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COMMENTARY

Measurement of chemotherapy-induced alopecia—time to change

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Abstract Data on chemotherapy-induced alopecia (CIA) as a side effect of cancer treatment are scarce. CIA is given minimal attention in clinical trials and in the literature. However, when asking the patients with cancer for their opinion, CIA appears to have a major impact, particularly on body image and quality of life. Currently, there is no commonly used measure to evaluate CIA; It is time to improve the management and measurement of CIA.

Keywords Alopecia · Chemotherapy · Side effect · Data quality

Commentary

Chemotherapy-induced alopecia (CIA) can visually turn a healthy person into a cancer patient. It stigmatizes and can be devastating for patients [1]. When searching for reference values of CIA to estimate the added value of scalp cooling, data related to CIA appears to be scarce. Several qualitative studies, predominantly nursing related, describe the impact of CIA and interventions for coping with it, but the incidence of CIA is rarely quantified in observational studies or clinical trials. The medical literature abounds with studies on the incidence and interventions for side effects of chemotherapy (e.g. prevention of nausea and vomiting), but only a minimal number of studies describe CIA prevention.

Although CIA is not life threatening, is unlikely to lead to dose reduction and hardly leads to rejection of chemotherapy, it should be incorporated as an important patient-reported outcome measure in pharmaceutical trials; If there are no survival benefits between cytotoxic treatments, quality of life issues such as CIA may be decisive. CIA also gets minimal attention in the widely used cancer-specific quality of life questionnaires, such as the European Organization for Research and Treatment of Cancer (EORTC) or the Short Form-36 (MOS SF-36).

Some clinician-rated measures do exist for assessing CIA, for example those from the World Health Organization (WHO) [2] and the Common Terminology Criteria for Adverse Events (CTCAE) [3]. However, in phase II and III clinical trials of 3 weekly docetaxel monotherapy regimes of 100 mg/m^2, the reported incidence of CIA differed from 42 % (grades 1–4) of the patients in one study to 100 % (only grades 2+3) in another [4]. For docetaxel 75 mg/m^2 monotherapy or combined with cisplatin or capecitabine, CIA was reported in 40–89 % of the patients [4].

The wide range of percentages reported make detecting significant differences in CIA almost impossible, and no reliable estimation can be made. In addition, the recent emergence of techniques to prevent CIA requires appropriate clinical trials to explore efficacy and this will require better measurement tools.

The current version 4.0 of the CTCAE [3] has only two grades for alopecia. Despite including a more comprehensive description of the grading of severity of CIA in contrast to previous versions, the quality of subjective reporting with this tool in forthcoming trials may not improve.

Researchers who focus on CIA obviously do not feel the CTCAE to be distinctive enough. A review of 85 papers and abstracts since the 1970s about the effectiveness of scalp

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cooling has shown the grading has rarely been used [5]. There is also no way of making comparison between studies because at least 34 different Likert scales were used, in addition to visual analogue scales, pictorial assessments, etc.

Who is best to complete the measure? Medical doctors (MDs) mainly use the CTCAE to indicate urgent interventions. In the case of CIA, because the value of hair is individual and personal, we believe such a measure should be patient reported.

There may be some ignorance of the impact of CIA by oncological professionals—is this a problem? Do MDs truly recognize the impact of hair loss on the patients' daily life? The view seems to be that it is 'temporary' and 'only cosmetic'. MDs are used to accepting it as a foregone conclusion, and patients also therefore seem to take it for granted. As long as patients do not seek answers about hair loss, MDs will not mention the topic and tend to leave it to the nurse specialist [6]. And even then, CIA tends to only be mentioned during the pre-chemotherapy consultation, but the impact of CIA and coping with this is hardly addressed when CIA is apparent [7].

So, why bother? For breast cancer patients, the impact of CIA is much higher than expected by MDs and nurses [8]. It is not only a problem for women with breast cancer; CIA is also an important side effect for many other cancer patients, including males [4, 9, 10]. The impact of the condition is neither related to age or ethnic background. Many patients report that losing their hair was disruptive, even though they thought they were prepared for it. Although many patients choose to wear a wig, they report that their 'baldness' is still there when they look in the mirror. It constantly reminds them about their disease, even on good days between chemotherapy treatments. Whilst the support of close relatives on hair loss is helpful, patients who choose not to wear a wig are regularly shocked about the 'cruel compassion' they receive from total strangers [7].

Based on current practice, patients are reasonably well informed about the particular chemotherapy regimens which rapidly cause total CIA. Most professionals will tell their patients that they will completely lose their hair within 3 weeks after the first cycle of high dose 5-fluorouracil (500 mg/m^2), epirubicin (80, 90 or 100 mg/m^2) and cyclophosphamide (500 mg/m^2) (FEC). That might be an overestimation, whilst the literature shows 62–88 % of patients with WHO grade 3 alopecia [11–13].

For many chemotherapies, the severity and pattern of CIA seems certainly not as evident as for FEC. In patients facing the prospect of CIA, this information is important when choosing to spend money for a wig and/or take the option of scalp cooling. Prevention of the suffering from CIA is crucial, but if the added value of scalp cooling is minimal, extra time and costs [14] should be considered. Another important reason for drawing attention to information about CIA is the occurrence of permanent alopecia, e.g. after the frequently used sequential scheme of FEC followed by docetaxel [15].

An international multidisciplinary group is researching into the prevention of CIA with interventions such as scalp cooling. In order to evaluate and compare the outcomes and to determine the added value of scalp cooling, an internationally common measure for CIA is needed. For research purposes, the objective hair mass index may be used in parallel [16]. Ideally, both data from scalp-cooled and non-scalp-cooled patients should be collected in a registry, preferably pooling data of several countries. To better manage CIA, more evidence-based data on investment in time and costs of scalp cooling would also be worthwhile.

In a recent editorial about 'toxicity of cancer treatment', it was stated that better quality data for toxicity outcomes are needed [17]. Whilst reporting of all side effects might indeed be improved, the grading of the severity of alopecia is a high priority. It is time for a real change in how CIA is managed and measured. Education and altered attitudes and beliefs are the buzz words. This is a call to action.

Conflict of interest All authors declare to have no conflict of interest.

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