PREVENTION AND MANAGEMENT OF ACUTE RADIATION DERMATITIS BY THE TOPICAL AGENTS : A LITERATURE REVIEW

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Abstract

Objectives: To review historical and current published studies on prevention and management of acute radiation dermatitis.

Data sources: Research studies, Review articles, Standard text books

Conclusion: The literature showed no standard recommendation for the use of specific topical agents for prevention or management of acute radiation dermatitis. The researches studied on aloe vera gel, biafine cream, almond ointment, chamomile cream, Thêta-Cream® and topical vitamin E cream demonstrated negative results for prevention and reduction of radiation induced skin alteration. Some evidence suggested the use of topical steroid, topical sucralfate/ sucralfate derivatives, hyaluronic acid cream and MDS065D. However, more studies are needed to support the firm recommendation.

Key words : acute radiation dermatitis, topical agent, prevention

Radiation therapy is one of the standard treatments for cancer in present, but the common side effect that causes suffering symptoms to the patient is “radiation-induced skin reaction”. Because of the important functions such as temperature regulation, barrier functions, immunological, sensory and autonomic functions[1], when the skin was damage, the complications were occurred.

Normally, the skin is a continuously renewing organ, but when it was irradiated, radiation will interfere with normal maturation, reproduction and repopulation of germinative epidermal and hair matrix cells, fibroblasts and the cutaneous vasculature[3-5]. The structural tissue damage from radiation occurs instantaneously, mediated by a burst of free radicals resulting in DNA damage and alteration of proteins, lipids, and carbohydrates. Each additional exposure or fraction contributes to inflammatory cell recruitment as well as to direct tissue injury5. Wound healing is further impaired by inhibition of normal granulation tissue, fibrogenesis, and angiogenesis. Acute radiation therapy induced skin injury is, therefore, a consequence of reduction and impairment of functional stem cells, endothelial cell changes, inflammation, and epidermal cell apoptosis and necrosis[3-5].

The Acute radiation dermatitis is defined as occurring within the first 6 months of irradiation, usually within 90 days[5]. There are various criteria used to define the severity of acute radiation dermatitis, but the common one is from The National Cancer Institute, that is Common Terminology Criteria for Adverse Events (CTCAE). In version 3.0 of CTCAE, dermatitis associated with radiation was graded in to 5 levels[6].

Grade1: Faint erythema or dry desquamation

Grade 2: Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema

Grade 3: Moist desquamation other than skin folds and skin creases; bleeding induced by minor trauma or abrasion

Grade 4: Skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site

Grade 5: Death

Prevention and management of acute radiation dermatitis can be a controversial subject as practices differ considerably between institutions and often also between individual practitioners. Inconsistencies in clinical management can lead to conflicting of the patients7-10.

The literatures showed difference results and recommendations for the use of topical agents, aiming to prevent or reduce acute radiation dermatitis7-39. The agents included and will be summarized for the results in this paper were steroid cream, sucralfate cream, aloe vera gel, biafine cream, almond ointment versus chamomile cream, hyaluronic acid cream, gentian violet, Thêta-Cream ®versus Bepanthol®Lotion, topical vitamin E, anionic phospholipid-based cream and MDS065D.

Topical Steroid

There were 8 studies about the effects of topical steroid on the skin of irradiated patients; the results can be summarized in to 2 categories

1st categories: positiive results

Bjornberg et al.11 studied the effects of betamethasone-17 valerate, vasline®(Unilever, Inc., New York, NY), Eucerin® (Beiersdorf AG, Wilton, CT) and no topical treatment in patients receiving experimental radiation administered in 4 equal areas on the inner thighs. During the 1st five weeks of treatment, the steroid cream performed better than the other creams and no treatment. After six weeks, statistical significant for the superiority of the steroid cream was not demonstrated over Vasline, although it still had a significantly better effect than Eucerin or no treatment

Bostrom et al.[12] compared the effects of topical steroid with emollient cream (0.1% mometasone furoate cream) versus emollient cream alone for prevention of acute skin reaction in women with breast cancer receiving radiotherapy. The results showed that 0.1% mometasone furoate cream significantly decreased acute radiation dermatitis in term of lower maximal erythema score and grade 4 or greater skin reaction (6/24 patients, 25%, vs 15/25, 60% in orderly), but no significant difference in symptoms of pruritus or pain.

Shukla et al.[13] investigated the use of beclomethasone dipropionate spray versus no topical treatment to the irradiated axilla of breast cancer

patients. They founded more evidence of wet desquamation in no topical treatment than the steroid group (36.66% vs. 13.33% respectively) and concluded that the use of opical steroid (beclomethasone dipropionate spray) for skin during radiotherapy significantly reduces the risk of wet desquamation of the skin.

Shapour et al.[14] compared the use of topical betamethasone 0.1% to prevent acute radiation dermatitis (ARD) caused by chest wall irradiation in breast cancer patients, comparing to the use of petrolatum or no topical treatment. The results showed that all patients developed some degree of ARD, the frequency and severity of which increased with time and reached the maximum at the end of the seventh week for all groups. Patients receiving betamethasone had less severe ARD than the other two groups throughout the course of the study, but this difference was significant only at the end of the third week (p =0.027). They concluded that prophylactic and ongoing use of topical betamethasone 0.1% during chest wall RT for breast cancer delayed occurrence of ARD but does not prevent it.

2nd categories: negative results

Gless et al.15 compared two different steroid cream, 1% hydrocortisone cream and 0.05% clobetasone butyrate in patients undergoing RT for breast cancer. The majority of patients using either cream derived benefit from its soothing effects, but patients using clobetasone butyrate developed more severe skin reaction. Although the result of hydrocortisone cream was better than the clobetasone cream, the authors did not recommended either cream as first choice treatment of radiation dermatitis because 96.4% of the hydrocortisone group and 88.5% of clobetasone butyrate group experienced a moderate to maximum skin reaction.

Portera ME[7] found no statistically significant difference in the duration or intensity of skin reactions with the prophylactic use of steroid cream (0.2% hydrocortisone valerate) and a placebo.

Løkkevik[16] presented clinical prospective study of 86 patients comparing Bepanthen cream with no topical treatment.in laryngeal and breast cancer patients receiving radiation therapy. The results showed no clinically relevant differences between groups. They concluded that the study did not indicate any clinically important benefits of using Bepanthen cream for ameliorating radiogenic skin reactions.

Schmuth et al.[17] compared treatment with topical 0.1% methylprednisolone aceponate (MPA) vs. 0.5% dexpanthenol cream in comparison to control group in a cohort of patients undergoing fractionated radiation therapy for breast cancer. The result showed no significant difference in the degree of skin reaction between patients. Neither topical treatment reduced the incidence of radiation dermatitis (19 of 21 patients developed radiation dermatitis, 76% > grade 2, 38% >/ grade 4).

Sucralfate Cream/ Sucralfate derivatives

Sucralfate is a non–absorbable, basic aluminium salt that address to positively charged proteins in the base of ulcers and thus creates a surface barrier protecting the ulcer from further irradiation which would normally delay healing. Sucralfate also

acts directly on prostaglandin synthesis; previous studies have shown that result in cytoprotection. It has an inflammatory effect, promotes angiogenesis, enhances epithelial regeneration and bind epidermal growth factor to tissue .Some studies have shown an antibacterial effect of sucralfate, although the mechanism is not understood [9] .Sucralfate cream was attended as an agent for radiation dermatitis since the 1990. Five trials have been conducted, and all of them showed demonstrated the positive results.

The 1st randomized clinical trial studied the protective effect of sucralfate on radiation dermatitis was done by Maiche A., et al.[18] The authors compared the efficacy of sucralfate cream to a base-cream in 50 breast cancer patients receiving postoperative electron beam therapy to their chest wall. Every patient used both creams, one on ether side of the scar. The result demonstrated that the skin treated with sucralfate cream was significantly better than the skin treated with placebo .Sucralfate delayed development of grade 1 and grade 2 skin reactions. The recovery time of skin lesion was faster on the areas treated with sucralfate cream. At the end of radiotherapy the area treated with sucralfate cream showed the lower grade of skin reaction than the placebo ones. The authors concluded that the acute radiation-induced skin reaction was statistically, significantly prevented by sucralfate cream.

Geoffrey Delaney, et al.[19] assed the value of sucralfate cream in the management of moist desquamation during radiotherapy in patients with cancer of head and neck, breast and other sites. The patients were randomized to received 10% sucralfate in sorbolene cream or sorbolene alone .Patient's pain and time to skin healing were assessed. The trial included 39 patients and terminated after 2 years due to poor patient accrual. Data analysis showed no significant difference between the two arms in either time from randomization to skin healing (14.8 vs. 14.2 days, p=0.86) or improvement in pain score (p=0.32). The authors reported that their trial was unable to show a difference in term of time to healing or pain relief in the treatment of moist desquamation by sucralfate. However due to a poor patient accrual they commented that an important-effect of sucralfate has not been excluded.

Evensen JE, et al.[20] tested for ability of sodium sucralfate octasulfate (Na SOS) in the reduction of radiation-induced skin alteration in head and neck cancer patients. They randomized 20 patients to receive either sodium sucralfate octasulfate (Na SOS) gel or a placebo. Skin reactions were scored using several variables. The authors report no significant difference in erythema,but the placebo group had less moist desquamation. In conclusion, they did not recommend sodium sucralfate octasulfate for the routine management of radiation-induced skin reaction.

Mary Wells, et al.21 randomized 357 patients with head and neck, breast and anorectal cancer to receive aqueous cream, sucralfate cream or no cream to irradiated skin. They aimed to investigate whether sucralfate or aqueous cream reduced acute skin toxicity during radiotherapy. The outcomes measured were acute skin toxicity, measured using a modified radiation therapy oncology group (RTOG) score, reflectance

spectrophotometry, patient diary card and dermatology life quality index (DLQI). The result showed no significant difference in the severity of skin reactions or levels of discomfort suffered by patients between the treatment arms. The authors concluded that there was no evidence to support the prophylactic application of either sucralfate or aqueous cream for the prevention of radiation–induced skin reaction.

De Rauglaudre G, et al.[22] evaluated the tolerance of topical application of the combination sucralfate /copper zinc salt in radiation dermatitis in breast cancer women .Patients were treated by photon or electron. The results showed good tolerance of the patients to topical sucralfate / copper zinc salt. Pruritus, pain and discomfort appeared, but the intensity was low. The soothing effect of the combination of these agents was considered satisfying or very satisfying by investigators and patients during the study, varying from 94 to 100 % of satisfaction. The researchers concluded that topical application of the combination sucralfate / copper zinc salt can be used in radiation dermatitis.

Aloe vera gel

A review of the literature suggested that topical aloe vera is useful for mind sunburn. Various animals' models suggest that aloe vera enhanced wound healing. It is claimed that aloe vera many reduce vasoconstriction, leukocyte and platelet aggregation at an injured sites. It may also improve wound oxygenation; increase rate of collagen formation reduced the amount of dead tissue at the wound site as well as being a potent macrophage activating agent [9].

Maurecon S.Williams[23] conducted two phase III randomized trials. The first one was double blinded study in 294 patients, comparing an aloe vera gel versus a placebo gel. The second trial randomized 108 patients to receive an aloe vera or no treatment. All patients in both trials were diagnosed of breast cancer with a planned course of radiation therapy to the breast and/or chest wall. Both the patients and healthcare provides rated skin reactions. The result demonstrated that maximum radiation-induced dermatitis severity scores and the weekly mean severity score were identical on both treatment arms during both of the trials. The authors concluded that dose and schedules of aloe vera gel in these two trials cannot prevent radiation-induced dermatitis.

Vagler, B.K., et al.24 made a systematic review of clinical effectiveness of aloe vera, due to a wide variety of its useness by general practitioners with a few data known about its allergy. They found only 10 studies that used aloe vera monoperperations. The summarized result concluded that topical application of aloe vera was not an effective prevention for radiation-include skin injuries.

Dana J. Dudek, et al.25 compared the acute skin reaction in patients undergoing radiation therapy for early breast cancer who use aloe vera gel on the irradiated skin to the acute skin reaction in patients who followed a routine normal skin care. The author found that the use of aloe vera gel did not increase the acute skin reactions due to irradiation and no evidence of toxic skin reactions from aloe vera (no signs of improvement nor increased toxicity) patients could safety use aloe

vera gel while undergoing radiotherapy.

Olsen DL, et al.[26] performed a prospective, randomized, blinded clinical trial to determine whether the use of mild soap cleansing and aloe vera gel versus mild soap cleansing alone would decrease the incidence of skin reactions in patients undergoing radiotherapy. The results showed that at low cumulative dose level (< 27 Gray), no difference existed in the effect of adding aloe vera to mild soap. But when the cumulative dose was high (> 27 Gray), there was benefit of delayed the skin change from radiation in the aloe vera/soap arm versus in soap arm only (5 weeks versus 3 weeks respectively). The author concluded that when the cumulative dose increase over time, there seemed to be a protective effect of adding aloe vera to the mild soap regimen.

Sue Heggie, et al.[27] conducted a phase III study involving 225 patients with breast cancer after lumpectomy or partial mastectomy, who required a course of radiation therapy. The aim of the study was to test the hypothesis that topical aloe vera was effective in reducing the radiation skin side effects of itching, erythema, pain and skin breakdown when compared with aqueous cream. The result demonstrated that aqueous cream was significantly better than aloe vera gel in reducing the incidence of dry desquamation and moderate more pain due to treatment. ($p<0.001$ and $p=0.03$ in orderly). The incidence of moderate or more itching was also reduced in the aqueous arm, although. It was not statistically significant difference. There was no significant difference between the treatment arms with respect to the incidence of moist desquamation. The authors concluded that aloe vera gel did not significantly reduce radiation - induced skin side effects.

Richard son J., et al.[28] performed a systematic literature review about aloe vera for preventing radiation – induced skin reaction. They searched the data from major biomedical database, specialist complementary and alternative medicine databases. Further more, unpublished and ongoing researches were also identified. Data from this review showed that there is no evidence from clinical trials to suggest that topical aloe vera is effective in preventing or minimizing radiation – induced skin reaction in cancer patients.

Biafine Cream

"Biafine" is a hypotonic, oil- in – water emulsion. It is reported to have non-steroidal anti-inflammatory properties, and enhance wound healing by recruiting macrophages to the wound bed, modifying the concentration of various immunoregulator and promoting the production of granulation tissue. Four trials have been conducted with Biafine with less favorable results.

J. Fisher, et al.[29] conducted a randomized phase III study in breast cancer patients undergoing breast irradiation. They aimed to compare the preventive effect for radiation-induced skin toxicity between biafine and best supportive care (BSC) BSC was defined as the institution's product of choice with 31% of patients receiving Aquaphor, 34% aloe vera ,19%other therapy and 16%reciving no skin care products. There was no overall difference between Biafine and BSC in prevention time to, or duration of radiation-induced dermatitis.

Ewa Szumacher, et al.[30] assed the effectiveness

of biafine cream as a prophylactic agent for radiation-induced acute skin toxicity and to evaluate health outcomes related to skin symptoms in women who underwent concomitant chemotherapy (CMF) and radiotherapy for breast cancer. There was no controlled group in this trial. They founded that during the 5 week course of radiation, the majority of the patients developed grade2 radiation dermatitis (82%). However no treatment delays or interruptions were observed because of skin toxicity. At the end of the study, 61% presented with little dryness or itchiness in the treated breast, 47% complained of little blistering and breakdown of the skin in the affected breast area, and 44% of patients complained of some trouble fitting brassieres. The data from this trial pointed out that. Biafine cream had no protective effect for radiation induced acute skin reaction.

Fenig E, et al.[31] investigated in breast cancer patients who received post operative radiotherapy. They evaluated the effects of biafine and lipiderm ointments (a lipid based moisturizing agent containing anti-pruritic properties) comparing to no topical treatment for the prevention of radiation dermatitis. The result showed no significant statistical difference in the degree of skin reaction between the two preparations compared to no topical treatment group. They concluded that neither biafine nor lipiderm seemed to have a radioprotective effect. P. pammier, et al.32 conducted a randomized phase III study to assess the effectiveness of calendula (Pommade au Calendula par Digestion; Boiron Ltd., Levallois-Perret, France) for the prevention of acute radiation-induced dermatitis of grade2 or higher during post-operative radiotherapy for breast cancer, compared with trolamine (Biafine; Genmedix Ltd, France) which is an oil in water emulsion that can enhance skin healing by recruiting macrophages and modifying the concentration of various immunomodulator. The result showed more effectiveness of calendula than trolamine. The occurrence of acute dermatitis of grade2 or higher was significantly lower (41%. vs. 63%, $p<0.01$) with the use of calendula than with trolamine. The authors concluded that calendula is highly effective for the prevention of acute dermatitis of grade2 or higher and should be proposed for patients undergoing post operative irradiation for breast cancer.

Almond ointment and Chamomile cream

Chamomile cream had been the standard treatment for skin protection during radiotherapy for the previous 10 years in Sweden. Maiche AG, et al.[8,9] compared almond ointment versus chamomile cream in 48 patients undergoing radiotherapy for breast cancer. The severity of skin reaction, pain, and itching were assessed. Both creams were used in each patients, one cream applied above the surgical scar and the other one applied below the scar. No statistically significant difference in the frequency of skin reaction between the two groups, although > Grade 2 skin reaction appeared later in the chamomile cream treated areas compared to the almond treated areas.

Patient's experience of pain and itching were not quantitatively analyzed, but the researchers reported no difference between the two treatment groups. The radiation dermatitis generally cleared within two weeks of the final radiation dose, but in some patients, it took up to 3 months, leading the

authors to report that neither cream can prevent radiation dermatitis.

Hyaluronic Acid cream

Hyaluronic acid is a polymer that has been shown to stimulate fibroblast and fibrin development, there by accelerating the granulation phase of healing. In animal models, it has been hypothesized that hyaluronic acid destroys the oxygen free radicals associated with impairing wound healing[10].

There is 1 clinical trial studied about the effectiveness of hyaluronic acid cream for reducing radiation induced skin toxicity by ionizing radiation in human by Vincenzo Lig uori, et al.[33]. They conducted a double-blind, randomized clinical study comparing hyaluronic acid 0.2% cream (Ialugen R) and placebo creams, provide by Bio-chimique S.A. (IBSA), Lugano, Switzerland. The study was performed in 134 patients receiving radiation treatment for head and neck cancer, breast or pelvic carcinoma.

Their aim was to analyzed whether the prophylactic use of a cream with hyaluronic acid postpones the first signs of acute radio-epithelitis and /or reduce its severity. Result indicated a statistically significant improvement in delaying the onset of skin reaction by the 3rd week. Acute radioepithelitis scores were significantly higher in placebo group than in hyaluronic group, starting from the control at week 3 and throughout the 6 week of treatment ($p<0.01$ from week 3 to week 7; $p<0.05$ at weeks 8 and 10) .The global judgments of the therapeutic efficacy at the end of treatment, by both the physician and the patient showed a significant difference in favor of hyaluronic acid group ($p<0.01$ and $p<0.05$ respectively). The therapeutic tolerability between the two groups showed no significant difference. ($p =0.18$ according to the physician and $p = 0.42$ from the patient's viewpoint). The author concluded that hyaluronic acid cream had a prophylactic role and suggested the use of this agent as supportive treatment to improve compliance and quality of life in patients undergoing radiotherapy.

Gentian violet

Mak, Suzanne S., et al.[34] created a prospective randomized clinical trial in 42 patients to compare the effect of a gentian violet topical application with that of a moist dressing (hydrocolloid) on the rate and efficacy of radiotherapy-induced moist desquamation, wound healing and the patients' satisfaction level with each method. The result showed that gentian violet significantly decreased wound size and reduced wound pain but the time required for healing was not statistically different between the two groups. However the treatment by gentian violet received significantly lower rating for dressing comfort and dressing aesthetic acceptance. The authors suggested that the causes may be from the skin discoloration and drying effects of the treatment, witch renders patients unable to move or stretch the skin. So gentian violet may not be a realistic method for treatment the skin reaction from radiation treatment.

Thêta-Cream®versus Bepanthol®Lotion

Thêta-Cream R (TheraCosm GmbH, Germany) was developed by French scientists. It was a new

formulation containing three active substances that are believed to influence radiation dermatitis. The tree active substanced were GM glucan, Hydroxy-prolisilan C and Matrixyl. GM glucan is a biological response modifier, promoting phagocytosis of macrophages and production of cytolytic, cytostatic factors reducing oxidative stress. Hydroxyprolisilan C is said to help in the rearrangement of lipids and collagen fibers decreasing the skin sensitivity to free radicals. Matrixyl should stimulate the synthesis of collagen I, III and IV, thus participating in the skin's regenerative process[35].

Bepanthol [R] Lotion is an oil-in water emulsion containing dexpanthenol, the alcohol derivate of panthothenic acid which is a component of coenzyme A. Acetye-coemzyme A, an active from of coenzyme A in the epithelium, is known to play a central role in lipid metabolism and for normal skin integrity. Extra supply of panthothenic acid may be thought to promote epithelial formation and regeneration and it is widely used in radiotherapy[35].

There was only one clinical trial conducted about Thêta-Cream [R] by Barbara Roper, et al. [35]. They evaluated the effectiveness of Thêta-Cream[R] in direct comparison with Bepanthol [R] lotion for preventing radiation dermatitis in breast cancer patients undergoing radiation therapy. The scoring of acute skin toxicity at 50 gray revealed no statistically significant difference between study arms. Mild itchiness and sporadic efflorescence were more frequently seen with Thêta-Cream [R]. A trend toward worsening skin marks was also noted with Thêta-Cream group. The Thêta-Cream group was reported more frequent sporadic efflorescence, worsening the skin marks and adverse events occurred in the users: suspected allergic reaction and the necessity for re-simulation twice. The authors concluded that they could not demonstrate any advantage of Thêta-Cream [R]. Higher costs and problems with skin marks prevent a general recommendation.

Topical vitamin E

The property of being a free radical scavenger causes vitamin E to be an interested topical agent from the past until now. Many clinical studies used vitamin E for reducing the skin changes from external causes, including radiation. Most of trials were about the ultraviolet light. However, data from the radiobiological knowledge shows that ionizing radiation can produce free radicals and damage tissues, including skin [1]. There are a few studies about the effect of vitamin E on this radiation type.

A. Dirier, M., et al.[36] investigated the preventive effect of antioxidant vitamin E on irradiation – included acute skin reaction in The New Zealand rabbits .The result showed no protective effect of vitamin E on the irradiated skin. The skin reactions were stronger in the area to which the 5% vitamin E studies or the solvent was applied than in the areas that received radiation treatment only. The authors hypothesized that the cause may from the vehicle induced free radical. There is only 1 clinical trial, investigated the effect of topical vitamin E on radiation induced skin alteration in the human being.

Nopadol Asavametha, et al.[37] compared the effectiveness of topical vitamin E and placebo on the reduction of ionizing radiation – induced skin reaction, intra-individually in head and neck cancer

patients. The results showed no statistically significant difference of the skin reaction between topical vitamin E and placebo (p=1.00). However, the degrees of skin changes were not severe in both groups. The authors hypothesized that moisturizing agents which were the ingredients of cream base of both preparations might decrease the severity of skin damage, probably by reducing the transepidermal water loss or from other mechanisms. They initially concluded that topical vitamin E cream did not make any difference of skin alteration caused by ionizing radiation when compared to the placebo.

Anionic Phospholipid – based cream

The APP skin cream (Ocular Research of Boston (ORB), Inc, Boston, MA) is an oil-in-water emulsion that was prepared in an FDA-approved facility under cGMP guidelines, but it is not commercially available. The active ingredients of APP cream are triglyceride and phospholipids preserved with benzyl alcohol, methyl paraben, propyl paraben and diaxolipinyl urea [38].

Thomas E Merchant, et al.[38] studied the effectiveness of APP cream in comparison with that of aloe vera gel in the prevention of radiation dermatitis in children with various diagnoses. Most common diseases were Hodgkin disease, CNS tumors, pediatric carcinoma and neuroblastoma. The children were treated with fractionated external beam irradiation .The total dose of radiation was greater than or equal to 23.4 Gray. The study demonstrated the superiority of a phospholipids-based cream over an aloe vera gel in the prevention of radiation dermatitis in children receiving more than 23.4 Gray. Subject skin comfort and dermatologic assessment were performed. The APP cream was favored during treatment for subject comfort variables of dry (p=0.002), softness (p=0.057), good feeling (p=0.002) and smoothness (p=0.012). The APP cream was also more efficacious during treatment for the dermatologic variables of dryness (0.013), erythema (p=0.002) and peeling (0.008) .Grouped common toxicity criteria scores were supportive of APP cream (p=0.004).

MDS065D

MDS065D (Sinclair pharmaceuticals Ltd, Godalming, UK) is a non steroidal medical device registered in the United State and Europe for the symptomatic treatment of radiation dermatitis (RD). MDS065D is water – in-oil cream with barrier-forming, hydrating and anti – inflammatory properties that can minimize the side effects of radiation on the skin. It's formulation containing hyaluronic acid (HA), shea butter, glycyrrhetinic acid (GrA), Vitis vinifera and telmesteine [39].

Maria Cristina LEONARDI, et al.[39] conducted a double-blind, randomized, vehicle - controlled clinical study comparing the efficacy of MDS065D with vehicle (an emollient base cream) in minimizing acute skin reactions and associated symptoms during and after radiation therapy for breast cancer. The results showed a statistically significant difference between vehicle and MDS065D groups regarding the maximum severity of skin toxicity (p<0.001), symptoms of burning within the radiation field (p=0.039) and desquamation (p=0.02), in favor of MDS065D group. No significant differences were observed concerning pain, itching and dryness.

The authors concluded that MDS065D may be

considered a safe and one of the available effective treatments in the prevention and minimization of skin reaction, and associated symptoms induced by radiation.

Discussion

A review of the literature examining radiation-induced skin toxicity clearly demonstrates that no standard treatment recommendations exist for the prevention or management of radiation induced skin toxicity. Thus, management is based on clinical experience, physician preference, and availability of topical agents. Quality and quantity of studies evaluating the used of topical agents did not allow for specific recommendations in prevention and management of acute radiation dermatitis.

Topical steroid and sucralfate creams have been the most promising topical agents in the prevention and treatment of acute radiation dermatitis. Some evidence suggested that the use of topical steroid cream or topical sucralfate/ sucralfate derivatives had a radioprotective effect, but more studies are needed to support the firm recommendation.

Aloe vera gel has not been shown to provide any major benefit, although one small study (by Osten et al.) reported that it prolonged the time to skin damage at high dose of radiation therapy. None of the trials demonstrated positive effects of topical biafine, almon ointment, chamomile cream, Theta-Cream and topical vitamin E cream on acute radiation-induced skin toxicity by ionizing radiation in human. So these topical agents are not recommended in clinical practice, until proven others.

One small trial showed benefit of gentian violet in the reduction of skin toxicity, but it was improper for the application due to skin discoloration and drying effects. There were limited evidence to support the use of hyaluronic acid cream, anionic phospholipid-based cream and MDS065D for the prevention and management of acute radiation induce skin toxicity. More evidence is needed to support firm recommendation.

However, most of the studies mentioned above have been conducted with small sample size which can render the result significant. Much of the trials have been written about women undergoing irradiation to the breast; there fore, result many not be generalized to all treatment fields. New researches need to have a larger sample sizes and need to be conducted with patients undergoing therapy for various cancers, so the results can be proven with greater statistical significant and can be more generalized.

Reports of the clinical trials are conflicting; which may result, in part, from the difference of scales used to measure the severity of radiation dermatitis. So if we want to reference the result of researches for the judgments and choosing the appropriate prevention and management for this common skin problem, a stand staging system for severity of radiation dermatitis is necessary. Then, the result can be interpreted and generalized.

In addition to conducting more trials with previously studied agents, research should be done on new products. However, the researchers also be aware of potential patient allergic reaction and side effects of the new topical agents that will be used in the trials.

In conclusion, acute radiation dermatitis is a

very common side effect of patients receiving radiation therapy. It cause many suffering symptoms to the patients and disturbs their daily life activities. Many topical agents are claimed to be an effective agents for prevention and management of this common problem, but the scientific researches are limited, and the results showed confliction or weak evidence base. Future researches must be conducted to provide betters evidence for the topical agents that are appropriate for the prevention and management of acute radiation dermatitis.

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