Efficacy and safety of cooling helmets for the prevention of chemotherapy-induced alopecia : a prospective study of 911 patients (pts)

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Background

Chemotherapy induced alopecia (CIA) is one of the most common and distressing side effects of chemotherapy (CT), especially for women following breast surgery, which can lead to severe psychological stress. Scalp cooling can prevent CIA in selected CT regimens through its physiological effects :

- Perfusion to the hair follicles significantly reduced by vasoconstrictionreduction of drug uptake by cells
- Reduced cellular uptake of chemotherapeutic agents
- Reduced biochemical activity

Data and information on scalp cooling is limited

- as a whole only 64 studies in the last 35 years
- only 8 randomized studies, of small population size
- only 14 studies matched with a historical control
- efficacy and safety of cooling helmets have never been assessed in a single published prospective study of more than 150 pts

Post 1985 studies show efficacy of modern scalp cooling approach in “classical” chemotherapy regimens (mainly intermediate-dose-anthracyclins based) with refrigerated pre-cooled gel caps (or “cooling helmets” CH) and continuous controlled cooling systems. However there is only limited published data available using modern chemotherapy regimens.

There are also concerns that scalp cooling can have an undesirable protective effect on tumour cells which could increase the risk of scalp, skull or even brain metastasis (Cephalic events (CE)) (FDA statement 1990, 1995).
There is very limited data available on patient tolerance to scalp cooling and its impact on quality of life.
Individual ‘prognostic’ factors regarding scalp cooling efficacy need to be assessed.
More data and research on these topics is therefore needed.

Methods

Due to uncertainties on safety and efficacy of scalp cooling, the first project of a randomized study was rejected by the ethics committee, who requested additional research data.

A prospective study of two parallel cohorts was therefore implemented in 8 centers previously routinely using refrigerated pre-cooled gel caps.

Only two types of gel caps could be used in this study : Elasto-Gel, Akromed INC, Penguin, MSC Ltd helmets

All participating centers followed the same common scalp cooling protocols with accuracy on :

- Refrigeration cooling time of gel caps
- Correct fitting of CH to the patients scalp
- Time between each change of gel cap
- Pre-CT cooling time
- Post-CT cooling time
- The protocol was customized for the different CT regimens and for each CH type

Patients were informed on the state-of-the-art information on scalp cooling and those who agreed to participate in the study gave written informed consent and were included according to their willing in 2 separate cohorts:

- Group A : pts agreeing to wear CH ; gel caps could be given up at any time of the study in case of ineffectiveness, intolerance, or at patient’s request.
- Group B : pts not agreeing to wear CH.

The principal objective was efficacy, assessed both by the physician (grade of alopecia) and the patient : self assessed scale of severity of alopecia and consecutive discomfort, registration of the percentage of pts not needing a wig or headband
Secondary objectives : tolerance, safety, quality of life (QoL), identification of predictive factors of CH efficacy.

Inclusion criteria :

- CT regimen with alopeciant drugs of short half-life and short infusion time (namely : adriamycin, epirubicine, docetaxel, cyclophosphamide < 750 mg/m², topotecan, irinotecan)
- written informed consent

Exclusion criteria :

- hematologic malignancies
- previous skull or brain radiotherapy
- previous alopecia (including androgenic alopecia)
- known cephalic soft tissue skull or brain metastasis
- CT regimens with etoposide, paclitaxel, ifosfamide, cyclophosphamide > 750 mg/m².

Assesments made :

- Wig requirement, self-questionnaires (visual assessment scale) on CH tolerance, CIA grade and straight discomfort, Qol questionnaires (EORTC QLQ C30 + body image module) were recorded at study entry, at each CT cycle and 1 month after last cycle
- Date of hair regrow was recorded in case of alopecia
- CE events were prospectively recorded during a minimum 2 years follow-up (FU).

Results

From 2002 to 2006, 911 pts were included in 8 centers and analysed
770 in Group A and141 in Group B. Data are presented with a median follow-up of 36 months

POPULATION

Epidemiologic factors were well balanced between the 2 groups

	All patients 911 patients	Group A with CH 770 patients	Group B without CH 141 patients	p
Median age	54 (29-80)	54 (29-80)	56 (30-78)	NS
Gender	Males 3,8%	3%	8.50%	NS
	Females 96,2%	97%	91.50%	
Tumour site				NS
Breast	93%	95%	86.40%	
Colorectal	3%	2%	6.40%	
Misc.	4%	3%	7.20%	
CT regimens				
Anthracyclin or/and docetaxel ≤ 75mg/m² (AT)	456 (50%)	386 (50%)	70 (49,6%)	NS
Anthracyclin or/and docetaxel > 75mg/m² (AT)	426 (46.8%)	364 (47%)	62 (44%)	NS
Topo-II inhibitors (T2)	29 (3.2%)	20 (3%)	9 (6.4%)	NS

Scalp Cooling discontinuation

reason	%
Ineffective	84
Intolerance	14
Patient’s request	2

SAFETY

	All patients 911 patients	Group A with CH 770 patients	Group B without CH 141 patients	P
Cutaneous sclap metastases	1 (0.1%)	1 (0.13%)	0	NS
Sub-cutaneous scalp metastases	2 (0.21%)	2 (0,26%)	0	NS
Skull bone metastases	2 (0.21%)	2 (0.26%)	0	NS
Brain metastases	31 (3.4%)	28 (4.1%)	3 (2.1%)	NS
All cephalic events		4.30%	2.90%	0.43

EFFICACY

Success Rates (no wig or headband required) :
46.3 % in Group A
31.2 % in Group B
(S, p = 0.0017)

	All patients 911 patients	Group A with CH 770 patients	Group B without CH 141 patients	P
Global success rate (no wig or headband)	44.1	46.3	31.2	0.0017
AT regimens	52,4	56,2	28,8	0.001
AT regimens	31.4	32.7	24.1	NS
T2 regimens	92.9	90	100	NS

Conclusions

Scalp Cooling is an effective method for the prevention of CIA for intermediate dose (≤ 75 mg/m²) anthracyclins and/or docetaxel regimens
High dose (> 75 mg/m²) anthracyclins and/or docetaxel regimens need further investigation with more efficient cooling systems
(ie continuous cooling systems such as Paxman coolers and Dignitana Dignicap systems)

Scalp Cooling is a safe procedure and does not increase the risk of cephalic events. Our data confirmed other published data.
6514 Pts with follow-up on scalp metastases reported including this study
21 cases of scalp metastases = 0,3%
To be compared to the 0,25-1% rate reported in the natural history of breast cancer (German and Dutch registry 2008)

In our opinion scalp cooling should be offered to motivated pts wanting to try to avoid CIA in selected CT regimens and after a thorough search of exclusion criteria.

Data on patient’s alopecia and disconfort assesments, quality of life and predictive factors of CH efficacy are pending and will be presented later.

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