon gamma [34,35]. All of these factors play a significant role in stimulating the proliferation of cells, including hair follicle cells, which leads to an increase in the rate of cell division and, consequently, promotes hair growth. For this reason, PRP has been used in the treatment of various types of alopecia, including those of diverse etiology [34]. Clinical trials are currently underway to assess the effectiveness of PRP therapy in women with breast cancer who have experienced alopecia due to hormonal therapy (endocrine therapy-induced alopecia, EIA) and chemotherapy

(chemotherapy-induced alopecia, pCIA) [36]. In the context of CIA, potential benefits of PRP treatment for this condition have been observed. Although most studies are limited to animal models, particularly in rats [37], it has been shown that PRP therapy can have a positive effect on preventing chemotherapy-induced hair loss, including after the use of substances such as etoposide, cyclophosphamide, and Ara-C.

Microneedling. Microneedling, also known as dermaroller therapy, involves creating numerous tiny punctures in the skin using fine needles. This process leads to the formation of micro-injuries that trigger biological reactions in the body, such as angiogenesis (the formation of new blood vessels) and the release of various growth factors. Additionally, it activates signaling pathways, including the expression of Wnt proteins, which play a key role in tissue regeneration, and stimulates collagen production, which is essential for maintaining skin structure and elasticity [39]. This mechanism improves microcirculation in the skin, leading to better oxygenation and nourishment of tissues, as well as promoting the regeneration of skin cells and its renewal. Microneedling has found widespread application in the treatment of various types of alopecia, particularly androgenetic alopecia, which is one of the most common causes of hair loss in both men and women [43]. Androgenetic alopecia is related to the action of sex hormones and genetic predisposition, leading to the miniaturization of hair follicles and a weakening of hair growth. In this case, microneedling aims to improve follicle activity and stimulate the growth of new hair. According to the literature, microneedling is used both as a monotherapy and in combination with various active substances, especially those that promote hair growth, such as minoxidil. Studies suggest that the synergistic effect of microneedling and active substances can lead to more effective therapeutic outcomes, improving both hair density and length, as well as the health of hair follicles [38]. Despite its broad effectiveness, microneedling has limited efficacy when used alone, particularly as a monotherapy. An analysis of 22 clinical studies on androgenetic alopecia (AGA) that included microneedling revealed that six studies focused on microneedling as monotherapy. Of these, only one showed a significant increase in hair count, and two studies observed an increase in hair length. In the remaining three studies, no noticeable effects were found, suggesting that the microneedling technique alone may not be sufficiently effective for treating AGA in the long term [41, 42, 48, 49, 50, 51]. On the other hand, combining microneedling with minoxidil, one of the most commonly used drugs in hair loss therapy, shows clearly better results. Minoxidil works by dilating blood vessels in the scalp, improving the delivery of oxygen and nutrients to hair

follicles, thereby stimulating their activity. When combined with microneedling, minoxidil can penetrate deeper into the skin, leading to improved hair density and follicular activity [45, 47]. There is increasing evidence in the scientific literature that the combination therapy based on these two methods yields more satisfactory results in treating alopecia compared to using a single therapy. Although microneedling has gained popularity as an effective treatment for hair loss, there is still a significant research gap, particularly regarding its application in the treatment of other forms of alopecia, such as CIA. The literature lacks studies that definitively confirm the efficacy of microneedling in the treatment of CIA, indicating the need for further detailed clinical and experimental research in this area.

PBMT. Another promising treatment for Chronic Inflammatory Alopecia is **photobiomodulation therapy**, also known as **Low-Level Laser Therapy (LLLT)**. This therapy involves the use of light radiation, particularly red light in the wavelength range of **630–655 nm**, which allows it to interact with cellular structures in the deeper layers of the skin. Initially, laser therapy was primarily used to support wound healing processes, showing anti-inflammatory, pain-relieving, and tissue-regenerating effects. Over time, it has also been applied in the treatment of alopecia, in both women and men, due to the discovery that it can improve the health of hair follicles and stimulate the growth of new hair [31,32,33]. The mechanism of action of **PBMT** is based on the interaction of light with skin cells, including fibroblasts and cells in the hair follicle. This phenomenon triggers a series of biological reactions, such as increased ATP production, activation of signaling pathways, and regulation of growth factors. These effects lead to the transition of hair follicles from the **telogen phase** (the resting phase), in which they are inactive and no new hair growth occurs, to the **anagen phase** (the active growth phase), during which intensive cell division and hair growth take place. By using phototherapy, the activity of hair follicles is restored, ultimately improving their function and promoting the regeneration of hair [31]. Additionally, photobiomodulation therapy has anti-inflammatory properties, which are particularly relevant in treating chronic inflammatory skin conditions like CIA. In CIA, inflammation can damage hair follicles and inhibit their function, leading to gradual hair loss. PBMT, by modulating the inflammatory response, can support skin regeneration and improve microcirculation around the hair follicles, facilitating their renewal and activating the growth of new hair. One of the commercially available devices for LLLT is the **HairMax LaserComb**, which has been approved by the U.S. FDA for the treatment of **AGA**. The HairMax LaserComb is one of the most commonly used

devices for photobiomodulation therapy, utilizing laser technology for hair loss treatment. It is designed for home use and allows for regular administration of low-energy light therapy in daily settings. Preclinical studies on rats aimed at assessing the effectiveness of this technology in treating CIA have shown promising results. Rats were administered various chemotherapy drugs, including etoposide, cyclophosphamide, and other chemotherapy agents, as well as a combination of cyclophosphamide and doxorubicin. The group of rats treated with PBMT showed faster fur regrowth compared to the control group — an average of 5 days faster hair growth [52]. These results suggest that PBMT could be an effective therapeutic option for CIA, but further studies, particularly clinical trials with human subjects, are needed to draw definitive conclusions. Currently, three clinical trials are underway to evaluate the effectiveness of this therapy in CIA patients [53,54,55]. Low-level laser therapy does not have to rely solely on red light. It is also possible to use other wavelengths, such as **blue light (453 nm)**, which has potential therapeutic effects in the treatment of alopecia. Within the mitochondria of hair follicle cells, there are opsins, which act as signaling molecules responsible for regulating the cell cycle, reducing apoptosis (programmed cell death), and extending the anagen phase. Studies have shown that these opsins react to blue light, which can stimulate repair and regenerative mechanisms within the hair follicles. In **ex vivo studies**, application of **3.2 J/cm² of blue light** resulted in increased expression of proteins **OPN2** and **OPN3** in hair follicles and deeper layers of the skin [56]. In the same study, no significant therapeutic effects were observed with red light at **689 nm**, suggesting that the response to different wavelengths may vary depending on tissue characteristics and the type of therapy. In conclusion, **photobiomodulation therapy** stands out as one of the most promising treatments for **Chronic Inflammatory Alopecia**. It is relatively inexpensive, safe, and virtually free of side effects. A key advantage is its suitability for home use, enhancing treatment accessibility and comfort. Devices for photobiomodulation therapy are available on the market and are user-friendly, making them easy to incorporate into daily practice. When combined with other treatment methods, such as **scalp cooling** or the use of active substances, phototherapy can form an effective and comprehensive therapeutic strategy for inflammatory hair loss. However, further studies, particularly large-scale clinical trials, are necessary to fully assess its effectiveness and long-term outcomes in CIA treatment.

Conclusions

Each year, cancer is diagnosed in over 20 million people worldwide. The vast majority of patients undergo treatment, which, with advances in medical science, is becoming increasingly

effective. Unfortunately, many patients still face side effects associated with treatment. The most common adverse effects of chemotherapeutic agents include nausea, vomiting, fatigue, hematological abnormalities, and alopecia, which is one of the most visible and stigmatizing consequences. For many individuals, hair is a significant aspect of their appearance, a means of self-expression, a confidence booster, and, particularly for women, an essential attribute of femininity. Nearly half of oncology patients consider hair loss the most traumatic aspect of their treatment. Chemotherapy targets the fastest-dividing cells in the body—cancer cells—but is non-selective and also damages cells in hair follicles, leading to hair loss in approximately 65% of oncology patients. Such drastic changes in physical appearance can be highly stigmatizing, and studies show that up to 10% of patients may refuse treatment due to fear of alopecia. CIA is typically a temporary condition, with hair regrowth occurring within six months of completing treatment. However, effective and reliable methods to prevent hair loss during chemotherapy are still lacking. Currently, the U.S. FDA has approved only one method to reduce hair loss—scalp cooling. Chemotherapy, being an invasive treatment, limits the use of certain hair-loss-preventing drugs with clinically proven efficacy, such as Minoxidil or Bimatoprost. The selection of cytostatic drugs also influences the risk of hair loss. Agents that most severely damage hair follicles include topoisomerase inhibitors like irinotecan. Chemotherapeutic agents like docetaxel or paclitaxel, which belong to the group of microtubule stabilizers, result in hair loss in up to 80% of patients. Conversely, the lowest risk of CIA is associated with the use of antimetabolites like methotrexate. The scalp cooling method, approved by the FDA for the prevention of hair loss during chemotherapy, induces local vasoconstriction by cooling the scalp. Vasoconstriction reduces blood flow to hair follicles, thereby decreasing the penetration of chemotherapeutic agents. Additionally, the cold environment reduces cellular metabolic activity, further limiting drug uptake. Currently, the most commonly used cooling systems include Elastogel, Penguin, and cooling machines such as Paxman or DigniCap. Scalp cooling methods are generally well-tolerated by patients, with the most commonly reported adverse effects being headaches and chills. A distinctly different approach for preventing hair loss during chemotherapy is photobiomodulation therapy (PBMT), also known as low-level laser therapy. Its mechanism of action involves the application of light, particularly in the red spectrum, which penetrates deeper skin layers to stimulate ATP production, activate signaling pathways, and promote the generation of growth factors. To date, PBMT has shown promising results in animal studies, and clinical trials involving humans are underway. The use of platelet-rich plasma (PRP) may also contribute to reducing

chemotherapy-induced alopecia (CIA). PRP, derived from the patient's peripheral blood, is a source of numerous growth factors, hormones, peptides, and anti-inflammatory cytokines. Injecting the scalp with PRP can stimulate hair growth and potentially reduce the risk of hair loss during chemotherapy. Microneedling is another therapy aimed at creating minor injuries in the scalp to induce angiogenesis and stimulate the release of growth factors. However, microneedling as a monotherapy has debatable therapeutic value. The most significant results are achieved when combined with Minoxidil, though its use is contraindicated during chemotherapy. The issue of hair loss during chemotherapy remains unresolved despite rapid advances in medicine. Emerging therapies to mitigate hair loss still show moderate efficacy or remain in the clinical trial phase. Developing treatment methods, such as those based on monoclonal antibodies or targeted therapies, could potentially reduce the incidence of this complication. For now, however, chemotherapy-induced hair loss remains a therapeutic challenge for oncologists. The potential benefits of introducing effective CIA prevention methods include better patient tolerance of the disease burden and reduced social stigma. These measures would also likely improve treatment acceptance and significantly lower the proportion of patients who refuse therapy out of fear of hair loss. Oncology care should adopt a holistic model that focuses not only on treating cancer but also on ensuring the psychological and physical well-being of patients.

Disclosure

Author's contribution:
Conceptualization: IO, KJ
Methodology: MK, KJ
Software: MK, MC
Check: KJ, MJ
Formal analysis: MK,
Investigation: MC, IO
Resources: MJ, IO
Data curation: IO
Writing-rough preparation: IO, MC
Writing-review and editing: KJ, MJ
Visualization: MC, MJ
Supervision: KJ, MK, IO

Project administration: IO, MC

Supplementary Materials: They have not been provided.

Funding Statement: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

All authors have read and agreed to the published version of the manuscript.

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