

# Effectiveness of Hydrogel Cap for Chemotherapy-related Alopecia

Study conducted in South Africa

TOPIC: to measure the effectiveness of a scalp cooling device used to prevent hair loss in patients receiving chemotherapy for breast cancer.

INTRODUCTION: Epi-Doxorubicin/Doxorubicin is an Anthracycline anti-neoplastic agent widely used to treat breast cancer. Hair loss is one of the most distressing side effects associated with this drug, especially as many of the women treated already have altered body images. The effectiveness of scalp cooling using the cold cap was studied in 87 women from our private Oncology Centre. These patients all received Anthracycline based chemotherapy for breast cancer. 43 patients chose to use the cold cap and fell into the experimental arm. The other 44 patients did not use the cold cap but were willing to enter the control arm. Similar patients with similar regimes were used on both arms of the study. Previous studies have already been done on Anthracycline induced alopecia and found to be successful, i.e., 85% success (Lemanager, et al, 1997).

However, these were not local studies. Therefore we needed to do our own study for local statistics.

PATIENT SELECTION: 87 women with breast cancer receiving Anthracycline based chemotherapy were selected. The chemotherapy regimes used were:

- CAF - (Cyclophosphamide , Doxorubicin and 5 FU)
- CFF - (Cyclophosphamide, Epi-Adriamycin and 5 FU)
- CA - (Cyclophosphamide & Doxorubicin)
- CE - (Cyclophosphamide & Epi-Adriamycin)
- VE - (Vinorelbine & Epi-Adriamycin)

The doses for Doxorubicin and Epi-Adriamycin ranged between 50 to 60 mg/m<sup>2</sup>. The experimental arm consisted of 43 patients. The mean age of this group was 48 years. The control arm consisted of 44 patients. The mean age of this group was 54 years. 13 patients had prior chemotherapy (Mitoxantrone, Vincristine, 5 FU and Cyclophosphamide). Patients who had scalp metastases, prior radiotherapy to the scalp, the presence of baldness or hair loss were ineligible to the study. The presence of liver metastases or abnormal ALP and GGT were recorded at baseline. The hair loss of each patient was assessed prior to each cycle.

METHOD: Scalp cooling was achieved by using the *Elasto-Gel™* Hypothermia Cap made of a glycerine based hydrogel. The *Elasto-Gel™* cap was placed in the deep freeze for a minimum of 12 hours prior to use. The temperature at which the cap was kept had to be below minus 25° - 30°C. Before placing the cap on the patient's head, the hair was wet and a non-woven bonnet was moistened with cold water and put on the scalp to improve thermal conductivity and induce an initial temperature drop. The exposed skin on the forehead and ears were protected from frostbite using cottonwool or gauze. The cap was then snugly placed over the patient's head and

maintained in place for 1 hour. The Anthracycline was infused 15 minutes after positioning of the cap and the cap remained in place at least 15 minutes after ending the infusions. Hence the total cold cap usage was 1 hour. To improve hair protection, the nurse gave some advise to the patients; no vigorous brushing after treatment, minimum shampooing and conditioning of hair - restricted to once weekly, no permanent hair wave or color to hair during period of chemotherapy, and to have a short hair cut. The patients were followed up until the end of chemotherapy or total hair loss. The hair loss was measured by the nurses administering the chemotherapy. Evaluation of alopecia took place before each chemotherapy cycle and for at least 3 consecutive cycles. Evaluation of hair loss was based on the WHO (World Health Organization) criteria for alopecia:

- Grade 0 - No hair loss
- Grade 1 - minimal hair loss
- Grade 2 - moderate hair loss
- Grade 3 - patchy alopecia
- Grade 4 - complete but reversible alopecia.

Success was defined as alopecia  $\leq$  Grade 2 and according to the patient had no need to wear a wig. If a decision was made by the patient to wear a wig, whatever the grade of alopecia, this was considered a failure.

**RESULTS: TABLE 1 Anthracycline - induced Alopecia**

Grade of Alopecia	No of Pts Arm		Experimental		No of Pts		Results Exp	Results Control
	No	%	No	%	No	%		
Grade 0	5	11.6%	0	0%	N = 39	N = 2		
Grade 1	23	53.5%	0	0%	90.7%	4.5%		
Grade 2	11	25.6%	2	4.5%	= Success	= Success		
Grade 3 + wig	1	2.3%	7	15.9%	N = 4	N = 42		
Grade 4 + wig	3	7.0%	35	79.5%	9.3%	95.4%	= Failure	= Failure
<b>Total</b>	<b>43</b>	<b>100%</b>	<b>44</b>	<b>100%</b>				

**RESULTS:** 87 patients received Doxorubicin/Epi-Doxorubicin based chemotherapy for breast cancer. 43 of these patients were in the experimental arm and used the cold cap. 6 patients received CA, 1 CAF, 8 CE, 20 CEF, 7 POLY and 1 VE. 44 patients fell into the control arm without the cold cap treatment. Similar chemotherapy schedules were used in the control group whereby one had CA, 2 CAF, 11 CE, 22 CEF, 5 POLY and 3 VE. The dose of Doxorubicin/Epi-Doxorubicin was 60 mg/m<sup>2</sup> for all regimes except poly which was 50mg/m<sup>2</sup>. The dose intensity was calculated for both groups and the mean for the experimental group was 29.05 and 28.5 (mgs per week) for the control group.

All the patients entered in this study were evaluable. The mean age for the experimental group was 48 years and 54 years for the control group. 5 patients in the experimental arm received prior chemotherapy consisting of CMF/CNV as compared to 8 in the control group with the same previous chemotherapy. The ethnic denomination for both arms of the study were similar with the majority of patients being white (84% in the experimental group and 79% in the control group). The other denominations were Colored (n = 1), Asian (n = 13) and Black (n = 2). Although the cold cap was offered to black patients, they refused and preferred to wear wigs.

The majority of the patients in both arms of the study fell into early stage breast cancer (T2 N1 M0 = 75%) and thus received adjuvant treatment only. 4 patients had liver metastases in the experimental arm and 2 patients in the control arm. No patients entered this study with scalp metastases. The number of chemotherapy cycles ranged from 3 to 12 in total.

Looking at the results in Table 1 it can be seen that 53.5% of patients in the experimental arm experienced Grade 1 hair loss and a total of 90.7% had less than or equal to Grade 2 hair loss. This was considered a success with the use of a cold cap. They did not need to wear wigs. This was compared to 79.5% of patients in the control arm who did not wear the cold cap and had Grade 4 alopecia and needed to wear wigs.

DISCUSSION: Hair loss in women with breast cancer receiving Anthracycline based chemotherapy is a highly emotional issue and the wearing of a wig uncomfortable and embarrassing. Any efficient method to reduce or prevent hair loss should be made available to the patients. Despite this, relatively few trials evaluating the efficiency of the different techniques have been done.

Some techniques used to induce scalp hypothermia range from bags with crushed ice, frozen cryogel packs, caps containing cryogel and an insulation, caps connected to cooling devices using air or fluid with a thermostat. Studies done by Lemanager, et al (1997), using the Spenco hypothermia cap containing cryogel gave good hair preservation results. Between 80 and 85% with Epi-Rubicin at 50 mg/m<sup>2</sup> and Docetaxel at 100mg/m<sup>2</sup> were considered a success.

The rationale for the use of cold caps in scalp cooling is cutaneous vasoconstriction and the inhibition of temperature dependent metabolic pathways into the cell. Doxorubicin/Epi-Doxorubicin is rapidly excreted following bolus injection therefore a relatively short period of cooling is required. We were able to maintain a degree of hypothermia of the scalp during chemotherapy which lasted an hour in total. Success in the prevention of hair loss was achieved with an overall rate of 90.7% in our study. Assessment of the exact temperature of scalp hypothermia was not done in our study. Limited data is available regarding the measurement of the degree of scalp hypothermia. Often this is uncomfortable and quite difficult to do. Hair preservation can be achieved clinically at temperatures around - 25°C.

According to previous studies (1) the degree of hair loss is both drug and dose dependent. 85% success in preservation of hair was achieved using FEC with doses of Epi-Doxorubicin at 50 mg/m<sup>2</sup> and this dropped to 64% success when doses of Epi-Doxorubicin increased to 100 mg/m<sup>2</sup>. In our study using CEF with Epi-Doxorubicin at a dose of 60 mg/m<sup>2</sup>, a success rate of 90.7%

was achieved. The actual dose intensity of Doxorubicin/Epi-Doxorubicin was calculated for each group of patients which was 29.05 mg/week in the experimental arm and 28.5 mg/week in the control arm. Thus it can be shown that the actual dose was 95% of the intended prescribed dose for both arms of the study. The dose intensity for the experimental arm was slightly higher than the control arm and despite this the results were favorable for the experimental arm.

There was no scalp secondaries recorded in patients for our study over the past two years. Not much is said in the literature about scalp secondaries and scalp cooling. However, there was one study done by Dean, et al, who found that 0.025% of patients in their 7,300 patients studied experienced scalp metastases. Lemanager, et al (1997) states that over a period of 15 years no incidence of scalp secondaries were recorded in the patients who had used the cold cap in their practice. Therefore scalp cooling is a relatively safe method of hair preservation.

Liver metastases and the rate of hair loss have been correlated in previous studies (2 & 3). Doxorubicin/Epi-Doxorubicin is difficult to excrete in liver metastases. Therefore, the duration of the drug in the body is longer and hair loss in these patients is more predominant. However, we did not find this in our study due to the small number of patients included with liver secondaries.

Overall, the cold cap was well tolerated with minor complaints of discomfort due to cold. A few patients complained of unpleasant cold sensations and mild headaches. This was relieved when the cold cap was removed at the end of the chemotherapy. Most of the patients said that having the cold cap was preferable to losing the hair. Thus it can be concluded that although Anthracycline Cytotoxic Agent, Doxorubicin/Epi-Doxorubicin almost inevitably causes alopecia, this can be prevented by a simple procedure using a cold cap. The cold cap is safe and well tolerated by patients with no major side effects.