

Chemotherapy-Induced Hair Loss

R. M. Trüeb, MD

Center for Dermatology and Hair Diseases Wallisellen, Zurich, Switzerland

ABSTRACT

Chemotherapy-induced hair loss occurs with an estimated incidence of 65%. Forty-seven percent of female patients consider hair loss to be the most traumatic aspect of chemotherapy and 8% would decline chemotherapy due to fears of hair loss. At present, no approved pharmacologic intervention exists to circumvent this side-effect of anticancer treatment, though a number of agents have been investigated on the basis of the current understanding of the underlying pathobiology. Among the agents that have been evaluated, topical minoxidil was able to reduce the severity or shorten the duration, but it did not prevent hair loss. The major approach to minimize chemotherapy-induced hair loss is by scalp cooling, though most published data on this technique are of poor quality. Fortunately, the condition is usually reversible, and appropriate hair and scalp care along with temporarily wearing a wig may represent the most effective coping strategy. However, some patients may show changes in color and/or texture of regrown hair, and in limited cases the reduction in density may persist.

Key Words: chemotherapy, hair loss, scalp cooling, minoxidil, hair care, wig

Chemotherapy-induced hair loss is considered to be one of the most traumatic factors in cancer patient care. Hair loss can negatively impact individual perceptions of appearance, body image, sexuality, and self-esteem, as well as deprive patients of their privacy, because this treatment-related outcome is readily associated with having cancer by the lay public. Forty-seven percent of female cancer patients consider hair loss to be the most traumatic aspect of chemotherapy and 8% would even decline treatment for fear of this impending side-effect.^{1,2}

Incidence of Chemotherapy-Induced Hair Loss

The overall incidence of chemotherapy-induced hair loss is estimated to be 65%.³ The prevalence and severity of this type of hair loss are variable and related to the selected chemotherapeutic agent and treatment protocol. There are multiple classes of anticancer drugs that can induce alopecia (Table 1), with frequencies of chemotherapy-induced hair loss differing across the four major drug classes: >80% for antimicrotubule agents (e.g., paclitaxel), 60%-100% for topoisomerase inhibitors (e.g., doxorubicin), >60% for alkylators (e.g., cyclophosphamide), and 10%-50% for antimetabolites (e.g., 5-fluorouracil plus leucovorin). Combination therapy consisting of two or more agents usually produces higher incidences of more severe hair loss, when compared with monotherapy.³

Pathobiological Considerations

Chemotherapy-induced hair loss is a consequence of direct toxic insult on the rapidly dividing cells of the hair follicle. While hair loss from anticancer therapy has traditionally been categorized as acute diffuse shedding that is caused by dystrophic anagen effluvium, more recently, it has been

highlighted that, in fact, chemotherapy-induced hair loss may present with different pathomechanisms and clinical patterns. Evidence exists suggesting that the hair follicle may respond to the same insult that is capable of stopping mitosis with both shedding patterns, i.e., dystrophic anagen effluvium and telogen effluvium.⁴ Accordingly, the hair may fall out very quickly in clumps or gradually. When mitotic activity is arrested, numerous and interacting factors may influence the shedding pattern. One of these factors is the mitotic activity of the hair follicle at the moment of the insult.

Agents that usually cause hair loss	Agents that sometimes cause hair loss	Agents that unusually cause hair loss
Adriamycin	Amsacrine	Carboplatin
Cyclophosphamide	Bleomycin	Capecitabine
Daunorubicin	Busulphan	Carmustine
Docetaxel	Cytarabine	Cisplatin
Epirubicin	5-Fluorouracil	Fludarabine
Etoposide	Gemcitabine	Methotrexate
Ifosphamide	Lomustine	Mitomycin C
Irinotecan	Melphalan	Mitroxantrone
Paclitaxel	Thiotepa	Procarbazine
Topotecan	Vinblastine	Raltritrexate
Vindesine	Vincristine	6-Mercaptopurine
Vinorelbine		Streptozotocin

Table 1. Cytotoxic agents that can cause hair loss³

A primary characteristic of the anagen hair follicle is that the epithelial compartment undergoes proliferation, with the bulb matrix cells exhibiting the greatest proliferative activity in building up the hair shaft. The abrupt cessation of mitotic activity leads to weakening of the partially keratinized, proximal portion of the hair shaft, resulting in narrowing and subsequent breakage within the hair canal. The consequence is hair shedding that usually begins at 1 to 3 weeks after initiation of chemotherapy. Due to its long anagen phase, the scalp is the most common location for hair loss, while other terminal hairs are variably affected depending on the percentage of hairs in anagen. Normally, up to 90% of scalp hairs are in the anagen phase, and as such, hair loss is usually copious and results in alopecia that is quite obvious. In addition, chemotherapy given at high doses for a sufficiently long duration and with multiple exposures may also affect hairs of the beard, eyebrows, and eyelashes, as well as axillary and pubic regions.

When hair is in late anagen phase, during which the mitotic rate slows down spontaneously, it simply accelerates its normal path to telogen, while mitotically inactive phases (catagen and telogen) are not affected. Since anagen duration is diminished in androgenetic alopecia, the

probability is increased that the antimitotic insult strikes hairs that are close to the resting phase, resulting in telogen effluvium. Furthermore, synchronization of hair cycles also plays a role, and again in androgenetic alopecia, the hair cycles tend to synchronize due to the shortened duration of anagen. Consequently, even a minor antimitotic insult can produce marked hair loss.⁵

Generally, the hair loss is reversible, with hair regrowth typically occurring after a delay of 3 to 6 months. In some patients, the new growth shows changes in color and/or texture. Hairs may be curlier than previous or they may be gray until the follicular melanocytes begin functioning again, but these differences are usually temporary. Permanent alopecia has been reported after chemotherapy with busulfan and cyclophosphamide following bone marrow transplantation,⁶ and it has also been associated with certain risk factors, including chronic graft-versus-host reaction, previous exposure to X-ray, and age of patients.⁷

Therapeutic Potential for Prevention or Reversal of Chemotherapy-Induced Hair Loss

A number of inhibitive measures have been proposed and tried in an effort to limit chemotherapy-induced hair loss. Of the treatments investigated thus far, scalp cooling (hypothermia) has been the most widely used and studied, though most published data on this method are of poor quality. Of the 53 multiple patient studies published between 1973 and 2003 on the results of scalp cooling for the prevention of chemotherapy-induced hair loss, seven⁸⁻¹⁴ of these trials were randomized. In six^{8,9,11-14} of the seven randomized studies, a significant advantage was observed with scalp cooling. The favorable results were most evident when anthracyclines or taxanes were used as the chemotherapeutic agents. Some studies have raised concerns about the risk of scalp skin metastases after cooling.^{15,16} Currently, scalp cooling is contraindicated for those with hematological malignancies and its use is controversial in patients with non-hematological malignancies who undergo curative chemotherapy.¹⁷ Patients undergoing scalp hypothermia commonly report feeling uncomfortably cold and experience headaches.

To date, no approved pharmacologic option exists for the prevention of chemotherapy-induced hair loss. Among the therapies evaluated in cancer patients thus far, the topical hair growth promoting agent minoxidil was able to shorten the duration, but it did not prevent chemotherapy-induced hair loss.¹⁸ Minoxidil also failed to induce significant regrowth of hair in busulfan- and cyclophosphamide-induced permanent alopecia.¹⁹

Advances made in understanding the pathobiology of chemotherapy-induced hair loss, in conjunction with the investigation of several experimental pharmacologic approaches, may offer some optimism. However, the inherent vulnerability rests with the rapid cell proliferation of hair follicle keratinocytes during anagen that renders the structure susceptible to the effects of chemotherapeutic toxicity. A strategy that protects against chemotherapy-induced hair loss may involve arresting the cell cycle in order to reduce the sensitivity of the follicular epithelium to cell cycle-active antitumor agents. Inhibition of cyclin-dependent kinase 2 (CDK2), a positive regulator of the eukaryotic cell cycle, may represent a potential approach that arrests the cell cycle. Potent small-molecule inhibitors of CDK2 are currently being developed using structure-based methods.³ Ultimately, a successful therapeutic candidate should selectively target the hair follicle and avoid interfering with the efficacy of anticancer treatment. In view of the fact that cancer is usually treated with a combination of chemotherapy drugs, an effective mitigation strategy would likely require agents that are effective for different chemotherapeutics with distinct mechanisms of action. Moreover, variations in patient characteristics must also be taken into account, as the pattern of chemotherapy-induced hair loss is patient-specific.

Suggestions for Routine Management

Even if chemotherapy-induced hair loss cannot be prevented, it can be managed. Anticipating hair loss, coming to terms with the inevitability of hair loss, and maintaining a proactive disposition are the key steps in successfully coping with chemotherapy-induced hair loss.

Recommendations for hair care include:²⁰

- Avoiding physical or chemical trauma to the hair (e.g., bleaching, coloring, perming, using curling irons or hot rollers). Implementation of gentle hair care strategies should be continued throughout chemotherapy.
- Using a satin pillowcase, which is less likely to attract and catch fragile hair; using a soft brush, washing hair only as often as necessary; and using a gentle shampoo.
- Cutting hair short or shaving hair. Short hair tends to look fuller than long hair, and when the hair is shed, it is less noticeable when it is short. Moreover, hair that has been cut short may help patients to ease the transition to total alopecia.
- Shaving the head may be easier for securing a wig or hairpiece.

Patients can be encouraged to plan for an appropriate head covering in advance. Clinicians should be mindful that the use of a head covering as the hair falls out is a very personal decision. For women in particular, chemotherapy-induced hair loss involves a confrontation with the very nature of their disease, while for men it is often viewed as a normal and inevitable consequence of treatment. Depending on individual patient preference, temporarily wearing a wig or another type of head covering until the hair regrows may be the most effective way of dealing with this condition, while at the same time this measure can protect the scalp from sun and cold exposure.²¹

Conclusion

The major medical approach to prevent or minimize chemotherapy-induced hair loss remains scalp cooling, while topical minoxidil may speed up hair regrowth. Since chemotherapy-induced hair loss cannot be reliably prevented, it is recommended that a management scheme be devised in advance which focuses on treatment expectations and making patients as comfortable as possible with their appearance before, during, and after anticancer therapy.

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