Chemotherapy induced alopecia and strategies to manage its impact

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Abstract
Chemotherapy-induced hair loss is a common and distressing side effect of some chemotherapy agents, and is ranked as one of the top three most distressing side effects by patients. Hair loss (alopecia) is more prominent on the scalp but affects the eyebrows, eyelashes, beard, axillary and pubic hair and typically begins within the first three weeks of starting chemotherapy. Patients report lower quality of life, high levels of distress, negative body image and feelings of loss of control associated with their alopecia. For most patients regrowth occurs after treatment completion but the colour and structure of hair can be altered, prolonging the negative impact on patient sense of wellbeing. The impact of chemotherapy-induced alopecia on patients is underestimated by many health professionals. Management is typically to camouflage the loss by wearing a wig, head scarf, or hat/turban. Scalp cooling with coolant based devices to reduce chemotherapy-induced alopecia has been available in Europe for more than a decade, but has only recently been introduced in Australia. Scalp cooling works by reducing local concentration of chemotherapy agents and decreasing metabolic uptake by hair follicle cells. Given the significance of hair loss to patients, further research to ameliorate this common side effect of chemotherapy treatment is urgently required.

Chemotherapy induced alopecia

Hair loss (alopecia) is a common and visible side effect of chemotherapy.¹ The incidence and severity of chemotherapy-induced alopecia (CIA) depends on both the type and dose of chemotherapy agents. Alkylating agents (cyclophosphamide, ifosfamide), anthracyclines (doxorubicin, daunorubicin), antimicrotubule agents (docetaxel, paclitaxel), and topoisomerase inhibitors (etoposide) are known to cause the most severe CIA and hair loss is greater when chemotherapy agents are administered intravenously, particularly when they are administered in combination.¹,² Hair loss typically starts seven to 14 days after infusion and can be diffuse or patchy and may occur suddenly or gradually over time.³,⁴ Newer chemotherapy drugs can reduce the level of CIA however current protocols often involve administration in combination with traditional agents. Although hair loss is more prominent on the scalp because the scalp has greater proliferation of hair, CIA affects all parts of the body such as the eyebrows, eyelashes, beard, axillary and pubic hair.

Hair loss occurs because chemotherapy agents are designed to disrupt the mitotic and metabolic process of cancer cells. Unfortunately, rapidly dividing cells such as hair follicles are also affected. The rapid hair growth, as well as high blood flow around the hair bulb results in disturbances of normal hair-shaft production and hair-follicle cycling, causes breakage of the hair shaft and hair shedding.²,⁴ However the mechanism of action is still being identified and it is unclear whether the blood concentration or the exposure time of hair follicles to cytotoxics is more important for the toxic effect.¹

Generally, CIA is reversible, with regrowth typically occurring three to six months after the completion of chemotherapy.⁴ There is little research exploring the regrowth of hair on other parts of the body, however, reports suggest that for 60% of patients who lose scalp hair, regrowth results in changes to hair colour and structure.⁵ New hair is often grey or differs in colour due to distortion of the pigmentation process during chemotherapy, and is typically coarser, grows more slowly and is thinner.⁶ It may therefore take considerable time before patients’ return to their pre-treatment
appearance, adding to patients' sense that cancer continues to impact them post treatment. Sad, a small number of patients experience permanent hair loss. Permanent hair loss is most commonly observed in those patients receiving high dose chemotherapy prior to bone marrow transplantation possibly due to epithelial hair-follicle stem cell involvement, however it has also been reported in a small number of patients with breast cancer receiving adjuvant anthracyclines and taxanes.

**Psychological impact of hair loss**

Although CIA is not life-threatening, temporary for the majority of patients and is unlikely to lead to dose reduction, it causes significant distress to most patients. Of concern, is the influence on patient treatment decision-making, with approximately 8% of patients refusing chemotherapy due to the fear of hair loss. The importance of CIA to patients is underscored by its ranking as one of the top three most distressing chemotherapy side effects and although being aware of CIA as one of the side effects of treatment, patients report not being prepared emotionally for the impact hair loss. Despite the prevalence of CIA, there have been relatively few studies that have explored the impact of CIA on patients, with much of what we know based on small qualitative studies exploring chemotherapy side effects more generally. These studies confirm hair loss results in lower quality of life, high levels of distress, negative body image and feelings of loss of control. Even before commencing chemotherapy many patients experience anticipatory distress associated with hair loss, with approximately one-third of patients mentioning hair loss during their first consultation with the oncologist.

The impact of CIA for patients is underscored by a study by Jayde et al that qualitatively explored the experience of CIA in Australian women with ovarian cancer. This study found CIA to be the most distressing aspect of the ovarian cancer experience. Similarly, in a study with early breast cancer patients, hair loss was considered more distressing than losing a breast. In both of the studies, CIA represented a public confirmation of a cancer diagnosis and for women with ovarian cancer particularly, highlighted patient fears of mortality. Despite the high levels of patient distress reported across studies, surveys of oncology health professionals' attitudes to hair loss indicate that they frequently underestimate the impact on patient wellbeing. Furthermore, a recent study conducted in Australia (Shaw et al, in press) highlighted ambivalence among health professionals to intervene, even when recognising the negative impact of CIA on patients.

**Body image**

Hair loss has a significant negative impact on many women's self-confidence and body image resulting in lower social, physical, and total wellbeing than female patients without alopecia. In 28% of young women with breast cancer, low body image as a result of hair loss contributes in part to sexual problems experienced. Additionally, Frith and colleagues found that body image to be poorer during treatment, but it did not return to pre-treatment levels when hair returned. Negative body image is compounded with loss of eyebrows and lashes as hair loss challenges women's conceptualisation of femininity and attractiveness and men's sense of masculinity leading to poor post-treatment adjustment. Although much of research related to hair loss has focused on women, particularly those with breast cancer, there have been some studies that report CIA is also a distressing side effect for males and similar levels are reported across tumour groups. There is some suggestion that hair loss is more threatening to women's sense of self, however Hilton and colleagues argue that while women are more distressed at losing hair above the eye line, men are more concerned at hair loss from other parts of the body such as face and limbs. Furthermore, the impact on body image is not age-related, with both younger (<50 years) and older patients reporting decreased body image related to CIA. Patients with recurrent disease also report higher distress associated with hair loss. Patients further report hair loss influences social confidence and role performance, with loss of facial hair impacting negatively on an individual's ability to express themselves.

**Illness representation**

Studies that focus on the meaning of CIA to patients highlight the link between hair loss and illness representation. CIA is perceived as a visual indication of illness. For some, the hair loss is a constant reminder of their cancer. However for others, CIA represents a public acknowledgement of cancer and patients report losing control over to whom they choose to disclose their diagnosis. Women with children report that hair loss causes distress to their children and was one of the most difficult side effects for partners to come to terms with.
Strategies to manage hair loss

Providing information on hair loss and teaching self-care strategies to minimise alopecia have been found to facilitate coping and adjustment to CIA, although health professionals rarely provide emotional support or counselling to patients. Typically both women and men take active steps to manage their hair loss as soon as it becomes noticeable. However some women find the act of cutting their hair or shaving their head as a traumatic blow and experience difficulties looking at themselves in the mirror. Many women camouflage CIA by wearing a wig or head cover, particularly in public. Wearing a wig is a compensation for the changed appearance and is aimed at trying to look normal again for both self and others. Other patients choose to shave their head when CIA begins due to both practical and emotional considerations. Both men and women report shaving reduces the physical sensations such as itching and reduces the need to clear fallen hair from pillows and the shower. Shaving rather than waiting for hair to fall out is reportedly a strategy used by some to gain control over CIA. Pre-emptively purchasing wigs and head covering was also reported to be another means women sought to come to terms with their altered appearance and gain a sense of control over CIA. This is particularly important when some much of cancer treatment is out of the patient’s control. Strategies to manage non-scalp hair loss are limited, although pharmaceutical agents to reduce eyelash loss are being trialled (K. Morris, personal comm).

Some patients see CIA in a more favourable light, choosing to consider alopecia as reflective of “strong therapy” that will translate into better survival. Despite these patients being less concerned about hair loss, reports suggest that patients who do not hide their hair loss can experience stigma as they are perceived as breaking social norms by not covering up. Male patients reported generally less pressure to hide their baldness although others perceived negative assumptions about them were made based on their bald status.

Scalp cooling

Scalp cooling is a supportive care intervention that is increasingly being utilised in many cancer centres as a strategy to reduce CIA. Scalp cooling has been available in cancer centres in Europe for more than a decade but it is a relatively new technology in Australia. Although application has evolved from frozen caps requiring frequent changes (e.g. Penguin Cold Caps) to continuous cooling of the scalp with super-cooled liquid gel caps (e.g. Paxman Orbis, Dignitana Dignicap) over recent years, the principles of scalp cooling involve concurrent cooling of the scalp during chemotherapy, as it is hypothesized the vasoconstriction reduces blood flow to hair follicles during peak plasma concentrations of chemotherapy agents, which in turn reduces its cellular uptake. Scalp cooling reduces biochemical activity making hair follicles less vulnerable to the damage of chemotherapeutic agents. Efficacy may be related to the achievement of scalp skin temperatures below 18°C.

There is a growing body of literature confirming scalp cooling is an effective treatment to reduce chemotherapy-induced hair loss. A recent meta-analysis summarising the available data confirmed scalp cooling significantly reduced CIA (RR 5 0.38, 95% CI 5 0.32–0.45). Additionally, a large cohort study conducted through the Dutch Scalp Cooling Registry confirmed 50% of the patients with scalp cooling had good hair preservation, with a range of between 8% (TAC chemotherapy) to 94% (docetaxal). The study also reported that higher dose and shorter infusion time, older age, female gender and non-West-European type of hair significantly increased hair loss during scalp cooling. Despite the variability the technology is reported to be well-tolerated and there is high patient satisfaction. For example, Betticher and colleagues found that scalp cooling reduced the risk of hair loss by 78%, with adverse events experienced by 3.3% (n=8) of participants and only 30 of 199 patients (12.6%) receiving scalp cooling discontinuing due to tolerability issues such as headaches, sensation of cold or pain. Concern that protection of the scalp from chemotherapy might lead to an increased risk of scalp metastases has not been borne out in large breast cancer cohorts.

Current research

Although the technology has been available in Europe for more than a decade, scalp cooling has until recently been unavailable in Australia. Introduction of scalp cooling into cancer centres requires a significant change to current clinical practice. Uptake in Australia has been primarily driven by individual oncologists or cancer nurses and access has been largely limited to patients with breast cancer in a few metropolitan centres. Ongoing research to identify the barrier and facilitators to wider
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implementation is currently underway. Internationally, there is research being conducted to build the evidence-base for scalp cooling, both in terms of greater understanding of treatment protocols and on investment in time and costs of scalp cooling from a health service perspective. Additionally, recent explorations of the scalp cooling and CIA literature have highlighted the need for a common objective measure for CIA. A consortium of Australian, Dutch and UK researchers is currently validating such a measure. Randomised controlled trials will then be feasible to address issues such as determining optimal cooling times for different regimens. Pharmaceutical agents applied topically or as an injectable to prevent CIA and enhance regrowth are also being tested, although promising agents identified in animal models have failed to translate to effective treatments in humans. Preliminary research to identify agents that may reduce the loss of eyelashes is also ongoing. (K. Morris, personal communication)

Chemotherapy-induced hair loss is a common side effect of chemotherapy. Hair loss is more prominent on the scalp but affects the eyebrows, eyelashes, beard, axillary and pubic hair and typically begins within the first three weeks of starting chemotherapy. Many patients experience psychological distress, report lower quality of life body image issues associated with this form of hair loss that are in addition to their cancer diagnosis. Management is typically to alter drug choice, or to camouflage the loss by wearing a wig, head scarf, or hat/turban. Scalp cooling is the most effective prevention strategy for chemotherapy-induced alopecia. Further research to optimise scalp cooling treatment protocols and identify pharmaceutical agents to prevent alopecia is urgently required.

Additional links:
COSA 2016 Conference breakfast session: Scalp cooling: Why it’s cool and how to keep you cool
Mater Hospital – Scalp cooling system (information for patients and hairdressers)

References


