SAFETY AND EFFECTIVENESS OF SENSOR-CONTROLLED SCALP COOLING TO PREVENT ALOPECIA IN PRIMARY BREAST CANCER PATIENTS RECEIVING NEOADJUVANT OR ADJUVANT EPIRUBICIN, TAXANES, OR BOTH

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Abstract # P6-11-14

INTRODUCTION

Chemotherapy (Ctx)-induced alopecia (CIA) is a common side effect of systemic anti-cancer treatment. Although not life-threatening and mostly reversible, CIA produces a deep emotional impact in many patients (pts) involved, particularly in women. A recent German survey showed that CIA is even the most distressing adverse effect in 1509 women exposed to Ctx for breast or female genital tract cancer [Schilling, 2016] In the past, sensor-controlled scalp cooling (SCSC) has demonstrated to be effective in preventing CIA in the majority of pts [Friedrichs, 2014; Van den Hurk, 2014; Cigler, 2015; Shin, 2015]. Nevertheless, SCSC is infrequently used in many countries including Germany due to both safety and feasibility concerns. However, recent reviews showed that SCSC does not increase the risk of developing scalp metastasis nor is it associated with a negative impact on patients´ survival [Lemieux, 2015, Rugo, 2017a]. Two randomized US studies have shown that SCSC is effective to prevent CIA in primary breast cancer (PBC) subjected to taxane-based Ctx whereas little effect has been found in those also treated with doxorubicin [Nangia, 2017; Rugo, 2017]. In a German randomized trial, however, patients exposed to anthracylines did not compare unfavorably in terms of CIA, which may be attributable to the exclusive use of epirubicin instead of doxorubicin [Smetanay, 2017]. This retrospective analysis was initiated to gain detailed information about the effectiveness and safety of SCSC using the Paxman cooling system (Paxman Inc., Huddersfield, UK) in a real-world population of German female outpatients with PBC exposed to neoadjuvant (NACT) or adjuvant (ACT) CIA-inducing Ctx.

METHODS

79 pts who underwent SCSC alongside with Ctx for PBC from 2014 to 2017 were identified from our database of whom 41 had NACT, (51.9%), and 38 had ACT (48.1%). 56 pts (70.9%) were subjected to dose-dense (dd) Ctx (i. e. Ctx-free intervals of ≤ 14 days) whereas the remaining 23 patients had non-dd Ctx (29.1%). At time of diagnosis, 44 (55.7%) pts were premenopausal (55.7%) and 35 (44.3%) were postmenopausal. The following Ctx regimens were used: epirubicin-based (E), 1 (1.3%); taxane-based (T), 23 (29.1%); epirubicin- and taxane-based (ET), 55 (69.6%). Detailed patients´ characteristics are summarized in Table 1. Pts were exposed to SCSC during every Ctx course with a 60 min pre-Ctx cooling period and a 90 min post-Ctx rewarming time (Figure 1, 2). All pts were advised to take 600 mg ibuprofen or 500 mg naproxen-sodium orally prior 1 h prior to start of SCSC. CIA was quantified according to the Dean score (DS) determined 3 wks after the last Ctx cycle (Table 2). SCSC related adverse effects were recorded according to the Common Terminology Criteria of Adverse Effects (CTCAE) scale, version 4.03. Data were analyzed regarding feasibility indicated by the SCSC completion rate, quality of hair preservation (success: DS 0-2, failure: DS 3-4), reasons of SCSC discontinuation, and safety. The primary endpoint was feasibility indicated by the SCSC completion rate. Secondary endpoints were quality of hair preservation with DS 0-2 qualified as success and DS 3-4 qualified as failure, reasons for discontinuation of SCSC, and safety. Moreover, the following parameters were investigated in regard to the success of SCSC: menopausal status (pre- vs postpenopausal), NACT vs ACT, dd Ctx vs non-dd Ctx, E- or ET-based Ctx vs T-based Ctx. Subgroups were compared by Fisher´s exact tests and Chi square tests, respectively. For all statistical analyses, p<0.05 indicated significance.

RESULTS

55 pts (69.6%) completed SCSC, whereas 24 pts (30.4%) discontinued SCSC. Three weeks after completion of Ctx, hair preservation was qualified as complete (DS 0) in 36 pts (45.6%), partial (DS 1-2) in 19 pts (24.1%), and insufficient (DS 3-4) in 24 pts (30.4%) (Table, 2, Figure 3). Among pts who prematurely stopped SCSC, lack of success (CIA) was the main reason in 18 (22.8%). Headache or earache was reported in 2 pts (1.3 %), and local discomfort in 4 pts (5.1%). Side effects were all not severe and resolved quickly after cessation of SCSC. SCSC was equally effective in most analyzed subgroups (Table 3). The relative risk (RR) to experience CIA was 1.11 (CI: 0.82-1.54) for post- vs premenopausal pts, 1.11 (CI: 0.83-1.53) for ACT vs NACT, and 1.03 (CI: 0.70-1.38) for dd Ctx vs non-dd Ctx. Pts receiving E or ET had a significantly higher RR for SCSC failure: 1.39 (CI: 1.04-1.81, p=0.035). However, the success rate in this group was still 62.5%, thus virtually indicating a clinically meaningful benefit of SCSC in pts exposed to epirubicin

Table 1: Characteristics of 79 primary breast cancer patients

Age (years)	
median	50.0
range	21-82
Menopausal status	**n (%)**
pre-/perimenopausal	44 (55.7)
postmenopausal	35 (44.3)
Intention of chemotherapy	**n (%)**
neoadjuvant	41 (51.9)
adjuvant	38 (48.1)
Schedule of chemotherapy	**n (%)**
conventional (non-dose-dense)	23 (66.7)
dose dense (dose-dense)	56 (33.9)
Type of chemotherapy	**n (%)**
epirubicin-based (E)	1 (1.3)
taxane-based (T)	23 (29.1)
epirubicin- and taxane-based (AT)	55 (69.6)

Table 2: General outcome of sensor-controlled scalp cooling

Outcome	Percentage of hair loss	n (%)
Success		
Dean score 0	0%	36 (45.6)
Dean score 1-2	1-50%	19 (24.1)
Failure		
Dean score 3-4	51-100%	18 (22.8)
Discontinuation due to adverse effects	n. a.	6 (7.6)

Table 3: Outcome by subgroup

	Success rate n (%)	Relative risk (95% CI)	p
Menopausal status			
pre-/perimenopausal	32/44 (72.7)		
postmenopausal	23/35 (65.7)	1.11 (0.82-1.54)	0.623
Intent of chemotherapy			
neoadjuvant	30/41 (73.2)		
neoadjuvant	25/38 (65.8)	1.11 (0.83-1.53)	0.625
Schedule of chemotherapy			
conventional	16/23 (69.7)		
dose-dense	38/56 (67.9)	1.03 (0.70-1.38)	0.999
Type of chemotherapy			
taxane-based	20/23 (87.0)		
epirubicin-based (+ taxanes)	35/56 (62.5)	1.39 (1.04-1.81)	0.035

Table 4: Safety of sensor-controlled scalp cooling in primary breast cancer patients

	Proportion (%)
Scalp cooling completed	55/79 (69.6)
Scalp cooling discontinued	24/79 (30.4)
Reasons for discontinuation	
lack of success (hair loss)	18/79 (22.8)
adverse effects	6/79 (7.6)
headache	*1 (1.3)*
earache	*1 (1.3)*
local discomfort ("feeling cold")	*4 (5.1)*

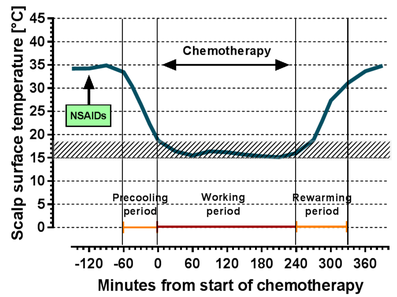

Figure 1: Temperature profile during sensor-controlled scalp cooling for a chemotherapy protocol of 4 hour duration. The shadowed area represents the optimal cooling temperature range.

CONCLUSIONS

- Sensor-controlled scalp cooling using the Paxman system is feasible and safe in patients receiving neoadjuvant or adjuvant chemotherapy for primary breast cancer.
- Nearly 70 percent of patients achieved a satisfying hair preservation and did not need to wear a wig, results which are in good agreement to other studies in primary breast cancer.
- Adverse effects related to scalp cooling were all not severe and rarely the reason of discontinuation.
- Menopausal status, and both intent and type of chemotherapy did not significantly affect the likelihood to benefit from sensor-controlled scalp cooling.
- Patients receiving epirubicin had a significantly higher risk for alopecia. However, the 62.5 percent success rate achieved in this subgroup indicated a clinical meaningful benefit.
- The latter result contrasts the US findings which may be largely attributable to the use of epirubicin instead of doxorubicin.

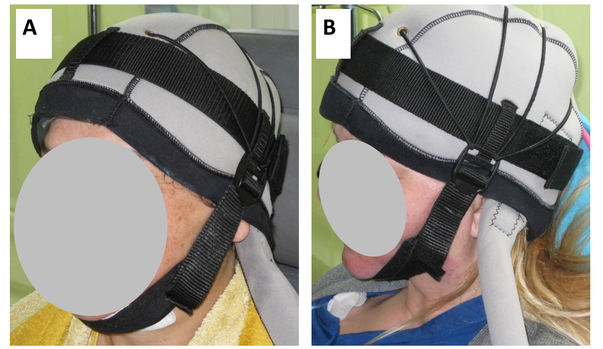

Figure 2: The Paxman cold cap correctly positioned in two patients with primary breast cancer during chemotherapy. **A**, half profile view; **B**, profile view.

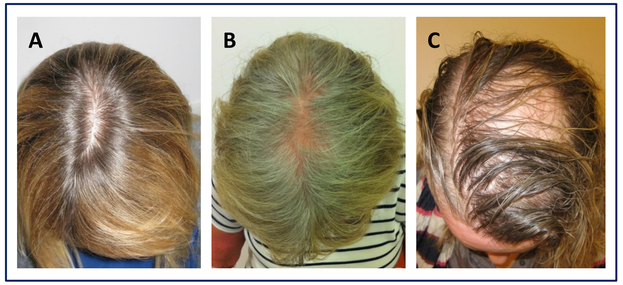

Figure 3: Results of sensor-controlled scalp cooling using the Paxman system in three breast cancer patients three weeks after cessation of chemotherapy. **A**, Dean score 0: 42 year old premenopausal patient after neoadjuvant chemotherapy with 12 x paclitaxel/carboplatin weekly → 4 x dose-dense epirubicin/cyclophosphamide. **B**, Dean score 1: 59 year old postmenopausal after secondary adjuvant chemotherapy with 12 x paclitaxel/carboplatin weekly for local recurrence after exposure to prior epirubicin/cyclophosphamide and tamoxifen for primary breast cancer. **C**, Dean score 2: 48 year old patients after adjuvant chemotherapy with 4 x dose-dense epirubicin/cyclophosphamide → 12 x paclitaxel weekly, the patient was fully satisfied and abstained from wearing a wig during the whole duration of chemotherapy.

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