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REVIEW ARTICLE

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What is wrong with the 30-year-old practice of scalp cooling for the prevention of chemotherapy-induced hair loss?

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Abstract Since about 1970 scalp cooling has been used to prevent chemotherapy-induced hair loss, one of the most common and emotionally distressing side effects of cancer therapy. Generally accepted opinions, uncertainty and controversy, topics to study and recommendations for improving the results of scalp cooling are the subjects of this article which was also presented at the MASCC Symposium, June 2003, Berlin.

Keywords Scalp cooling · Hypothermia · Cold cap · Chemotherapy-induced hair loss · Alopecia

Introduction

A recent review of the literature of the 30-year-old practice of scalp cooling has shown that there are still many questions to be answered (E.G. Grevelman and W.P.M. Breed, unpublished data). This may be due to the rather short history of supportive care, the very limited interest shown by oncologists in this subject, the underestimation of the impact of temporary hair loss on patients, the difficulties of clinical trials in these areas, especially of the necessary multicentre trials, the small number of preclinical studies in which the biochemical and biophysical processes playing a role in the hair loss have been investigated, and possibly also the lack of financial support.

There are fewer than 100 reports of scalp cooling for the prevention of chemotherapy-induced hair loss. This is far fewer than the number of reports on other side effects of chemotherapy such as nausea, vomiting and bone marrow toxicity. Moreover, the reports often contain merely one method of scalp cooling in a limited number of patients, regularly without control patients. There have been only six randomized clinical studies in which cooling and no cooling have been compared. Although patients are concerned about hair loss, the developmental history of scalp cooling makes one feel ashamed. The progress in the understanding and prevention of chemotherapy-induced hair loss is moderate and insignificant in comparison with progress in understanding other side effects of chemotherapy. The frequency of applied scalp cooling varies in European countries. For example, at present it is used only in fewer than 5% of the hospitals in the Netherlands, while it is much more generally used in the surrounding countries.

In this article the conclusions drawn from published results from more than 2000 cooled patients over 30 years of scalp cooling are first discussed, followed by a presentation of the most important areas of uncertainty and topics that need further study to improve our knowledge, and finally the beneficial results of scalp cooling in the care of patients.

Generally accepted opinions

Scalp cooling effectively prevents chemotherapy-induced hair loss

The efficacy of cooling has been demonstrated in five out of six randomized studies, the findings of which are

supported by many convincing nonrandomized studies with historical controls. Especially when anthracyclines or taxanes are used, good results have been shown. In general at least 50% of patients have a good to excellent response to scalp hypothermia. However, this percentage may be too high because of a publication bias.

Chemotherapy-induced hair loss is distressing

Although chemotherapy-induced hair loss is temporary, it is one of the most feared side effects of cancer therapy. This topic was also discussed at the MASCC Symposium by Marco Mulders, psychologist.

Hair loss is a common side effect of cytotoxic drug therapy

The potential for hair loss differs markedly among the different cytostatics. The ability of individual agents to cause hair loss depends upon the dosage, route and schedule of administration and combination with other cytostatics.

Current preventive measures to reduce chemotherapy-induced hair loss mainly focus on scalp cooling

Since about 1970 many measures have been tried: tourniquet, medicaments and scalp cooling. Of these, scalp cooling is now the most commonly used.

The side effects of scalp cooling are acceptable

The majority of patients tolerate cooling very well and its side effects are not frequent and not serious. Side effects are rarely a reason for stopping the cooling.

Protection of unrecognized tumour cells by cooling

The fear that cooling prevents the cytotoxic effect of chemotherapy on tumour cells in the scalp skin is only justified in some clinical situations. Scalp cooling should not be given if clinical manifestations of scalp skin metastases or haematological malignancies with generalized haematogenic metastases (e.g. lymphoma, leukaemia) are present and chemotherapy is given with a curative intent. Also scalp cooling should not be given in the rather rare conditions of cold sensitivity, cold agglutinin diseases, cryoglobulinaemia and cryofibrinogenaemia.

Cooling machines have some advantages over cold caps

Cooling machines are less time-consuming for the nursing staff than cold caps, which require changing several times, and are more appropriate for studying the relationship between the degree of cooling and hair preservation.

Uncertainty and controversy

The prevalence and severity of hair loss as a side effect of new drugs is often poorly described, and reports concerning the effects of many older drugs are conflicting.

Does scalp cooling improve the quality of life? Scalp cooling effectively prevents chemotherapy-induced hair loss, and chemotherapy-induced hair loss is distressing. Consequently, scalp cooling would be expected to improve quality of life. However, this hypothesis has not yet been proven.

The dose-response curve is unknown. Only Gregory et al. (1982) have demonstrated in 24 patients a relationship between the degree of cooling and the degree of hair-loss prevention. Does the required decrease in temperature depend on the peak blood level of the cytostatic drug? The many problems of skin temperature measurement during scalp cooling make it very difficult to study the relationship between skin temperature and hair loss.

The optimal cooling time required before and after chemotherapy infusion is unknown. Does the required cooling time depend on the half-life time of the cytostatic drug? Is temperature more critical if there are high drug concentrations and is cooling time more critical if the half-life time of the drug is long? No thorough studies have been conducted investigating these areas.

There is the theoretical possibility of protection by scalp cooling of unrecognized tumour cells present in the scalp skin against the cytotoxic effect of chemotherapy leading to an adverse influence on the course of the disease. In the case of solid tumours there are no indications that this fear is justified. However, although such protection of tumour cells is unlikely in solid tumours, and scalp cooling is widely applied in the adjuvant setting, this topic has not received sufficient attention, and a very large long-term clinical study has to be done.

Other areas of uncertainty include: how to evaluate the effect of scalp cooling on hair preservation; evaluating hair loss according to WHO criteria; determining the circumstances under which a patient will wear a wig or a shawl; and how to evaluate patient contentment. Furthermore, the efficacy, patient tolerance, user discomfort and costs of the various systems of scalp cooling have not been compared systematically.

Topics to study

With the goal of improving patients' quality of life by means of scalp cooling, the following topics for study are suggested:

- Biochemical and biophysical processes playing a role in chemotherapy-induced hair loss
- Reliable, noninvasive measurement of the temperature at the levels of the hair follicle and the skin surface during cooling
- The influence of variation in size and shape of the scalp, various kinds of cold caps, various cooling systems, various methods of application of cold caps, the number of hair layers and wetting of the hair on scalp skin temperature and hair loss prevention
- Relationship between the degree of decrease in scalp temperature, decrease in blood flow and hair preservation
- Processes (biophysical, psychological) playing a role in side effects and tolerability of scalp cooling
- Further development of computer models to assess the crucial parameters in the design and user protocol of scalp cooling
- Costs of scalp cooling and wigs

Recommendations for improving the results of scalp cooling

Intensive cooperation between clinical, psychological, biophysical, biochemical and technical groups has to be achieved to gain more insight into the processes in hair follicle cells leading to chemotherapy-induced hair loss and how scalp cooling can be optimized. In this field, the role of cancer nurses in research in building the evidence-base as to how scalp cooling prevents hair loss, as stimulated by European Oncology Nursing Society, is central. Only together will it be possible to initiate studies leading to guidelines and improvements in the results of scalp cooling and quality of life in patients requiring chemotherapy.