EFFECT OF PELSAN CREAM ON SKIN EPITHELIAL REVITALISATION DURING RADIOTHERAPY AFTER SURGICAL PROCEDURES AND CHEMOTHERAPY

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ABSTRACT

Radiodermatitis, or radiation induced skin reactions occur in the majority of patients receiving ionizing radiation treatment. Typical effects are erythema (redness) and dryness of the skin, burning, itching, fibrosis, and ulceration. The impact and assessment of radiodermatitis includes clinical effects and the subjective experiences of patients.

Objective: a clinical study was conducted to evaluate the effect of a dedicated regenerative cream (Pelsan) in patients with malignant tumors in the ENT region, breast cancer surgery, and chemotherapy, undergoing radiation therapy.

Patients and methods: 60 patients received treatment with Pelsan cream prior to, during, and after radiotherapy. Clinical effects were compared to 60 patients exposed to the same radiation therapy regime using a skin cream or lotion they customarily use at home.

Results: a total of 120 patients were observed between February and May 2015. In the treatment group ….patients advanced to grade…, whereas in the control group

Conclusions: Topical treatment with Pelsan is effective as a preventative measure retarding the onset and the degree of damage (grade of radiodermatitis).

Key Words: Radiation therapy, radiotherapy, radiodermatitis, malignant invasive breast tumors, RISR radiation induced skin reaction, ENT region.

INTRODUCTION

Radiation therapy after surgery is a standard and integral procedure for the treatment of malignant invasive breast tumours.

The radiation dose to be applied on the breast is initially limited by acute reactions,later on by irreversible toxic radiation damage.Today, the radiation dose to be applied on a tumor or its seat is defined and determined by several prognostic factors such as: tumor size, histo-pathological report, histological tumor differentiation, degree of lymphovascular and perineural invasion, performance status, proliferation index (Ki-67 index), and hormonal and nodal status.
Complications during radiation therapy correlate directly with applied (tumor) dose.

Earlier, during orthovoltage radiotherapy (external beam radiation level 200-500 kV), which gives its maximum effect on the skin surface, the appearance of skin redness (radiation skin erythema) was a sign to stop radiotherapy.

On the other hand, during the application of high-energy photons and electrons, energy radiation from 4 MV and 6 MV (megavolts), there is a reduced negative effect on the skin as the maximum dose absorbed is below the skin surface (At 4 MV photons, 1 cm below the skin surface; at 8 MV focal dose, 2 cm below the skin surface).

According to the RTOG classification (Radio Therapeutic Oncology Group), acute cutaneous complications during and after the radiation treatment are classified into 4 stages [1]:

Grade 0 - without complications
Grade 1 - slight erythema or dry desquamation
Grade 2 - moderate erythema or moist desquamation, moderate skin edema
Grade 3 - confluent, moist desquamation more than 1,5 cm, pitting edema
Grade 4 –ulceration or skin necrosis

[1)] Common Toxicity Criteria version 2.0, DCTD, NCI, NIH, DHHS. Cancer therapy graduation programme. RTOG: Late radiation morbidity scoring system. Revised March 23 1998. Published April 30 1999) Version 4; adverse events.

Late complications of the skin after mastectomy and partially operated breast could occur after several months or even years. Those are telangiectasia, hyperpigmentation, scleroderma, fibrosis, or atrophy of the skin.

Principelle Pelsan is a skin regenerator cream used after exposure to ionizing radiation. In addition to its antibacterial effect, the cream has hydrating strength (creating a wet environment), enabling rapid recovery of damaged skin and restoring its normal structural and physiological characteristics. It does not contain metal ions and can be used regularly throughout radiotherapy.

The cream is composed of: Bisabolol (the active ingredient of chamomile) which prevents inflammation, soothes irritated and inflamed skin and has antibacterial effect, Jojoba extract from a bushy plant which oil is great for skin hydration, and Shea butter obtained from the kernel of a fruit tree that grows on the African continent. Shea Butter penetrates the epidermal layer of the skin, it helps to restore the elasticity of mature skin, prevents cell damage, stimulates cellular activity, and revitalizes rough skin damaged by radiation. The product also contains Willow extract with antibacterial effect.

During radiation therapy of malignant tumors, skin changes that appear may be early or late, and acute or chronic. Early or acute changes occur within 6 months after starting treatment, and late after 6 months.

Skin erythema on irradiated skin is the earliest change and occurs in the first week of radiation as a result of dermal capillary congestion. The skin becomes red, edematous, warm, and painfully sensitive.
The level of radiation dermatitis depends on several factors: the type and dosage of ionizing radiation, the size of the radiated field, the applied daily dose, the fractionation regime, total tumor dose, and skin condition before starting radiation therapy.
Dry desquamation occurs as a result of a reduction in the germinative layer of the epidermis, because cells from this layer replace destroyed cells from a peeled layer. This phase is characterized by itching and peeling of large epidermis areas. The intact epidermal cells increase its number and replace the destroyed epidermal cells in a period of three to four weeks.
Moist desquamation occurs if all the cells in the basal layer of the epidermis are destroyed, after a period of 4 weeks, because in that time all squamous cells becomes desquamated and fall away from the skin surface. As there are no new cells, the serum slowly passes from dermal capillaries on the surface.
Necrosis or ulceration of the skin can also occur as a complication of radiation therapy.
Changes in skin pigmentation - skin hyperpigmentation (resulting from increased melanin production in melanocytes) is the result of the ionizing effect and the activation of the enzyme tyrosinase, which convert tyrosine into melanin.
By splitting, melanin cells move to the upper skin layers and it becomes darker - hyperpigmented.
Suppression of the sebaceous glands caused by ionizing radiation results in a dryness of the skin. Dry skin and reduced fat on the skin surface leads to the development of fissures, infections and can cause skin necrosis.
Epilation (hair loss) is a reversible process that occurs at the end of the second week of radiation therapy. It happens as the result of disruption of mitotic activity in the germ cells of hair follicles. Hair regrowth begins at the end of the second month and lasts until the end of the first year.
Skin telangiectasia (local capillar dilatation) are late sequelae of radiation and result from endarteritis obliterans, due to the development of subendothelial fibrosis in epidermis capillaries.
Epidermis atrophic changes and dermis fibrotic changes are the late effects of radiation. The epidermis becomes thin and translucent. Acute inflammatory changes in the dermal tissue, followed by a reparative process, are transformed into mature connective tissue with marked hyalinization. This skin can be easily injured and wounds heal very slowly.

RESEARCH GOAL

The research goal is to determine the effect of Pelsan cream in the revitalization of the epithelium of the skin during radiation therapy in patients with malignant tumors of ENT region (tumors of the base of the mouth, tongue, epipharyngeal and tumors in hypopharynx, larynx and thyroid gland), breast cancer surgery, and chemotherapy.

MATERIAL AND METHODS; inclusion and exclusion

The research was conducted in a prospective study that included a total of 60 patients with postoperative radiotherapy indicated by the local Oncological Commission, from mid-February 2015 until the end of May the same year. During the fractioned radiation treatment, Pelsan cream was applied to 60 patients (40 patients with breast cancer and 20 patients with tumors of ENT region).

The study was performed on patients who had radiotherapy during a period of 15 to 33 working days. The youngest patient was a 37 years old and the oldest 82 years old.
The treatment was carried out daily by applying cream to the skin surface after radiotherapy fraction.The treatment was continued two weeks after finishing radiotherapy.
The product is packaged in bottles with dispenser and is easy to use. Before the start of radiation treatment, an oncologist had verbal contact with each patient, introducing the topical use of the cream, method of application, and included a patient after obtaining written consent. All patients who had previous radiotherapy, patients who have a disease of the connective tissue or ulceration and bleeding of the skin, patients who have not adequately healed surgical incisions or skin diseases (eczema, psoriasis, erithema) and patient who have diabetes were excluded from this Study.

Fractionated radiotherapy was applied by linear accelerators with photon energies 6 and 15 MV flanked from radiation field in breast cancer and a number of 3D tumours of ENT region.

Radiation fields are verified before starting radiation therapy, after half of the planned treatment and at the end of treatment.
The following variables were observed: Radiodermatitis (gradus1-4), redness, inflammatory reaction (itching, dry, flaked skin) and allergic reactions.
Of the total number of patients included in the study (40 patients with breast cancer and 20 patients with tumors of ENT region), 6 patients with breast cancer and 4 patients with tumors of ENT region reported a change in the form of radiation dermatitis was grade 2 (moderate erythema or beginning of moist desquamation) and grade 3 (confluent moist desquamation at more than 1.5 cm of the skin).
Other patients did not have skin lesions (grade 0) or the observed changes were in the form of mild to moderate erythema without desquamation – Grade 1 (Figure 1).

A) before radiotherapy B) after 16 fractions C) after 25 fractions

Figure 1. Without complication after radiotherapy

A) beginning of radiotherapy

B) halfway through radiotherapy

C) at the end of the radiotherapy

Figure 2. Without complication during and after radiotherapy treatment

Radiation dermatitis grade 2 and 3 was recorded in 6 patients who received standard fractionated radiation therapy (Tu Dose 50 Gy in 25 fractions with a boost) made after partial or radical mastectomy (Figure 3), and (Figure 4) patients with radiotherapy in ENT region.

A) after 4 fractions of radiotherapy

B) after 14 fractions of radiotherapy

C) after 25 fractions D) after 14 fractions of radiotherapy

Figure 3. Radiation dermatitis Grade 2 and 3

A) at the beginning of radiotherapy B) at the end of radiotherapy

Figure 4. Radiation dermatitis Grade 2 and 3

Moist desquamation (Figure 5, 6 and 7) occurs if all the cells of the basal layer of the epidermis are destroyed, after a period of 4 weeks, because then all squamous cells become desquamated and fall off from the skin surface. As there are no new cells, serum passes from dermal capillaries on the skin surface.

Figure 5. Cutis excoriation and vesiculae in the axillary region during 22 fractions of radiotherapy sessions for breast cancer.

Figure 6. Moist desquamation at the end of radiotherapy – Tumor in the ENT region (25 fractions + 10 boost fractions)

Figure 7. Moist desquamation during radiotherapy after 21 fractions

Figure 8. Allergic reaction with makulo-papular efflorescence on the skin after 14 radiation therapy sessions and application of Pelsan cream. Termination of Pelsan therapy.

Ulceration in the neck (Figure 9) after radiotherapy (28 fractions) and Pelsan cream therapy. Therapy was terminated.

Figure 9

Skin hyperpigmentation (Figure 10) due to increased melanin production in melanocytes induced by ionizing radiation after the complete radiation therapy (TD50Gy / 25 fractions).

Epilation-hair loss (figure 10b) is a process that appeared at the end of the third week of radiation as a result of disruption of mitotic activity in the germ cells of hair follicles. This process is reversible. Hair regeneration begins at the end of the second month and lasts until the end of the first year.

Figure 10a - hyperpigmentation

Figure 10b - epilation

CONCLUSION

The results of the study with Pelsan cream showed that the application of this preparation during a fractioned radiation regime plays a significant role in the prevention of higher radiation dermatitis grades (G2, G3 and G4). Pelsan cream provides normal skin moisture, hydrates the skin, reduces inflammation and in a high percentage (about 85% of patients) reduce redness of the radiated region. Since Pelsan does not contain pharmaceutical ingredients, toxicity of this product is not expected. There are no known interactions between Pelsan and other medications. Application of Pelsan cream is recommended during radiation therapy and to continue until at least two weeks after radiotherapy.

References

1. Rollmann DC, Novotny PJ, Petersen IA, Garces YI, Bauer HJ, Yan ES, et al. Double-Blind, Placebo-Controlled Pilot Study of Processed Ultra Emu Oil Versus Placebo in the Prevention of Radiation Dermatitis. Int J Radiat Oncol Biol Phys. Elsevier; 2015 Jul 1;92(3):650–8.

2. Yoo H, Kang JW, Lee DW, Oh SH, Lee Y-S, Lee E-J, et al. Pyruvate metabolism: A therapeutic opportunity in radiation-induced skin injury. Biochemical and Biophysical Research Communications. Elsevier Ltd; 2015 May 8;460(3):504–10.

3. Zenda S, Ishi S, Akimoto T, Arahira S, Motegi A, Tahara M, et al. DeCoP, a Dermatitis Control Program using a moderately absorbent surgical pad for head and neck cancer patients receiving radiotherapy: a retrospective analysis. Japanese Journal of Clinical Oncology. 2015 Apr 28;45(5):433–8.

4. Manas A, Santolaya M, Ciapa VM, Belinchón B, Tully F. Topical R1 and R2 Prophylactic Treatment of Acute Radiation Dermatitis in Squamous Cell Carcinoma of the Head and Neck and Breast Cancer Patients Treated With Chemoradiotherapy. Eplasty. 2015;15:e25.

5. Herst PM. Protecting the radiation-damaged skin from friction: a mini review. J Med Radiat Sci. 2014 Apr 28;61(2):119–25.

6. Kerns SL, Ostrer H, Rosenstein BS. Radiogenomics: Using Genetics to Identify Cancer Patients at Risk for Development of Adverse Effects Following Radiotherapy. Cancer Discovery. 2014 Feb 4;4(2):155–65.

7. Chan RJ, Webster J, Chung B, Marquart L, Ahmed M, Garantziotis S. Prevention and treatment of acute radiation-induced skin reactions: a systematic review and meta-analysis of randomized controlled trials. BMC Cancer. BioMed Central Ltd; 2014;14(1):53.

8. Pazyar N, Yaghoobi R, Ghassemi MR, Kazerouni A, Rafeie E, Jamshydian N. Jojoba in dermatology: a succinct review. G Ital Dermatol Venereol. 2013 Dec;148(6):687–91.

9. Kim JH, Kolozsvary AJJ, Jenrow KA, Brown SL. Mechanisms of radiation-induced skin injury and implications for future clinical trials. Int J Radiat Biol. 2013 May;89(5):311–8.

10. Knipping S, Grünewald B, Hirt R. Medical honey in the treatment of wound-healing disorders in the head and neck area. HNO. 2012 Aug 19;60(9):830–6.

11. Miller RC, Schwartz DJ, Sloan JA, Griffin PC, Deming RL, Anders JC, et al. Mometasone furoate effect on acute skin toxicity in breast cancer patients receiving radiotherapy: a phase III double-blind, randomized trial from the North Central Cancer Treatment Group N06C4. Int J Radiat Oncol Biol Phys. 2011 Mar 31;79(5):1460–6.

12. Schnur JB, Love B, Scheckner BL, Green S, Wernicke AG, Montgomery GH. A Systematic Review of Patient-Rated Measures of Radiodermatitis in Breast Cancer Radiotherapy. American Journal of Clinical Oncology. 2010 Sep;:1–8.

13. Tanum ELSBRH. Skin Treatment with Bepanthen Cream Versus No Cream During Radiotherapy: A randomized controlled trial. 2006 Nov 17;:1–6.

14. Moolenaar M, Louwrens Poorter R, Paulus Gerardus Van Der Toorn P, Willem Lenderink A, Poortmans P, Cornelis Gerardus Egberts A. The effect of honey compared to conventional treatment on healing of radiotherapy-induced skin toxicity in breast cancer patients. Acta Oncol. 2006 Jan;45(5):623–4.