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Evaluation of efficacy of QR678® and QR678® Neo hair growth factor formulation in the treatment of persistent chemotherapy-induced alopecia caused due to cytotoxic chemotherapy—A prospective pilot study

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Abstract

Background: Cancers are one of the main reasons of morbidity and mortality globally. Chemotherapy-induced alopecia (CIA) is one of the most alarming, terrifying, and traumatic adverse effects. A range of therapeutic measures has been suggested to alleviate CIA, but at present, there is no accepted pharmacological therapy that can assure prevention or management.

Aim: The aim of the present study was to evaluate the efficacy of QR 678 Neo® therapy in the treatment of persistent chemotherapy-induced alopecia in women and men treated with cytotoxic chemotherapy for breast and lung cancers, respectively.

Methods: A total of 8 male patients with history of lung cancer and 12 female patients with history of breast cancer in the age range of 25-60 years, with WHO classification of grade I and II persistent alopecia who had undergone chemotherapy treatment, were selected for the study. At each visit, 1.5 mL solution of QR 678® was injected into the scalp skin of patients. A total of 8 sessions were performed at an interval of 3 weeks each. All the patients were evaluated with standard global photography, video microscopic assessment, and patient self-assessment questionnaire at baseline, 6 months, and 1 year.

Results: Marked improvement was seen in the global assessment score at 6 months (mean-8) which was maintained even after 1 year. Mean score increase in hair count at 6 months was 12.71 which further increased at 1 year. High satisfaction score was given by patients for slowing of hair loss (mean = 4.2) and also for overall hair growth. For appearance and growth of hair, the mean value was 3.4 and 3.8, respectively.

Conclusion: The formulation of QR 678® and QR 678® Neo showed to be significantly safe and efficient for chemotherapy-induced alopecia in both men and women. Improvement in hair growth was maintained even at 1 year of follow-up. No patient had any severe adverse effects, and injections were also easily bearable by most of them.

KEYWORDS

chemotherapy-induced alopecia, hair loss, QR678, QR678 Neo; hair growth

1 | INTRODUCTION

Cancers are one of the main reasons of morbidity and mortality globally, with 14 million new instances each year. The prevalence of cancer in India is 70-90 per 1 lakh population, and the frequency of cancer is reported to be about 2.5 million, with over 800 000 new cases and 550 000 deaths happening per year.[1]

Cancer patients undergo numerous physiological and psychological health transitions that may influence their perceptions about their personality, body appearance, and communal interactions.[2,3]

Chemotherapy is one of the most implicated treatment therapies for cancer and involves lengthy intervals of therapy including several appointments, prolonged hospitalization, and numerous adverse effects involving nausea, vomiting, diarrhea, exhaustion, lack of appetite, and alopecia.[4,5]

The average rate of chemotherapy-induced hair loss is 65%.[6,7] Chiewchanvit et al reported that 75.6% of patients acquired alopecia related to chemotherapy agents.[8] Chemotherapy-induced alopecia (CIA) is one of the most alarming, terrifying, and traumatic adverse effects among other adverse effects.[9-12]

Knowing that hair is a major indicator of physical appearance, attraction, and unique personality for women, hair loss adversely affects the feeling of femininity, identity, elegance, perception of appearance of the woman, body image, and self-esteem that contributes to self-disappointment and low post-treatment amendment.[13,14] Alopecia is a major source of stress for people with cancer.[15]

Alopecia rated 3rd in 1983 and 2nd in 2002 in a survey to assess which chemotherapy adverse effect patients have witnessed the most.[16,17] In research in which women with breast cancer were questioned to document and evaluate their adverse effects, alopecia rated 1st to 5th of all adverse effects.[18-20] Very often, hair loss has been identified as even more tougher than breast loss.[11,21]

CIA is an external evidence of disease.[22] It is a visible predictor of the existence of life-threatening disease.[23,24] Alopecia is most frequently a psychologically painful condition that can be stigmatized and may contribute to frustration, humiliation, depression, guilt, helplessness, and fear.[25,26]

Alopecia-inducing chemotherapy treatments will last for minimum 9 months, though most frequently for up to 21 weeks, while patients may have to contend with bald head or fine hair for estimated up to 9 months.[27] Even if the frequency and extent of hair loss are linked to the group and the amount of drugs prescribed, more than 80% occurrence of alopecia is recorded with antimicrobial agents, 60%-100% with topoisomerase inhibitors, >60% with alkylating agents, and 10%-50% with antimetabolites.[7]

While most of the CIA is reversible, certain patients experience loss of or insufficient hair growth even years after the completion of chemotherapy, considered persistent or chronic alopecia. A review of women with breast cancer who obtained docetaxel following doxorubicin and cyclophosphamide showed a prevalence of 6.3% for persistent alopecia. While not popular, it is difficult to determine which patients are likely to face persistent CIA involvement.[28]

Even though not life-threatening, alopecia appears to be one of the extremely frightening and frustrating adverse effects of chemotherapy for patients.[16,29] Acknowledging and managing the CIA is also a huge challenge. A range of therapeutic measures have been suggested to alleviate chemotherapy-induced alopecia but at present, there is no accepted pharmacological therapy that can assure CIA prevention or management.[6]

In 2010, Kapoor and Shome developed a bioengineered, recombinant formulation composed of a mixture of growth factors called QR678® hair growth factor formulation.[30] The effectiveness and safety of QR678® intradermal solution has been proven for alopecia in male and female pattern hair loss.[31]

QR678 Neo® preparation is a plant-derived polypeptide solution that biologically mimics the behavior of QR678® and comprises of a particular concentration of Sh-polypeptide-9 (bio-mimicking VEGF), Sh-polypeptide-1 (bio-mimicking bFGF), Sh-oligopeptide-2 (bio-mimicking IGF-1), Sh-polypeptide-3 (bio-mimicking KGF), copper tripeptide, and Sh-oligopeptide-4 (bio-mimicking thymosin β4) suspended in a sterile injectable medium.[31]

A research was first performed in an animal trial to assess its safety and effectiveness which was comparatively free from side effects.[31] Additionally, an open-label, observational, single-arm interventional clinical study was performed using QR678®. Results showed that the combination of several growth factors in QR678® and QR678 Neo® is safe and equally efficient for both male and female pattern hair loss.[30]

The aim of the present study was to evaluate the efficacy of QR678® and QR678 Neo® therapy in the treatment of persistent chemotherapy-induced alopecia in women and men treated with cytotoxic chemotherapy for breast and lung cancer, respectively.

2 | MATERIAL AND METHODS

2.1 | Study design

A prospective clinical study was conducted following acceptance by the review board of the Institutional Ethics Committee. A total of 20 male and female patients with a diagnosis of lung cancer and breast cancer, respectively, between age group of 25-60 years, with a history of having taken chemotherapy for their disease, were chosen for the study. Signed, written, and informed consent has been received from all the candidates.

2.2 | Inclusion criteria

A total of 8 male patients with history of lung cancer and 12 female patients with history of breast cancer in the age range of 25-60 years, who had undergone chemotherapy treatment, were selected for the study (Figure 1).

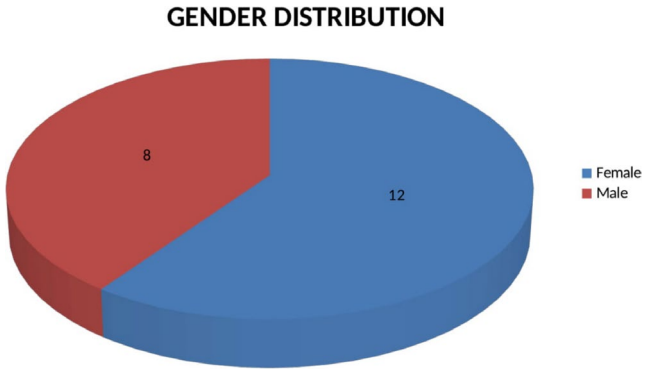

FIGURE 1 Distribution of patients according to gender

Patients with following criteria were included in the study:

- Patients diagnosed with lung cancer and had been treated with vincristine, etoposide (VP-16), and cyclophosphamide-like chemotherapeutic drugs.
- Patients diagnosed with breast cancer and had been treated with tamoxifen, cyclophosphamide, carboplatin, and 5-fluorouracil-like chemotherapy drugs.
- Patients who had completed the chemotherapy treatment 6 months before onset of study and had persistent CIA.
- Patients who had not shaved their head.
- Patients who had not undergone any other chemical treatment for alopecia.
- Patients who willing to complete 8 sessions of the hair treatment which was being studied.

According to WHO classification for CIA, patients with grade I and II alopecia were included in the study.[22]

WHO classification for CIA.

Grade I: Minimal hair loss
Grade II: Moderate patchy hair loss
Grade III: Complete but reversible hair loss

2.3 | Exclusion criteria

- History of chronic hair loss before chemotherapy treatment.
- Concomitant use of cold cap or any other CIA anti–hair loss treatment.
- Patients on other ongoing anti-neoplastic therapy or drugs with potential effect on hair growth.
- Patients with serious drug allergy, autoimmune/hematologic disorders, seborrheic dermatitis, or other scalp skin disease.
- Pregnant and lactating women.
- Patients who had recently started or stopped oral finasteride/spironolactone/oral contraceptives and/or minoxidil were excluded from the study to avoid the bias due to confounding factors.

Also, patients were not allowed to change hairstyle or use any hair color in the due course of treatment.

2.4 | Injection technique used for scalp

All these patients were assessed with standard global photography and videomicroscopy at baseline, 6 months, and 1 year, and also with patient self-assessment questionnaire to evaluate the growth of hair and condition of the scalp at the end of the study. During each appointment, 1.5 ml of QR678® solution was administered into the scalp skin of the patients.

Several (average 60-70), small, and nearly painless intradermal injection shots were delivered using a 31 G needle using a nappage technique in obvious areas of alopecia. Each injection was given 1 cm apart with 0.02ml of quantity per shot. 8 sessions were provided at intervals of 3 weeks.

2.5 | Scalp assessment and evaluation

2.5.1 | Global photographic assessment

The frontal, vertex, and temporoparietal regions of the scalp were photographed utilizing a standardized method at baseline, 6 months, and 1 year. The photographs were analyzed by two blinded dermatologists on a scale of 0 to 10, where 0 indicated no progress and 10 showed maximum dense hair growth. The mean score was analyzed and averaged.

2.5.2 | Videomicroscopic assessment

With the aid of a ProScope optical handheld device, videomicroscopic images were taken at a location of 20 cm from the glabella, on the midline of the scalp. The photographs were taken to measure the hair count per cm^2 using advanced software (Trilogic Corporation, Moscow, Russia, Tricho. Technology version 1.5). The assessment was done using unpaired t test. GraphPad software, an online calculator for statisticians, was used to calculate the results.

2.5.3 | Patient self-assessments

Patients were given a validated hair growth questionnaire, which included four questions in section 1, where three were related to the treatment efficacy and one related to the satisfaction with the appearance of scalp hair. Patients valued each question between 0 and 5, where 0 is very dissatisfied to 5 is very satisfied with the treatment outcome at the end of therapy (Table 4). Section 2 had questions correlated to the adverse effects, and they were asked to tick the appropriate response (multiple ticks were allowed) (Table 5).

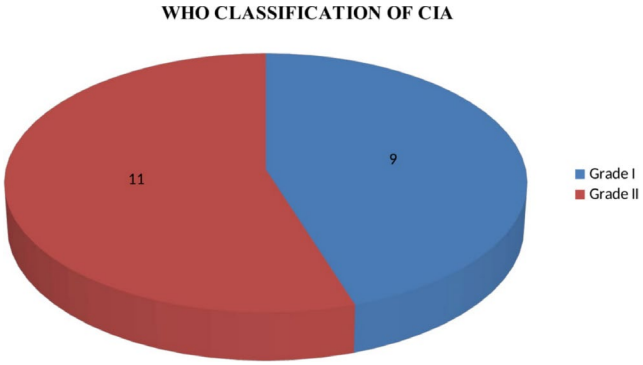

FIGURE 2 Demographic distribution of patients as per WHO classification of CIA

3 | RESULTS

The prospective clinical study was carried out from January 2018 to January 2020 after taking the approval from the Institutional Ethics Committee. The study included 20 total patients (12 female and 8 male) from 25 to 60 years of age, with history of breast or lung cancer, who had gone under chemotherapy treatment and completed it 6 months before start of the study, having CIA and who willingly underwent hair growth therapy with QR678®. As per WHO classification of chemotherapy-induced alopecia, 9 patients were in grade I and 11 were in grade II of alopecia (Figure 2).

3.1 | Global photographic assessment

Subjective assessment of the clinical photographs was done by 2 blinded dermatologist reviewers (Figures 3-5). Reviewers evaluated each photograph on a scale of 0 to + 10, where 0 shows no progress and 10 shows highest growth. The assessment was done at baseline, the end of 6 months, and 1 year. The mean value at the baseline was 4. Marked improvement was seen in the global assessment score at 6 months (mean = 8) which was maintained even after 1 year. It was also remarkable that only 1 person (5%) showed no response from QR678® (Tables 1-2, Figure 6).

3.2 | Videomicroscopic assessment:

Hair count (per cm^2) was evaluated by videomicroscopic assessment for every patient at 20 cm from the glabella. Assessment outcome was recorded at baseline, 6 months, and 1 year. Unpaired t test was done to find out the level of significance ($P < .005$). Result values have been mentioned in the table (Table 3). It was noted that there was a significant improvement in the parameter (Figure 7).

3.3 | Patient self-assessment

In section A, 4 questions were asked to assess the efficacy of the treatment and patient's satisfaction. They were advised to rate it on a scale of 0-5. High satisfaction score was given by patients for slowing down hair loss (mean = 4.2). For appearance of hair and growth of hair, the mean value was 3.4 and 3.8, respectively. In satisfaction score, highest satisfaction score noted for overall hair growth (Table 4, Figure 8).

In section 2, only 5% (N = 1) of patients reported uncomfortable pain during injection and only 10% (N = 2) patients reported itchy scalp after treatment. None of the patients reported increase in hair fall posttherapy (Table 5, Figure 9).

4 | DISCUSSION

The CIA specifically reveals the status of disease which decreases the living standards for people who are still dealing with the physical and psychosocial consequences of cancer.[32]

Chemotherapy-induced hair loss is the outcome of intense toxic insult to quickly dividing hair follicle cells. Hair loss can be diffuse or patchy, may include scalp and body hair or only scalp hair, and may arise abruptly or slowly over period depending on the individual and mode of therapy.[33]

Alopecia is a significant side effect of comprehensive cancer therapy. Well before chemotherapy starts, patients anticipate a strong psychological effect when hair loss actually is happening.[34-36]

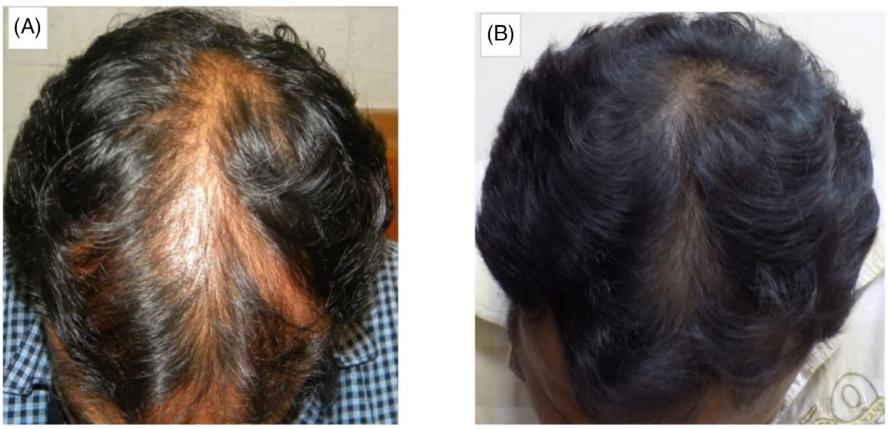

FIGURE 3 Patient 1 clinical photographs. A: Pretreatment. B: After 2 mo of 8th session

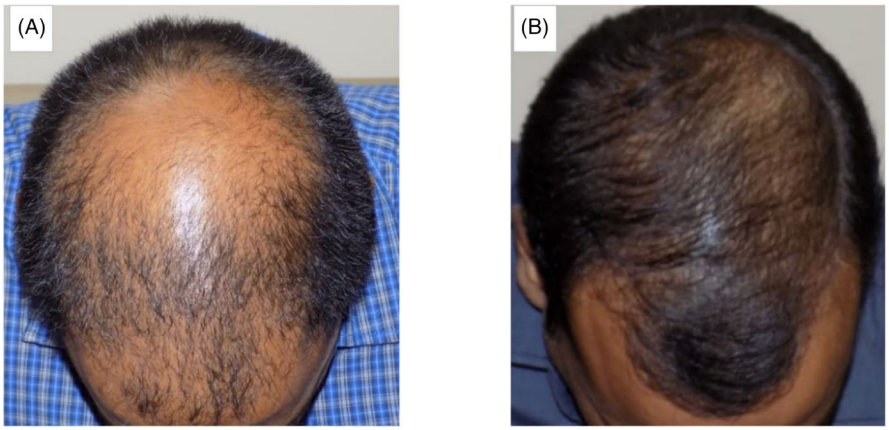

FIGURE 4 Patient 2 clinical photographs: A: Pretreatment. 4B: After 2 mo of 8th session

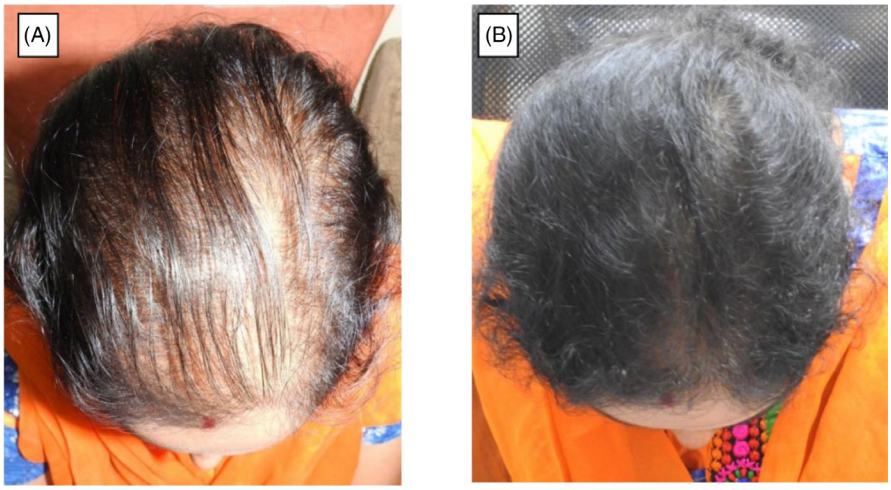

FIGURE 5 Patient 3 clinical photographs: A: Pretreatment. B: After 2 mo of 8th session

In a survey, 16.2% of patients said that they would have avoided therapy if it were not completely necessary and life-saving. A total of 14.5 percent felt sorry for beginning treatment that triggered hair loss.[37] It was reported that 8 percent of people considered rejecting chemotherapy due to possibility of CIA.[38] Nearly 40% of people with alopecia had marriage issues as a consequence of hair loss, and around 63% reported having career-related issues.[38,39]

Choi et al performed a survey of 168 patients with breast cancer in Korea, which revealed that 55.3% of female patients reported higher stress with alopecia.[2] Similar results were identified in a retrospective analysis conducted by Macquart-Moulin et al.[40]

Moreira and Canavarro reported that elevated rates of self-assessment indicate poorer psychological and social quality of life, greater rates of stress, and enhanced apprehension of other cancer patients' unfavorable assessments.[41] Patients may report suicidal thoughts and emotions regarding their image that continue far after diagnosis.[42]

There are two main types of chemotherapy-induced alopecia. The first, telogen effluvium, never includes more than 50 percent of scalp hair and, as a result, causes a degree of hair thinning that is sometimes more distressing to the individual than to outsiders. Anagen effluvium, the second main category of CIA, is the cause of hair loss most frequently identified with anticancer therapy in popular imagination.[43] As a consequence of this irregular weakening of the shaft, the hair either falls under slight force or breaks down before it reaches the scalp.[38]

Chemotherapy-induced hair loss is a significant adverse reaction in cancer patients seeking medical care. Careful guidance and strategies for coping with it should be part of the treatment of patients. The most common approach to chemotherapy-induced alopecia treatment has been to mask damage by using a cap, a head cover, or a hat/turban.[38]

Scalp tourniquets were one of the initial anticipated mechanisms for preventing chemotherapy-induced alopecia consisting of a blood

TABLE 1 Global Photographic Assessment by Reviewers 1 and 2

Reviewer	Baseline	6 mo	1 y
Reviewer 1	3.8	7.8	8
Reviewer 2	4.2	8.2	8.2
Mean	4	8	8.1

TABLE 2 Global Photographic Assessment by Reviewer 1 and 2 Patients showing no improvement and worsening

	No. of patients showing no improvement	No. of patients showing worsening
QR678®	1	0

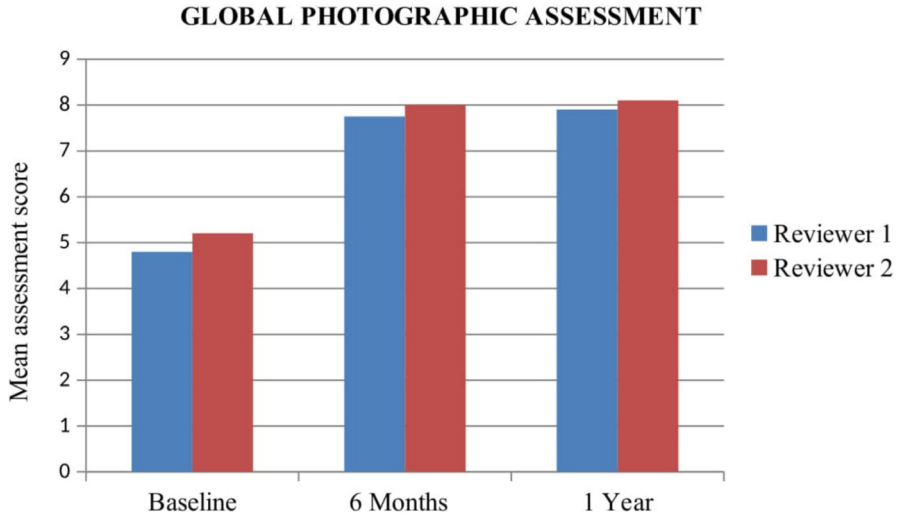

FIGURE 6 Global Photographic Assessment Score by Reviewers 1 and 2

	Mean value at baseline	Mean value at 6 mo	Mean at 1 y	δ	*P*-value
Hair counts at 20 cm (cm^2)	80.65	93.36	98.40	+17.75	<.001

TABLE 3 Mean score of hair counts post-QR678® hair injection treatment

pressure cuff inflated all over the scalp, creating a structural blockade of the scalp perfusion.[44]

Here, some of the commonly used treatment methods have been described with its efficacy and adverse effects.

4.1 | AS101

AS101 (the tellurium compound ammonium trichloro(dioxoethylene-O,O-)tellurate) has revealed efficiency in protecting human patients against chemotherapy-associated hair loss.[45] AS101 was recognized by Sredni and colleagues in the late 1980s and was originally tested in chemotherapy experiments for its ability to inhibit chemotherapy-induced neutropenia and thrombocytopenia.[46] In phase II trials of individuals with non-small-cell lung cancer, AS101 was also found to reduce the extent of alopecia.[45]

Sredni et al performed a comparative study and observed that less AS101 patients had extreme alopecia relative to controls and most had mild alopecia. The resulting variation between AS101 and placebo groups was statistically significant in two randomized trials of non-small-cell lung cancer patients undergoing combination therapy with carboplatin and etoposide. Among 44 cases, 26% of the AS101 group had no alopecia after 3 months contrast to 10% in the control group. Of the 58 cases, 37.2% vs. 20.4% have no alopecia following 3 months of AS101 vs. control groups.[45-47]

4.2 | Vitamin D

Vitamin D analogs have not yet established protection against CIA in humans; however, effectiveness has been demonstrated in animal models.[48,49] Topical calcitriol (1,25-hydroxyvitamin D) was

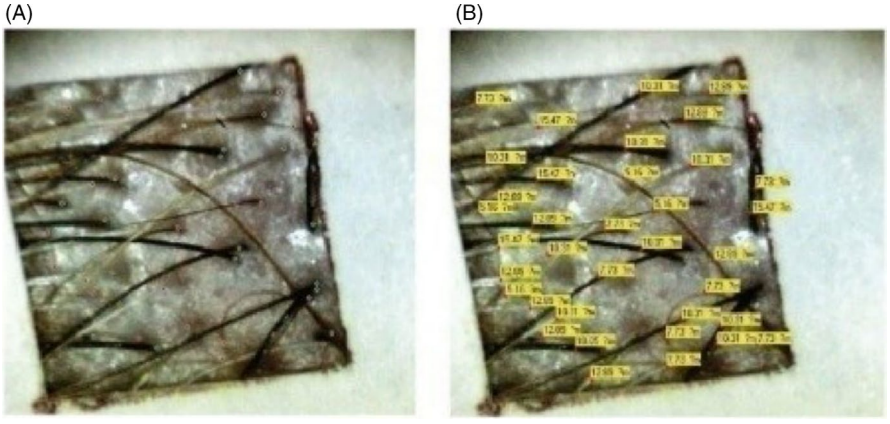

FIGURE 7 Videomicroscopic image showing hair count

FIGURE 8 Patient Self-assessment Questionnaire

studied in a phase I clinical trial utilizing three separate dosage and timeframes; all 12 patients in the treatment arm and 2 patients in the placebo arm experienced mild alopecia by 20-30 days past chemotherapy.[48] Likewise, no contrast was observed between topical calcipotriol and vehicle categories in a survey of 24 breast cancer patients undergoing cyclophosphamide, methotrexate, and 5-fluorouracil regimens.[50]

4.3 | Scalp cooling

Among the therapies so far tested, scalp cooling (hypothermia) was the most widely accepted and researched method.[51]

The mechanism of action is thought to be the outcome of two processes: (a) vasoconstriction, reducing blood circulation to hair follicles and restricting the absorption of cytotoxic agents, and (b) reducing follicle metabolism, rendering follicles less responsive to chemotherapy exposure.[52]

Betticher et al conducted prospective, nonrandomized, observational three-arm study of 238 patients with metastatic cancer, with 128 using Paxman cooling system, 71 using cooling caps, and 39 controls. Docetaxel drug was used weekly or every three weeks with or without other chemotherapy. Intervention result found for Paxman weekly was 93% reported successful WHO score of 0-2 or no wig use and for every three weeks, and 77% reported success. For cooling caps used weekly, 92% reported success, and for every three weeks, 73% reported success. Control result was for chemotherapy every three weeks, 26% reported successful WHO score of 0-2 or no wig use; for chemotherapy weekly, 83% reported success.[53]

Van den Hurk et al carried out a retrospective, nonrandomized, two-arm cohort analysis of 246 patients with various primary tumor variants (93% with breast cancer), 160 with Paxman cooling device and 86 controls. Various methods have been used. Complying with scalp cooling was strong, only 4 patients halted because of intolerance, and others decided to stop due to extreme CIA. No scalp skin metastases were identified from participated patients for 2 years to the next 4 years. Hair loss in scalp-cooled patients was slightly less severe than in non-scalp-cooled patients ($P < .0001$).[34]

The frequency of scalp metastases varied between 0.4% and 1.1% among patients that used scalp cooling relative to 0.3% –3% among those who did not use scalp cooling over two to nine years.[28,34]

It is contraindicated in patients with hematological malignancies, such as the mycosis fungoides and acute myeloblastic leukemia as per two case reports.[6] The side effects of scalp cooling involve pain, headache, and chills but logistic concerns relating to the usage of scalp cooling include provision of devices, conflicting reimbursement protection, and incorporation of use into the standard infusion center setup[54,5]

TABLE 4 Patient Self-assessment Questionnaire: Section 1 Patient satisfaction score

Que. No.	Question	Possible Responses (On a scale of 0-5)
1	Because of the treatment I have received since the start of the study, the appearance of my hair is	Lot better to a lot worse
2	Ever since the start of the study, how would you describe the growth of your hair?	Greatly increased to greatly decreased
3	Ever since the start of the study, how effective do you think the treatment has been in slowing down your hair loss?	Very effective to not effective at all
4	Compared to the beginning of the study, which statement best describes your satisfaction with the appearance of your hair overall?	Very satisfied to very dissatisfied

TABLE 5 Patient Self-assessment Questionnaire: Section 2 Adverse effects

Adverse effect	Tick the appropriate response(if noticed)
Itchy scalp	
Uncomfortable pain during injection	
Unsteadiness during injection	
Increase in hair fall	

4.4 | Minoxidil

In clinical trials, hair growing substance minoxidil (2% topical solution) was able to lessen the period of hair loss, but did not help to eliminate CIA in breast cancer patients undergoing adjuvant chemotherapy.[55]

Notably, 2% of topical minoxidil, although unable to prove significant efficacy as a prophylaxis against the CIA, demonstrated considerable efficacy as a hair regrowth booster in a double-blind randomized study on patients.[48]

Randomized trial was carried out by Madeleine Duvic et al with purpose to investigate the efficacy and safety of minoxidil in chemotherapy-induced hair loss. Twenty-two patients who had been diagnosed with adjuvant chemotherapy following breast cancer were enrolled in a study utilizing a 2% minoxidil topical solution or placebo in a randomized double-blind trial. There was a statistically significant variation (favoring minoxidil) in the period from maximal hair loss to first regrowth. Thus, the period of baldness was shortened (mean, 50.2 days) in the minoxidil group.[55] However, in a survey of 48 women with solid tumors, minoxidil could not prevent alopecia caused by doxorubicin-based chemotherapy.[56,37]

In fact, much of the work on the management of chemotherapy-induced alopecia concentrated on avoidance instead of facilitating recovery, studies on treatment of persistent chemotherapy-induced alopecia are scarce, and much of the available therapy seems to have multiple side effects also.

Since CIA cannot be effectively avoided, the only approach to cope with it has been to prepare patients accordingly with an emphasis on getting the individual as comfortable as possible about her/his image throughout and after cancer therapy.

In our study, we used bioengineered, recombinant formulation of growth factor QR678® in 20 patients. Some of the animal studies proved that growth factors protect against the hair fall and increase production of keratinocytes in the epidermis, such as epidermal growth factors (EGFs), fibroblast growth factor (FGF), and keratinocyte growth factor (KGF). EGF facilitates the proliferation of epidermal cells. It generates both stimulatory and inhibitory activities in the dermis and also stimulates catagen to delay the transition through the telogen process. FGF induces mitogenic activity in epidermal keratinocytes, and KGF induces epithelial cell proliferation in epidermis and dermal adnexa.[32]

In all assessment parameters, QR678® formulation is found to be significantly effective in 95% of the patients. No patient had any severe adverse effect, and injections were also easily bearable by most of them. No death or serious complication has been reported with the use of QR678® in the past. In our study also, no serious side effects were noted. However, few patients experienced side effects like itchy scalp.

We found marked improvement in global photographic assessment after 6 months of treatment and the results were maintained even after 1-year follow-up period. Also, in patient self-assessment scores, we found the highest satisfaction score in overall hair growth with QR678® therapy.

5 | CONCLUSION

Chemotherapy-induced alopecia is a crucial factor that has a major effect on cancer journey; however, CIA treatment and consideration of its psychosocial effects are not frequently highlighted in cancer care. Patients receiving chemotherapy report an altered body appearance, a sense of disparity, disapproval, and social isolation related to hair loss. Given the fact that the detrimental effects of the CIA are well known in the literature, there is still a shortage of

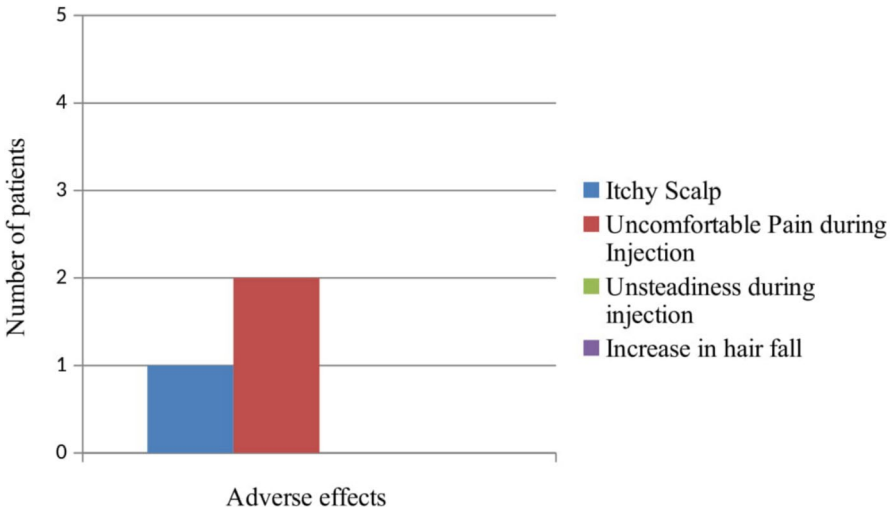

FIGURE 9 Adverse effects as evaluated at the end of the study

appropriate intervention for chemotherapy-triggered hair loss and the occurrence of irreversible hair loss following high-dose chemotherapy is on the raise. So far, no particular method has produced definite treatment for CIA in humans.

6 | LIMITATIONS

This is an open-label, noncontrolled, singe-arm pilot study, where the novel formulations of QR678® and QR678® Neo proved to be safe and efficacious for the CIA in both men and women, with no side effects. Even though the use of QR678® and QR678® Neo has shown good results in small pilot study, more controlled trials with longer follow-ups are needed to be performed to demonstrate effectiveness.

ACKNOWLEDGMENTS

Dr Debraj Shome conceptualized the study. Dr Rinky Kapoor, Dr Komal Doshi, Dr Sapna Vadera, and Dr Vaibhav Kumar wrote the manuscript. Ghanshyam Patel involved in statistics.

CONFLICT OF INTEREST

The authors have been awarded a patent from the United States Patent & Trademark Office (USPTO) and the Indian Patent Office administered by the Office of the Controller General of Patents, Designs and Trade Marks (CGPDTM) for the invented hair formulation, used in this study.

ETHICAL CLEARANCE

The ethical clearance has been taken from the review board of the Institutional Ethics Committee of The Esthetic Clinics.

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