



## The Most Apparent Aspect of Chemotherapy: Alopecia: Is It Possible to Prevent It?

### Kemoterapinin En Görünen Yönü: Alopesi: Önlemek Mümkün Mü?

Ayşe Arıkan Dönmez<sup>1</sup>

<sup>1</sup>Department of Internal Medicine Nursing, Faculty of Nursing, Hacettepe University, Ankara, Turkey.

#### Abstract

Alopecia is one of the most common side effects of chemotherapy. Hair loss in the chemotherapy process is an important side effect that can affect the individual physically, socially and spiritually in a negative way. Although hair loss is not a side effect to limit treatment dose or a life threatening condition, since it causes negative effects on patients, this problem should not be overlooked. The loss of hair can be traumatic for patients because it negatively affects body image. Since the late 1960s various methods have been used to prevent chemotherapy-induced hair loss. Although all these methods are not 100% effective, they provide high-quality hair protection. An important aspect of quality nursing care in the field of oncology is helping the patients to cope with the stressors caused by cancer and its treatment. The nurses are also responsible for ensuring and maintaining the best hair protection of the patients with cancer, preventing the complications caused by the treatment, preparing and supporting the patients to control the hair loss, providing the patient consulting service and training each member of the healthcare team. The aim of the present review was to investigate the etiology, risk factors, importance, and different prevention or management methods of chemotherapy-induced alopecia (CIA).

**Key words:** Alopecia, Chemotherapy, Symptom Management, Nursing

#### Introduction

Chemotherapy is one of the widely used treatment methods in cancer treatment. The main principle of this treatment is to stop or eliminate the growth and proliferation of the tumor cells without damaging the normal-healthy cells of the patient (1-4). Chemotherapy drugs, however, do not distinguish between rapidly dividing malignant cells and normal healthy rapidly dividing cells found in the oral cavity, gastrointestinal tract, bone marrow, and hair follicles therefore they can damage these cells by inhibiting the growth and proliferation of both cancerous cells and rapidly multiplying normal body cells. Accordingly, side effects such as stomatitis, nausea, vomiting, neutropenia and alopecia can occur as a result of healthy cells damage because of chemotherapy (1, 5).

Chemotherapy-induced alopecia (CIA) is one of the most common side effects that may affect patients' adjustment

#### Özet

Alopesi kemoterapinin en yaygın yan etkilerinden biridir. Kemoterapi sürecinde yaşanan saç kaybı bireyi fiziksel, sosyal ve ruhsal yönden olumsuz yönde etkileyebilen önemli bir yan etkidir. Saç kaybı doz sınırlamasını gerektiren veya yaşamı tehdit eden bir yan etki olmamasına rağmen, beden imajını olumsuz yönde etkilediği için hastalar üzerindeki etkilerinin göz ardı edilmemesi gerekmektedir. 1960'ların sonlarından beri kemoterapiye bağlı gelişen saç kaybını önlemeye yönelik çeşitli yöntemler kullanılmaktadır. Bu yöntemlerin bir kısmı tamamen etkili olmasa da, yüksek oranda saç korumasını sağlayabilmektedir. Onkoloji alanında kaliteli bir hemşirelik bakımı vermenin önemli boyutunu kanser ve tedavisinin yarattığı stresörlerle başetmede hastalara yardımcı olabilmek oluşturmaktadır. Bireyin saç korumasının sağlanması ve sürdürülmesi, saç kaybının kontrolüne yönelik bireylerin hazırlanması ve desteklenmesi, hastaya danışmanlık hizmeti ve eğitim verilmesi hemşirelerin sorumlulukları arasında yer almaktadır. Bu derlemenin amacı kemoterapi ilişkili saç kaybının etyolojisi, risk faktörleri, önemi ve farklı önleme veya yönetim yöntemlerini incelemektir.

**Anahtar kelimeler:** Alopesi, Kemoterapi, Semptom Yönetimi, Hemşirelik

to the disease and treatment and hinder their ability to cope with the illness (6). CIA, although not life threatening during chemotherapy, it can negatively affect the physical appearance, body image, sexuality and self-esteem (3, 7-11).

The incidence of CIA is specified as 65% (12) and usually occurs within 2-3 weeks after the first treatment cycle, and full hair loss occurs within 1-2 months, and the hair grows again within 1-2 months following the end of treatment (13, 14). Although CIA is one of the transient side effects, chemotherapy can cause permanent change in the structure or color of the newly growing hair by about 65% (13).

Since the late 1960's, there have been various studies and literature reviews about CIA prevention such as mechanical methods including tourniquet application, physical methods including scalp cooling and biological agents (13, 15-19), but our country does not have comprehensive literature on

whether it is possible to reduce or prevent this symptom. From this viewpoint, the aim of the present review was to investigate the etiology, risk factors, importance, and different prevention or management methods of CIA.

### The Importance of Hair

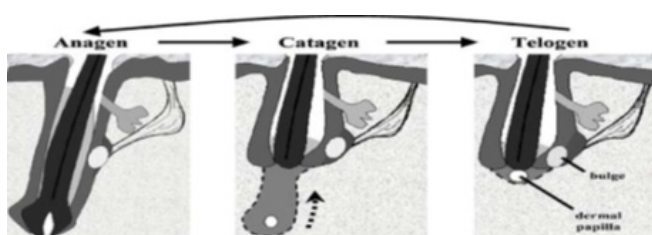
Hair has been a sign of aesthetic identity as well as being seen as a symbol of social, cultural, political, and religious environment throughout the history (8, 20). Hair, which is an important part of human beauty, has been accepted as a symbol of power, strength, freedom and superiority in the ancient times and different forms have been given to the hair according to the understanding and fashion of the living age and hair beauty has been an inspiration for poets and painters for centuries. The appearance of hair in society is often seen as an expression of health and well-being (6, 8). For this reason, the hair affects the body image and provides the body integrity. In addition to increasing the body image, experienced hair problems and related issues can also be an important source of stress (6, 8, 10, 13, 21). Hair loss can be perceived as a loss of attractiveness, individuality, declining reputation and illness, but in addition to aging, death and loss of sexuality. Hair loss also lead to decreased self-esteem and personality perception (6, 8, 10, 13).

A study comparing the CIA experiences of patients revealed that hair loss indicated the fact that they were “cancer patient” and it was a a sense of strangeness or shock (22). Hansen (23) reported that in her anthropological study the women equated hair loss with the loss of womanhood (femininity, sexuality and attractiveness), sickness and death. In another study, Choi et al (6) found that CIA distress was strongly associated with lower body image, overall health status, and psychosocial well-being in breast cancer patients. In another study comparing the men and women’s experiences of CIA found that while there were no differences between men and women with regard to body image in respect of degree of alopecia, the body image of the male and female patients who had partial or complete alopecia was lower than that in patients who had no alopecia (24).

### Hair Growth Cycle

Human hair follicles have 85-90% fast growing cells under normal conditions and this growth cycle consists of three main phases: anagen, catagen and telogen (25) (Figure 1).

Figure 1. Hair growth cycle



Reference: Wang J, Lu Z, L. J, Au1 S, Protection against chemotherapy induced alopecia. *Phar Res* 2006;23(11):2507

The growth rate of hair varies depending on race, sex, age and genetic characteristics (13). The growth rate of the hair was between 0.62-1.25 cm/month and 0.35 mm/day (21). The anagen phase, known as the developmental stage, undergoes about two weeks of cathogene stage at the end of the 1000th day. The resting phase, known as telogen, is completed at the end of about 100 days and enters the anagen phase again for cycling. In the hair the anagen stage is longer while the telogen stage is shorter. At the end of the telogen stage, a new hair body starts to be seen with new hair. An average of 50-100 telogen hair loss per day in a human scalp is normal. This hair loss can normally be seen during bathing, shaving or hair-brushing. Unless there is hair loss, at least 90% of the hair follicles in human hair are in the anagen phase, less than 10% in the telogen stage and only less than 1% in the cathogene stage (8, 21, 26, 27).

Many factors affect hair growth cycle and can lead to temporary or permanent hair loss. These factors include drugs, radiation, chemotherapy, dermatological diseases, chemical exposure, hormonal and nutritional factors, thyroid and immunological abnormalities, common and local skin diseases, scar formation, psychological or physiological stress (21). In particular, one of these factors, high doses of chemotherapeutic medication, can lead to partial or complete atrophy of the hair root causing hair damage in the hair shaft or root. Damage to the hair shaft results in partial atrophy or root necrosis, causing the hair to thin and break while root damage can result in complete hair loss. Depending on the root damage, the hair can be spontaneously poured or lost during brushing and washing (8, 13, 27).

Hair loss can be seen in the form of anagen and telogen hair loss. Two weeks after drug is given in anagen stage, hair loss occurs as sudden, diffuse and usually returns to the original state after the drug is discontinued. This type of hair loss is particularly evident by the effect of chemotherapeutic agents such as cyclophosphamide, doxorubicin and nitrosourea. In telogen type, hair loss is more prolonged and diffuse as compared to anagen type. The patient’s hair begins to dilute and a homogeneous hair loss appears. This type can regress spontaneously when the treatment is terminated (8, 28).

### The Risk Factors of Chemotherapy-Induced Alopecia

The incidence and severity of CIA can vary depending on many factors. These factors can be listed as the chemotherapeutic agent half-life in the body, the dosage, the route of administration, the type of chemotherapeutic agent, the treatment protocol (single or combined), the length of the infusion, nutritional and hormonal status, and the state of the hair (13, 21, 29, 30).

Intravenous high dose administration often leads to intense hair loss, while oral and low dose treatment protocols result in less hair loss. Hair loss is affected by increased metastasis-induced liver dysfunction, as drug elimination and metabolism are delayed. Drugs such as doxorubicin, epirubicin, docetaxel, paclitaxel, cyclophosphamide, vinblastine, bleomycin, topotecan and etoposide can cause severe hair loss while some chemotherapeutic agents (such

as fludarabine, estramustine, lomustine and cladribine) do not cause hair loss (13, 29-31).

Drugs that cause hair loss are classified into three categories: serious, moderate, and mildly causing hair loss (13, 31). (Table 1)

**Table 1.** Classification of Chemotherapeutic Drugs Causing Alopecia

Mild Alopecia	Moderate Alopecia	Severe Alopecia
Bleomycin	Busulfan	Cyclophosphamide
Carmustine	Nitrogen mustard	Daunorubicin
Fluorouracil	Floxuridine	Adriamycin
Hydroxyurea	Methotrexate	Vinblastin
Melphalan	Mitomycin	Vincristine
Dacarbazine	Teniposide	Vindesine
Cisplatin	Actinomycin	Ifosfamide
Cytosine arabinoside	Camptothecin	Etoposide
Thioguanine		Taxoids
Streptozocin		
Chlorambucil		
L – asparaginase		
Thiotepa		
Mercaptopurine		
Hexamethylmelamine		

Reference: Collett A, Al-Tameemi W, Durnill C, Hussain O, Georgopoulos N. The role of scalp cooling in the prevention of Chemotherapy Induced Alopecia. *European Journal of Clinical and Medical Oncology Special Edition* 2014; 65-9.

### Prevention of Chemotherapy-Induced Alopecia

Since the late 1960's oncologists and oncology nurses have used different methods to prevent chemotherapy-induced alopecia. The main purpose of these methods is to improve physical appearance by preventing hair loss, provide optimal social interaction and maintain body image (13). These methods can be listed as mechanical, physical and biological methods.

#### Mechanical Methods

These methods involve the tourniquets applied to the scalp. Scalp tourniquets are kept under pressure by means of bands applied around the head. They show their effects by reducing blood supply to the scalp during the time of peak plasma concentration of chemotherapeutic agents and so, cytostatic agents reach less to the hair follicles (13, 32). These tourniquets are usually applied 5 minutes before or just before chemotherapy infusion until 5, 7, 20, or 30 minutes following the administration of the chemotherapy agents. Researchers have described mild to moderate hair loss with this technique. The success and failure of this method have been discussed by many researchers. Some researchers stated that this method was ineffective because of this method is time-consuming, uncomfortable and could lead to ischaemic nerves damage (33). Besides Payne (34) stated that although scalp protection through cooling or tourniquet has been reported to minimize delivery of chemotherapeutic agents to the scalp thereby potentially decreasing the risk of hair loss, case reports of cutaneous metastases or spread, therefore this method is not recommended. Also, in a randomized controlled study, scalp tourniquet was found ineffective for preventing CIA (35). The authors of this study explained the two probable reasons for

ineffectiveness of this method are that the cytotoxic drugs are not all rapidly cleared from the blood and tissue-bound and that the hair follicles could not be well protected from drug effects for a long enough time because of patients' discomfort (35).

#### Physical Methods

The hypothermia used to prevent alopecia is a method that involves cold application to the head, which is defined and tested by most researchers (13). Since 1970, scalp cooling method has been used in various forms. In recent years, the interest in physical methods has been increased and they are preferred because they are more useful than mechanical methods and less disturbing to the individuals (13, 36).

From the past, various cooling systems have been developed, such as ice and cold liquid turban, cold air application and cryogel caps, which show 0% to 90% efficiency (8, 13). But ice and cold liquid turbans are becoming less popular after the development of cryogel caps. Generally, cryogel caps are more preferred than ice packs. Because it is easier and less uncomfortable to prepare and apply these caps, they do not cause any problems such as melting during treatment (8, 13).

Hypothermia applied to prevent CIA is one of the commonly used methods and there are many studies that describe the use of hypothermia (7, 27, 29, 37-40). It acts with three mechanisms: (1) it reduces the rate of cytostatic agent exposure by decreasing blood flow to the hair follicles via vasoconstriction, (2) reduces the temperature of scalp and (3) reduces the metabolic rate of the drug reaching the hair follicles (8, 13, 36).

Although there are several studies suggesting that scalp cooling is an effective method to prevent CIA (9, 11, 14, 27, 29, 31, 37-40), there are some debates about this method. In these debates, it is stated that scalp metastasis can develop after cold application process. In a retrospective cohort study, the metastasis incident is found to be 1.2% for women (6 incident in 553 patients) who had scalp cooling method and 1.1% for women (1 incident in 87 patients) who didn't have cold application treatment (41). In a meta-analysis, scalp metastasis incident is found 0.56% (12 in 2129 patients) (42).

In addition all these, scalp cooling method is contraindicated in cases of, hematological malignancies (leukemia, multiple myeloma, non-Hodgkins and other generalized lymphomas), cold sensitivity, cold agglutinin disease, cryoglobulinemia, cryofibrinogenemia, cold traumatic dystrophy, melanoma patients with adjuvant or curative chemotherapy (43). As a consequence, it is not recommended for all these cases.

#### Biological Methods

Biological methods are methods that focus on protecting the hair follicle or increasing hair growth.

a. 2% Minoxidil; It is indicated that when it is applied topically twice daily with hair, it induces hair growth and prevents hair loss in normal male pattern baldness (androgenic alopecia) and affects the hair follicles on the anagen stage (13, 16, 17). In a randomized clinical trial, topical minoxidil (2%) was shown to shorten the duration of CIA and lengthen the

time to maximal hair loss in breast cancer patients receiving 5-fluorouracil, doxorubicin, and cyclophosphamide (17).

b. Other biological methods; Steroid 5 alpha-reductase inhibitor (4MA), in animal experiments, hair growth modulators Cyclosporin (CSA) and FK 506 gave successful results (44-46). But there is still insufficient evidence of its use in humans. Imurent and interleukin 1 have been found to be effective on newborn mice to prevent Ara-C and doxorubicin induced hair loss. Folic acid has been shown to prevent hair loss when administered in combination with methotrexate. It has been reported that 69% of patients receiving doxorubicin did not develop hair loss when high-dose vitamin alpha-tocopherol was administered (15, 19, 47). As a result, studies for preventing hair loss of biological agents are still in use and its use in practice is not fully recommended (7, 13).

### **The Roles of Nurses in the Prevention of CIA**

The roles of nurses as an educator are crucial for preventing CIA. Nurses should be planned the patient education to prepare the patients for the preparation of the treatment and to reduce hair loss, so as to increase the compliance and participation of the people (48). To assess the severity of CIA, nurses can benefit from some scales, for example those from the World Health Organization (49) and the Common Terminology Criteria for Adverse Events (50).

The issues that need to be addressed during the preparation process for chemotherapy can be summarized as follows:

- Encouraging patients to express their feelings about their particular feelings, thoughts, and self-gaze,
- Encouraging patients to ask questions about health problem, treatment, prognosis,
- Preparing family members for physical and emotional changes,
- Encouraging visits of friends and family members,
- Creating opportunities to share these experiences with people who have similar experiences,
- Informing patients about the chemotherapeutic agents that will cause severe hair loss,
- Giving information about the use of hair dyes or perms during the treatment period can increase hair loss,
- Informing patients that hair loss is not only limited in the scalp, but also eyebrows, eyelashes, beard, axillary and pubic hair may also be lost,
- Giving information about the hair loss generally is reversible, with hair regrowth typically occurring after a delay of 3–6 months,
- Counselling patients about continuing their treatments even if they experience hair loss,
- Advising patients a convenient wig or scarf-head band before treatment,
- Giving opportunities for family members to share their fears and thoughts,
- Avoiding the use of intensive shampoo,
- Drying hair gently,

- Avoiding the use of electric hair stylers, buckles, tape, hair dyes and hair sprays,
- Preventing the hair from being pulled with tapes, buckles or pliers,
- Using of a large toothed comb,
- Avoiding a strong brush (8, 13, 30, 48).

Since patients have to cope with hair loss at their homes, it is also important to teach a variety of self-care practices so that the patients choose activities that are more appropriate for them. In this way, the patient can identify side effects and show willingness to self-care to alleviate these side effects (13).

### **Recommendations for prevention and management of CIA**

Although CIA does not menace life, it is an important side effect of chemotherapy and can negatively affect the physical appearance of patients, body image, sexuality, self-esteem, disease and treatment adjustment and the ability to cope with illness (3, 7, 9). Therefore, it is essential that healthcare professionals should also be aware of the social significance of hair. In this way, this problem, which is very important for patients, can be addressed in a sensitive and practical manner.

Coping with CIA remains a major problem in the management of cancer treatment. Significant progresses and several physical and pharmacological approaches to prevent and manage CIA have been studied. However, the most effective prevention strategies have yet to be developed. Even so CIA cannot be exactly prevented, it can be managed.

For the prevention and minimizing of CIA and its negative effects on the patients;

- Nurses and patients' family could help patients prepare for the CIA, thus minimizing the negative impact on cancer patients.
- Nurses should inform the patients about self-care strategies to take control and cope with CIA.
- Nurses should also advise patients to avoid physical and chemical trauma to the hair (e.g. bleaching, coloring and perming) and to shave their hair once the hair loss becomes prominent.
- Scalp cooling and 2% topical minoxidil are the best prevention and most effective methods that have been studied up to now, nurses may suggest these methods as appropriate for the clinical condition of the patient.
- Further research to optimise scalp cooling protocols and identify effective pharmaceutical agents to prevent CIA should be designed and studied in large populations, different chemotherapeutic agents and treatment protocols.
- Nurses may develop scales that they can assess the severity of CIA and determine its effects on the patient.
- Nurses may draw up protocols and guidelines for CIA prevention by pharmacological or non-pharmacological methods.
- To develop better therapeutic methods for the prevention CIA, nurses can be involved in randomized controlled and multidisciplinary studies.

## Conclusion

Patients can affect not only their physical appearance, but also the psychological side because of CIA, which leads to significant deterioration in body image and self-esteem as well. Although various studies including pharmacological and non-pharmacological methods have been performed, there is no method proven to be effective for the prevention CIA because of the limitations of these methods and debates on their effectiveness. However, CIA can be significantly reduced through non-pharmacological methods (particularly), facilitating patients' adjustment to the disease and treatment and favorably supporting the quality of life.

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