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SCALP HYPOTHERMIA IN THE PREVENTION OF CHEMOTHERAPY-INDUCED ALOPECIA

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Abstract

Alopecia is a common side effect of cancer chemotherapy, especially in combination with regimens with doxorubicin (Adriamycin). The effect of scalp hypothermia in connection with chemotherapy was evaluated as hair protection in 61 women with disseminated breast carcinoma, where earlier treatment routines had caused wig-requiring alopecia in nearly all patients. The cooling was performed with a gel-helmet (Hypotherm Gel-Kap). Of the 61 patients, 47 (77%) had no or slight, not wig-demanding hair loss, and 14 (23%) had severe (wig-demanding) hair loss. Seven patients had liver dysfunction; in 5 of these severe hair loss was observed; 2 had slight hair loss. Eighty-three per cent of the patients with normal liver function had no hair loss. Treatment tolerance was found to be good, and side effects were minimal. The method is found to be simple, effective and inexpensive, though still not technically optimal.

Many drugs used for cancer chemotherapy may induce alopecia, among these doxorubicin (Adriamycin) and cyclophosphamide. Alopecia is especially marked and frequent during cyclic treatment with Adriamycin given as single drug or in combination with other cytotoxic agents.

The last decade has seen several attempts to eliminate this psychologically and socially traumatising side effect of an already physically distressing treatment regimen.

Experiments to reduce the blood flow to the scalp by use of a tourniquet only met with little success (12, 13). However, since 1973 investigations have introduced hypothermic scalp treatment and with better results (1, 2, 4–11, 14). The results as well as the disadvantages reported in these investigations vary considerably; however they are not directly comparable as they have employed different regimens and doses of drugs. The studies report hair loss to have been avoided in 39 to 78 per cent of the cases.

The theory offers two explanations of the hair protective effect of scalp cooling during chemotherapy. First, the blood circulation of the scalp is reduced due to vasoconstriction. Secondly, the cellular uptake of drug is reduced. These factors offer particular advantages on administration of doxorubicin as the plasma concentration decreases rapidly in the first 30 min after intravenous injection due to rapid tissue distribution of the drug (3).

Since the late 70s, a combination chemotherapy regimen of cyclophosphamide, Adriamycin and 5-fluorouracil (CAF) has formed part of the treatment of Danish women with recurrent or primary metastazising mammary carcinoma. The treatment induced wig-requiring alopecia within one or two months in nearly all cases.

The aim of the present study was to investigate whether scalp cooling by Hypotherm Gel-Kap (Hospipharm, Düsseldorf, FRG) would prevent alopecia in a group of patients where earlier treatment routines without such use would have caused wig-requiring hair loss in all patients.

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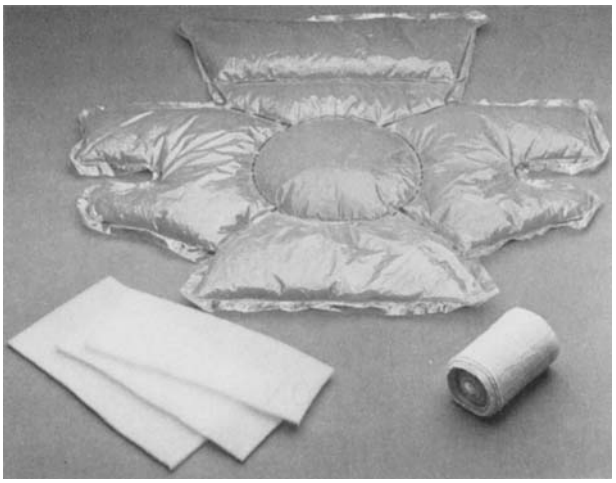

Fig. 1. The equipment used. Hypotherm Gel-Kap, disposable wash cloths and elastic bandage.

Fig. 2. Areas exposed to cold (ears, forehead) are protected with foam pads, the cap placed on the patient's scalp. (Published with permission of the patient.)

Fig. 3. The cap is secured with elastic bandage, patient is made comfortable with support for the head.

Material and Method

From October 1981 to October 1983, scalp hypothermia was applied to 65 women treated with CAF-chemotherapy. An intravenous bolus injection was administered on days 1 and 8 of a 28-day cycle; cyclophosphamide 400 mg/m^2, Adriamycin 25 mg/m^2, 5-fluorouracil 500 mg/m^2. Treatment was continued until one year after complete remission or until progressive disease was discovered. Dosage reduction was undertaken, e.g. by hematologic toxicity. The maximum cumulative dose of Adriamycin was 550 mg/m^2. All patients suffered from recurrent or primary metastazising mammary carcinoma. The mean age was 47.6 years (range 29–73). Consecutive patients were offered hypothermic treatment after being informed of the technique, side effects and anticipated results of the treatment.

Patients with cutaneous scalp metastases or with a poor general condition were excluded. The assessment only embraced patients who were evaluable at least 30 days after the second cycle, i.e. after 4 intravenous treatments. Two patients were therefore excluded because of death and 2 in consequence of progressive disease. The investigation thus included 61 patients.

The Gel-Kap was stored in a deep-freezer at −15 to −18°C, and a cooling of approximately 8 hours is recommended between treatments. The following materials were used: Hypotherm Gel-Kap; protectors for front, ears and if necessary neck (disposable wash cloth adjusted to size) and elastic bandage (Fig. 1). The treatment regimen was as follows: 1) The patients wets her hair. 2) Intravenous drip (before Gel-Kap as cooling may lead to peripheral vasoconstriction). 3) Exposed areas were covered (Fig. 2). 4) The Gel-Kap is applied—fixation by ordinary elastic bandage (Figs 2–3). 5) Patient sitting comfortably in bed/chair with neck support (Fig. 3). 6) Intravenous chemotherapy administered after 10–15 min. 7) Gel-Kap remains in place 30 min after chemotherapy, i.e. for a total of 45 min. Most of the patients were treated during single-day admission to the hospital.

Hair loss was recorded as: no hair loss, minor hair loss (not wig-requiring), or severe hair loss (wig-requiring). Patient and nurse jointly assessed the result. Clinical and hematologic (assessed from alkaline phosphatase and aspartate-aminotransferase) signs of liver metastases or impairment of the liver function before treatment start were recorded.

Table

Hair loss and liver function in 61 patients where scalp hypothermia was applied during cancer chemotherapy (per cent in parentheses)

	Hair loss	
	No + slight	Severe
Normal liver function	45/54 (83)	9/54 (17)*
Impairment of liver function	2/7 (29)	5/7 (71)*
Total	47/61 (77)	14/61 (23)

* $p<0.01$.

Results

During the treatment course, 34 patients (56%) had no and 13 (21%) had slight loss of hair. Thus, 47 patients kept enough hair to avoid wearing a wig (77%±11%, 95% confidence limits assessed by binomial approximation). Fourteen patients (23%±11%) suffered severe, wig-requiring hair loss (Table).

As appears from the Table, 7 patients suffered from impairment of the liver function, of whom 5 (4 with liver metastases, 1 with pericardiac accumulation and hepatomegalia) had severe hair loss. The remaining 2 (with liver metastases) suffered a slight hair loss, but none of the patients with impairment of the liver function kept all their hair. The Table also shows that 83 per cent of the patients with normal liver function had no or slight hair loss.

Hair loss generally occurred after 2, and in a few cases after 3 to 4, intravenous injections. Proper application of the Gel-Kap is important as a few patients had spots of hair loss presumably caused by inefficient local cooling. One patient with liver metastases and a slight hair loss developed a cutaneous scalp metastasis in 2½ months as the only patient in the material. Twenty-seven of the patients with no or slight hair loss were followed for 6 to 20 months during the continuous treatment, and no change in 'hair status' was seen; the remaining patients were followed from 2 to 6 months.

Two patients stopped with Gel-Kap treatment because of the associated additional psychologic stress (before: no hair loss; after: severe hair loss). The remaining patients found the treatment acceptable. A major inconvenience was, of course, the sensation of cold on the scalp, another was the weight of the Gel-Kap. A few patients developed side effects, such as short-term dizziness and headache when the cap was removed. None developed symptoms from ears or sinuses.

Discussion

The present investigation shows that in the actual regimen, scalp hypothermia can prevent hair loss. However, it should be considered whether hypothermia should be offered to patients with impaired liver function as it will constitute yet another distressing factor with little chance of a successful result for these patients. The reason for the lack of effect on this group of patients is presumed to lie with the more prolonged elimination of doxorubicin as this drug is primarily excreted by the liver. Another study has observed a similar outcome by impairment of the liver function (1).

Of the remaining patients who suffered significant hair loss, the cause is assumed to be either insufficient scalp cooling or a side effect of cyclophosphamide. Both 5-fluorouracil and doxorubicin are rapidly excreted from the plasma (half life <30 min), whereas cyclophosphamide is converted to active compounds by metabolism and does not reach maximal plasma concentration until 4 to 6 hours after administration. In the present study the doxorubicin dosage was relatively small (25 mg/m^2 corresponding to approximately 40 mg/a time × 2 every 4 weeks), and hair loss is expected to increase by greater dosages.

The combination of adjuvant chemotherapy and scalp hypothermia is problematic. In adjuvant treatment regimens scalp metastases cannot be accepted, although one may have to accept this as a risk in the treatment of advanced diseases. The routes of spreading of the relevant disease should therefore be realized before a possible initiation of hypothermic treatment, which should be avoided in the treatment of diseases with a high frequency of cutaneous metastases. Such 'misuse' of hypothermia has previously been described in the treatment of mycosis fungoides (15).

The technique has not yet become optimal. The weight of the Gel-Kap exposes the patient to discomfort, and lighter systems are in demand. Several solutions have been proposed, e.g. a helmet connected to a liquid thermocirculator or an air-conditioner where the load carried by the scalp is reduced. These systems also offer the advantage of a constant and adjustable temperature (10, 11). The

price of such units is high, but the operating costs are low. Temperature adjustment may prove a desirable feature once the optimal scalp temperature level has been established. Previous studies have found that the successful prevention of alopecia depends on the temperature, and an intra-cutaneous temperature below 22°C has been recommended (9).

The additional time used on each patient amounts to 5 to 10 min. The treatment has now been a routine for over 2 years without having required extra staff.

Hypothermia merits a wider use for the benefit of patients who undergo chemotherapy and for whom hair loss is yet another distressing aspect of a serious course of disease. The underlying principle is simple, but the method has to be further developed. In addition, further knowledge is required regarding the relation between scalp hypothermia and the pharmacokinetic properties of cancer chemotherapeutic agents.

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