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Cooling Cap- A Novel Approach Used In The Treatment Of Chemotherapy Induced Alopecia

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ABSTRACT

Alopecia is a temporary consequence of cancer chemotherapy that can be depressing to the patient. This condition is usually temporary, but the patient undergoes lot of emotional stress due to hair loss. Hence minimizing or relieving these kind of side effects is considered important in overall treatment as they boost the emotional status of the patient .Therefore, patients were counselled to purchase a wig or other head covering for the duration of their treatment. But these methods cannot reduce or inhibit hair loss, hence there arises a need to find an alternative method to reduce chemotherapy induced alopecia. Cooling of the scalp has proved to reduce chemotherapy induced hair loss. As of now, only one cold cap has been approved by the U.S. Food and Drug Administration (FDA). FDA approved the marketing of the DigniCap Scalp Cooling System in the United States on December 8, 2015. On July 3, 2017 the U.S. FDA cleared the expanded use of a cooling cap; the DigniCap is made by Dignitana, a company based in Sweden. The present article gives detailed explanation on mechanism of cooling caps, their advantages and drawbacks. The DigniCap® system consists of a snugfitting silicone cooling cap connected to a cooling and control unit Sensors in the cap monitor scalp temperature allowing the system to automatically regulate cooling temperature throughout the treatment, a separate safety sensor in the cap ensures that the temperature never drops below the freezing point of 32°F (0°C)

Key words: *Cooling cap, Alopecia, Chemotherapy, dignicap*

1.INTRODUCTION

Cancer is a name given to a collection of related diseases, which is caused by uncontrolled cell division. To control this rapid cell division we need to start chemotherapy to the patient. Chemotherapy works by killing cancer cells that are in the process of further duplication. As these drugs kill the dividing cells, there is a chance of killing healthy and normal cells which are actively dividing in areas such as hair follicles, nails, lining of mouth, lining of digestive system and bone marrow. Because of this, it leads to many side effects such as alopecia (hair loss), reduction in platelet count and inflammation in GIT.

The patient starts loosing hair after 2 weeks of chemotherapy treatment and continues till the chemotherapy is stopped, this could lead to mental stress. Patients were given topical medicine Minoxidil to treat alopecia, but it had many side effects such as unwanted facial hair growth, fast or irregular heartbeat, and weight gain. Hence there was a need to discover something new for reducing hair loss during chemotherapy. This need lead to a great innovation called cooling cap.

The cap also referred as hypothermia cap is a device used to cool the human scalp which is used in preventing hair loss in chemotherapy induced alopecia. It has been proved as the most effective way in treating the chemotherapy induced hair-loss. This encourages the patients to maintain positive attitude about the treatment. In 2015 Dignicap was the first FDA approved cooling cap for both the genders. More than a decade this diginicap was found to help the cancer patients successfully. It is now available at many of the infusion centers across the state.

The U.S. pivotal study has provided strong evidence that scalp cooling can be a safe and effective treatment to help mitigate alopecia among chemo patients. With the FDA clearance of The DigniCap® system, infusion centers may now provide this much-needed service to patients.

The DigniCap® Scalp Cooling System completed a rigorous multi-center clinical trial to receive FDA clearance and is indicated to reduce the likely hood of chemotherapy-induced alopecia in cancer patients with solid tumors.

The trial results demonstrated that The DigniCap® scalp cooling system is safe and effective for cancer patients undergoing many common chemotherapy regimes.

2. MATERIALS AND METHODS

The DigniCap® system consists of a snug-fitting silicone cooling cap connected to a computer-operated cooling and control unit. Coolant continuously circulates through channels in the cap, cooling the scalp during chemotherapy. A sophisticated system of sensors ensures that optimal temperature is continuously maintained throughout treatment. Lower scalp temperature in turn helps protect hair follicles from the damaging effects of chemo by reducing blood flow and cell metabolism. Worn tight on the head, hypothermia caps are typically made of a synthetic such as neoprene, silicone or polyurethane, and filled with a coolant agent such as ice or gel which is either frozen to a very cold temperature (−25 °C to −30 °C, or −13 °F to −22 °F) before application or continuously cooled by an auxiliary control unit.

2.1 Indication for use:

The DigniCap® Scalp Cooling System is indicated to reduce the likelihood of chemotherapy-induced alopecia in cancer patients with solid tumors.

2.2 Intended Use:

A cooling device intended to reduce or prevent the frequency and severity of alopecia during chemotherapy in which alopecia inducing chemotherapy agents are used.

2.3 Contraindications:

The use of DigniCap is contraindicated in pediatric patients.

The use of DigniCap is contraindicated in adult patients with:

• Cold sensitivity

• Cold agglutinin disease

• Cryoglobulinemia

• Cryofibrinogenemia

• Cold urticaria

• CNS malignancies (either primary or metastatic)

• Squamous cell carcinoma of the lung

• Small cell carcinoma of the lung

• Cancers of the head and neck

• Skin cancers including melanoma, squamous cell carcinoma, and Merkel cell carcinoma

• Hematological malignancies treated with curative intent by chemotherapy

• Solid tumor malignancies with a high likelihood of metastases in transit

• Patients who are scheduled for bone marrow ablation chemotherapy

• Patients who are scheduled to undergo skull irradiation

• Patients who have previously received skull irradiation

Scalp and/or cutaneous metastases have been reported in patients with non-small cell lung cancer, colon cancer, renal cell carcinoma, ovarian cancer, and bladder cancer. Patients with advanced forms of these cancers may be more likely to experience scalp metastases with the scalp cooling system.

Use of Scalp Cooling in the palliative setting in patients with metastatic cancer may also increase the risk for scalp metastases.

Use of scalp cooling with taxanes plus anthracyclines when used in combination has not been shown to be successful in preventing chemotherapeutic drug induced alopecia. DigniCap® Scalp Cooling System should not be used in these patients.

Scalp radiation can cause stenosis of small cutaneous vessels decreasing device effectiveness.

The effectiveness of this device in patients who have received previous chemotherapy has not been evaluated.

The risk of scalp-cooling may outweigh the benefits in patients receiving chemotherapeutic agents with low incidence of inducing alopecia.

Long-term effects of scalp-cooling and risk of scalp metastasis have not been fully studied.

Clinical studies have demonstrated variable success rates in patient reduction of chemotherapy-induced alopecia with scalp cooling since the outcome is dependent on multiple factors including chemotherapy regimen, dose, duration of drug infusion, chemotherapy drug metabolism, and concomitant comorbidities. Data have shown that women who experience hair loss in spite of using scalp cooling might have worse quality of life than women who did not have scalp cooling.

2.4 Warnings:

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2.5 Adverse events:

Most patients tolerate scalp cooling with The DigniCap® Scalp Cooling System very well. In the clinical study conducted in the U.S. for FDA clearance, three of 101 patients discontinued scalp cooling because of intolerance to the cooling.

Approximately half of the patients experienced a mild to moderate headache that was triggered or exacerbated by scalp cooling using The DigniCap® Scalp Cooling System.

Mild scalp pain was experienced by the majority of the patients, but rarely required pain medications to control the pain.

2.6 Long term adverse events:

When using scalp cooling, less chemotherapy is distributed to the hair cells, and cancer cells could theoretically survive locally within the scalp area. In cancer patients there has been a concern for scalp and skin metastases when scalp cooling patients. Based on medical literature, scalp and skin metastases are rare occurrences regardless of cancer stage (scalp metastases as first sign of recurrence occurs in 1 out of 4,000 patients, and in 1 out of 100 patients who already have other sites of metastasis). The observed risk of scalp metastasis does not seem to differ between patients who have and have not used scalp cooling

3. CLINICAL STUDY

A clinical study comparing hair loss in 117 breast cancer patients who used and did not use the DigniCap® Scalp Cooling System was performed. All patients had either Stage I or Stage II breast cancer and underwent at least 4 cycles of specific chemotherapy regimens. Sixteen of these women did not use the scalp cooling system and 101 patients used scalp cooling.
The average age of the women was 53.0 years (range 28 – 77); 77.4% were White, 10.4% were Black and 9.4% Asian. The most common chemotherapy regimen was docetaxel/cyclophosphamide for 4-6 cycles (75%, 76 of 89 for 4 cycles), with additional regimens including docetaxel/carboplatin (12%), weekly paclitaxel (12%), and docetaxel (1%). Docetaxel/carboplatin and docetaxel were given with HER2-targeted therapy.
The purpose of this study was to understand how well scalp cooling reduced hair loss. The women in the study evaluated hair loss by comparing before and after photographs of their hair using the Dean Scale.

Dean Scale:

- Grade 0: no hair loss
- Grade 1: > 0 up to 25% hair loss
- Grade 2: > 25 up to 50% hair loss
- Grade 3: > 50 up to 75% hair loss
- Grade 4: > 75% hair loss

Success was defined as a maximum Dean score of ≤ 2 using standardized photographs graded by the patient up to 4 weeks after the last chemotherapy treatment.
Patient satisfaction with using scalp cooling was evaluated with the Alopecia Self-Report questionnaire. Quality of Life and Body Image was evaluated using the EORTC-QLQ-BR23 Questionnaire and the Body Image Scale respectively.

3.1 Alopecia Self-Report*:*

Maximum Dean Score (Evaluable Population) (Table-1)

Dean Score	Patients using DigniCap®	Control patients
N	101	16
0 (No Hair Loss)	5 (5.0%)	0 (0.0%)
1 (Greater than 0 up to 25% Hair Loss	31 (30.7%)	0 (0.0%)
2 (Greater than 25 up to 50% Hair Loss)	31 (30.7%)	0 (0.0%)

3 (Greater than 50 up to 75% Hair Loss)	19 (18.8%)	1 (6.3%)
4 (Greater than 75% Hair Loss)	15 (14.9%)	15 (93.8%)

Of the 101 women in the study who used the DigniCap® Scalp Cooling System 67 women (66.3%) lost less than half of their hair, when followed for a month after the last chemotherapy cycle. In comparison, 16 women (100%) in the control group lost more than half of their hair.
Success rate was also analyzed by chemotherapy regimen. In patients who used DigniCap® Scalp Cooling System, success was documented in 83.3% ($p=0.022$) of patients receiving docetaxel/carboplatin, 60.2% ($p<0.001$) of those treated with docetaxel/cyclophosphamide, and 83.3% ($p=0.066$) of patients treated with a taxane alone. Success rate did not differ when analyzed by hair thickness, history of previous chemotherapy, median age, median body mass index, use of prior hormone replacement therapy, and menopausal status. At one month after the last chemotherapy treatment, almost half of the women who had used the DigniCap® Scalp Cooling System reported that they never used a wig, cap, scarf or other head cover due to hair loss.

3.2 Patient satisfaction:

Patients in the study filled out an Alopecia Self-Report questionnaire. Results clearly showed that 101 patients who had an average of 3.6 cycles of chemotherapy and used DigniCap® Scalp Cooling System were satisfied with the decision to use scalp cooling and expressed higher satisfaction with their hair quantity and hair quality as compared to controls. The patient reported satisfaction score (0 to 100), showed a mean score of 87.5 satisfaction with the decision to use scalp cooling, a mean score of 70.9 for hair quantity and a mean score of 69.1 for satisfaction with hair quality.
In patients using DigniCap® Scalp Cooling System, the Alopecia Self-Report questionnaire results showed thick hair in a mean 0.7 study cycles and no change in hair texture in 1.8 study cycles.
In contrast, the 16 patients in the control group had an average of 1.5 cycles before discontinuing reporting due to hair loss. Patient reported satisfaction score (0 to 100) of 25.6 for hair quantity, and a mean score of 37.6 satisfaction with hair quality. Alopecia Self-Report results indicated 0.9 cycles with no significant change in hair texture.

3.3 Quality of Life and Body Image:

Compared to patients who used the DigniCap® Scalp Cooling System, a greater number of patients in the control group had dry mouth, different than usual taste in food and drink, eyes were painful, irritated or watery, lost hair, upset at hair loss, felt ill or unwell, had hot flushes, had headaches, felt physically less attractive or less feminine due to the disease or treatment from baseline at the last cycle of chemotherapy and the one month follow-up.
Women who used DigniCap® Scalp Cooling System agreed strongly that hair is important for appearance at the baseline (82.2%), last cycle of chemotherapy (80.2%) and one month follow- up (78.7%), while women in the control group agreed strongly that hair is important for appearance at the baseline (50.0%) and the last cycle of chemotherapy (50.0%) and 66.7% at one month follow-up.

3.4 Adverse events**:**

Six women reported 7 adverse reactions caused by the DigniCap® Scalp Cooling System. These were headache (4 women), itchiness (1 woman), pain of skin (1 woman) and head discomfort (1 woman); none of these reactions were rated severe and one headache was the only reaction rated moderately severe and the rest were mild.
Three of 106 women discontinued use of scalp cooling because of cold discomfort, while 102 out of 106 women had a feeling of chilliness during the cooling down period.
Less than half of the women (43/106) reported that headaches were triggered or exacerbated by scalp cooling. Although headaches occurred, they were not reported at every cycle of scalp cooling.

4. CONCLUSION

Overall, the DigniCap® Scalp Cooling System appeared to be safe and well tolerated with only mild discomfort associated with the scalp cooling and effective in reducing the likelihood of chemotherapy-induced alopecia.

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