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How to manage radiation-induced dermatitis?

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Radiotherapy is one of the treatment methods available for cancer patients. More than half of all cancer patients treated with radiotherapy will experience radiodermatitis during their treatment. There are two commonly used scales to evaluate clinical manifestations: Common Terminology Criteria for Adverse Events (CTCAE) and the Radiation Therapy Oncology Group (RTOG) scale. According to them, the severity of radiation dermatitis ranges from mild erythema to moist desquamation and ulceration. Prevention methods for radiation dermatitis include proper skin hygiene, the use of topical corticosteroids, other non-corticosteroid agents and systemic drugs. Treatment of radiation dermatitis is guided by the severity of skin damage. In grade 1 it can be limited to moisturising the irritated skin field but in more severe reactions (grade 2–4) the use of dressing is essential. There is still a need to investigate new products, techniques or novel approaches to minimize, prevent or treat radiation dermatitis in patients undergoing radiotherapy.

Key words: radiation dermatitis, radiodermatitis, acute skin toxicity, radiotherapy

Introduction

More than half of all patients treated for cancer will receive some form of radiation therapy (RT). Irradiation affects not only the cancer cells but also normal tissues, often resulting in significant side effects during and after the completion of therapy [1–5]. Radiodermatitis is a side effect of radiation therapy. Radiation reactions apply to any tissue that is in the irradiated volume due to the topography. The tissues that are always in the volume to be treated include the skin. Skin complications arise after both irradiation and systemic treatment, i.e. chemotherapy or treatment directed at molecular disorders.

Radiotermatitis occurs only in irradiated volume. [1]. Radiodermatitis can occur as an early side effect during the actual treatment period or some months after the radiotherapy is completed. Skin changes can be experienced by 72–95% of patients undergoing radiotherapy and radiation dermatitis (RD) is the most common adverse reaction in the sites of radiation [2, 6, 7]. The severity of early skin radiation reactions depends on both the irradiation technique, the treatment regimens, i.e. a combination of systemic treatment, the fractional dose as well as the total dose, and also to a large extent, the individual predispositions of the patient. Late changes in the skin and subcutaneous tissue are most often manifested in the form of fibrosis, atrophy of the subcutaneous tissue and telangiectasia.

At present, due to the use of modern radiation techniques, fibrosis and telangiectasia are very rarely seen. All these clinical symptoms of radiation dermatitis are associated with discomfort, burning of the skin and also very often with pain. The described symptoms have a negative impact on the patient's

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quality of life. Radiodermatitis ranges from mild to severe and may be acute or chronic [8–10]. This review will discuss the risk factors, pathophysiology, clinical manifestations, prevention and treatment of radiation dermatitis.

Risk factors

The factors that may influence the response of the patient's skin to RT have been grouped into two categories: host factors that depend on the patient's biological characteristics and treatment-related factors. These factors may place the patient at increased risk of dermatitis and should be considered at the baseline skin assessment. The risk factors of developing radiodermatitis are summarised in table I. Patient-related factors:

- age,
- sun exposure,
- smoking,
- nutritional status, body mass index (BMI) >25,
- inflammatory skin disease – atopic eczema with sensitive skin,
- autoimmune diseases – sclerodermia, lupus erythematosus, rheumatoid arthritis.

Different body areas have different sensitivity to radiation. The most sensitive skin regions of the body are the anterior of the neck, face, extremities, chest and abdomen [11]. Skin folds are also susceptible to develop severe radiodermatitis due to a phenomenon called the "bolus effect". These areas are more likely to receive a higher dose of radiation and more prone to bacterial contamination and secondary infection [12]. Elderly, obese (BMI ≥25) patients and smokers are more prone to radiodermatitis [13–15]. Ex-smokers are also at higher risk of severe skin reactions, probably because of vessel changes [13]. In patients who have undergone breast reconstruction after surgical procedures, the skin is thought to be more susceptible to burns. This is due to the sensory and thermoregulatory changes that develop after surgery [16]. There are a few congenital diseases which can adversely influence the severity of radiodermatitis. Patients with pre-existing conditions, for example systemic lupus erythematosus [17] or ataxia telangiectasia [18], may experience increased frequency of severe forms of radiodermatitis.

Table I. Risk factors for radiodermatitis development

Category	Risk factor
intrinsic	advanced age [7, 87]
	BMI ≥25 [13, 14, 88]
	chronic sun exposure [14]
	comorbidities (e.g. SLE) [17]
	female sex [7, 88]
	location (skin folds) [12]
	poor nutritional status [87]
	previous breast reconstruction/implants [16]
	radiosensitive disorders (ataxia telangiectasia) [18]
	smoking [13, 87, 89].
extrinsic	concurrent chemotherapy [13, 22]
	dose rate [90, 91]
	dosing schedule [90, 91]
	EGFR inhibitors [21]
	radiosensitizers (e.g. paclitaxel, docetaxel) [22]
	radiation quality [20, 92, 93]
	total radiation dose [90]

Treatment-related factors

Treatment-related factors such as dose per fraction, total dose and radiotherapy techniques are very important and can influence the severity of skin reaction. The surface area exposed and the radiotherapy techniques used have an impact on developing radiodermatitis. Treatment delivered with a higher dose per fraction >2 Gy or a higher total dose means the skin area in question is at risk of developing sever radiodermatitis [19]. The use of bolus or lower energy beams has an impact on the skin's reaction. The total doses of radiation required to induce skin injury are summarised in table II.

New techniques such as intensity modulated radiotherapy (IMRT) can reduce the dose for skin and healthy tissue which is associated with a decrease in the severity of radiodermatitis compared with 3D conformal conventional radiation therapy [20]. Radiotherapy combined with chemotherapy or immunotherapy as well as anticancer therapies with EGFR inhibitors can be a factor as regards increased severity of radiodermatitis [21]. Some chemotherapeutic agents (for examples paclitaxel and docetaxel) can be a radiosensitizer. Combining treatment with radiotherapy: concomitant chemoradiotherapy, especially for head and neck cancers or gynaecological cancers, can lead to more sever skin reaction. Patients with advanced head and neck cancer who are referred for induction chemotherapy with

Table II. Dose-dependent acute skin changes with localized radiation dose [10, 11, 32]

Skin reaction	Radiation dose (Gy)	Onset
early transient erythema [32]	2	<24 hours
permanent epilation [11]	7	3 weeks
definite erythema [10]	12–20	2–3 weeks
hyperpigmenation [32]	≥20	2–4 weeks
dry desquamation [10]	20–25	3–4 weeks
moist desquamation [10, 32]	30–40/45–60	≥4 weeks
ulceration [10]	>40	≥6 weeks
dermal atrophy/necrosis [10]	>45	months
complete hair loss [32]	>55	2 months

5-fluorouracil followed by chemoradiotherapy can develop more severe radiodermatitis [22]. Some systemic treatment can sensitize skin cells for irradiation. It can be given before, simultaneous or after irradiation. The mechanism of these drugs is very similar to irradiation. It is a reason of more severe side effects. Radiation dermatitis which occurs in patients receiving cetuximab concomitantly with radiotherapy for locally advanced head and neck cancer have different pathophysiological and clinical characteristics. Bernier et al. proposed a new classification of radiodermatitis that takes into account the side effects of cetuximab on the skin of the entire body and the irradiated area.

Pathophysiology

Modern radiotherapy techniques is delivered mostly from accelerators which generate photons. The newest conformal radiotherapy treatment, especially of the head and neck regions or for children, uses protons beams [23]. Radiation therapy using high energy radiation kills cancer cells via free radicals. Free radicals are damaging deoxyribonucleic acid (DNA) and the cells are killed through the mechanism of of apoptosis. This way is called a direct mechanism. In 1906 Bergonie and Tricondeau [24] stated that any cells which are actively dividing are more radiosensitive than mature, non-dividing cells. This occurs not only in cancer cells, but also in healthy tissues. It is the reason why basal keratinocytes and hair follicle stem cells are the primary target for radiation, but also the activity of melanocytes is affected by radiation energy [25]. Radiation activates various cellular signalling pathways leading to activation and expression of many cytokines, vascular injury and activation in coagulation cascade [26]. Increased levels of IL-1 and TNF-α stimulate the production of metalloproteinases causing degradation of dermal matrix components and a disruption of the epidermal basal cell layer [27–30]. A vascular response occurs with extra-capillary cell injury and capillary dilation [31, 32]. Irradiation via free radicals changes the mitotic activity in the germinal cells of the epidermis [11, 33]. Free radical production is a very important mechanism for cancer treatment. It leads to cancer cell death and side effects not only for skin, but also for oral and gastrointestinal mucosa [11]. Free radicals also activate a cascade of pro inflammatory cytokines and cytokine TGF-β in the irradiated cells. It leads to death of the epidermal basal cell in indirect way.

Clinical manifestations

The first early skin changes occur within 1–4 weeks from the beginning of radiotherapy and persist during the treatment period [32]. The first clinical manifestations of radiodermatitis occur in the form of erythema (I grade according to the EORTC/RTOG scale), then dry exfoliation (II grade according to the EORTC/RTOG scale) appears; the next phase is wet exfoliation (III grade according to the EORTC/RTOG scale). Sometimes there are severe skin lesions in the form of ulcers (IV grade according to the EORTC/RTOG scale). The phase of wet exfoliation and ulceration (severity of reaction III and IV) is often accompanied by bacterial and fungal infection (tab. III) [35]. All these clinical symptoms of radiation dermatitis are associated with discomfort, burning of the skin and very often also with pain. The described symptoms have a negative impact on the patient's quality of life. Late changes in the skin and subcutaneous tissue are most often manifested in the form of fibrosis, atrophy of the subcutaneous tissue and telangiectasia. At present, due to the use of modern radiation techniques, fibrosis and telangiectasia are very rarely see. According to CTCAE version 4.0 [34], the severity of radiodermatitis can be graded on a scale of 0–5, and in RTOG 0–4.(tab. III, tab. IV). In both scales, grade 0 means no changes. In grade 1 changes occurs as an erythema (fig. 1). Erythema starts as a result of capillary dilatation and oedema in the dermis. Both these mechanism due to increased vascularity and obstruction [31, 36]. Erythema is dose dependent and can be asymptomatic. The erythema manifestation depends on a balance between pro-inflammatory and anti-inflammatory processes. [27]. Other skin changes that may be seen in grade 1 include: epilation and dyspigmentation [8]. Grade

Table III. Classification of radiodermatitis

	0	1	2	3	4	5
CTCAE [34]	none	faint erythema or dry desquamation	moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	moist desquamation other than skin folds and creases; bleeding induced by minor trauma or abrasion	skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site	death
RTOG [35]	none	erythema; dry desquamation; epilation	bright erythema; moist desquamation; edema	confluent moist desquamation; pitting edema	ulceration, hemorrhage, necrosis	

Table IV. Radiodermatitis score NCJ clasification

Radiation dermatitis NCI Common Terminology Criteria for Adverse Events (version 4.03)				
grade 1 (mild)	grade 2 (moderate)	grade 3 (severe)	grade 4 (life–threatening)	grade 5
faint erythema or dry desquamation	moderate to risk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	death

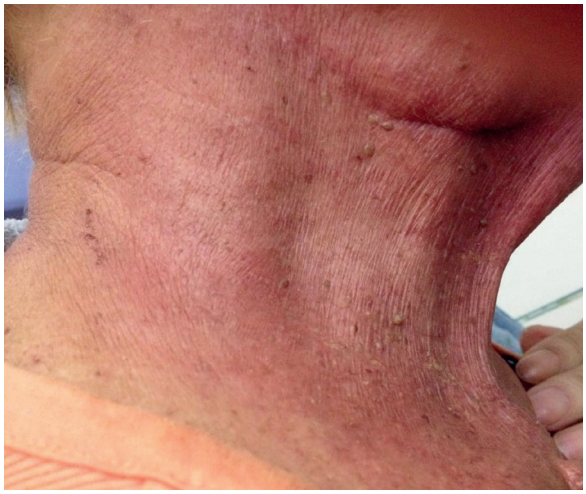

Figure 1. Faint erythema and dry desquamation (grade 1 RD)

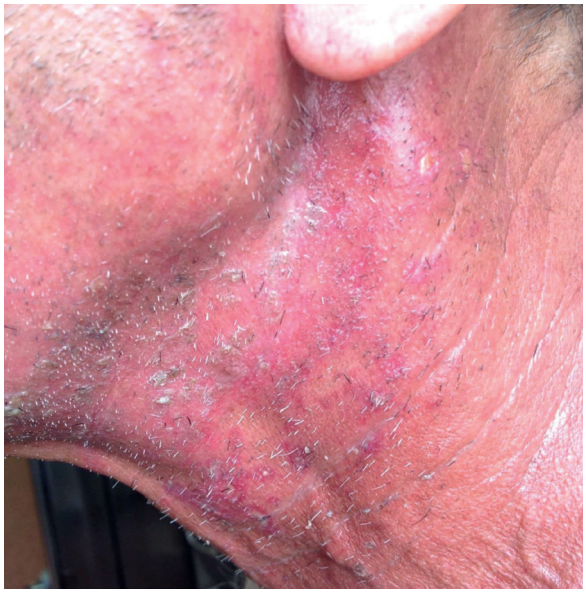

Figure 2. Grade 2 RD with moderate erythema and desquamation

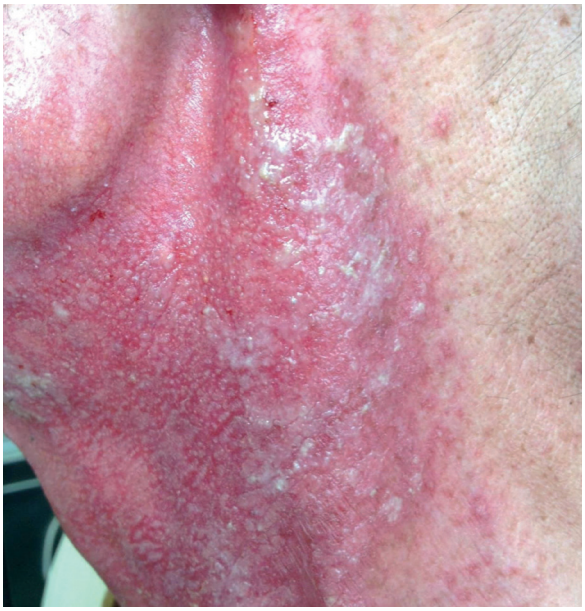

Figure 3. Grade 3 RD with moist desquamation and persistent erythema

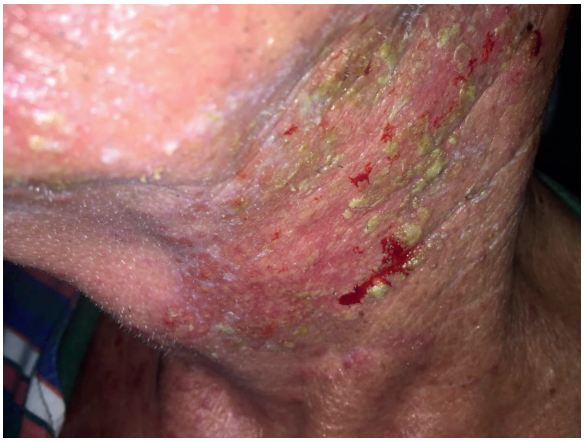

Figure 4. Moderate erythema with moist desquamation, spontaneous bleeding and bacterial infection (grade 4 RD)

2 appears very often in the forth or fifth week of treatment [33] as a dry desquamation. Dry desquamation can occur as a pruritus, an increase in melanin pigmentation or scaling – grade 2 (fig. 2) [33]. When the total dose of irradiation becomes higher than 50 Gy, the moist desquamation phase occurs. It happens mostly in the fifth week of treatment. [25]. Grade 3 changes consist of confluent moist desquamation (fig. 3), pitting and oedema may also be present. Grade 4 dermatitis is characterized by ulcers, haemorrhage, and skin necrosis (fig. 4). In most cases, the radiodermatitis is mild to moderate but about 20–25% of patients experience severe reactions [37, 38]. In the absence of infection, radiodermatitis is self-limiting and will resolve in 2–3 weeks with complete healing within 1 to 3 months [39, 40]. The reepithelization of

the denuded skin usually begins within 10 days [33]. Seldom acute radiation skin changes become consequential-late changes. These can lead to chronic wounds and skin necrosis [8]. Patients who underwent radiation therapy have skin hypersensitivity to UVA and UVB radiation. It lingers in varying degrees of severity over the rest of the patient's life.

The management of radiodermatitis

A lot of research has been carried out due to the serious problem of skin changes occurring after irradiation, as well as after systemic treatment. Thanks to this we can now assess the effectiveness of various methods of prevention and treatment of skin reactions [41–44]. Despite great commitment and the emergence of new publications every year, the unambiguous best practices for the so-called "golden standard" have still not been agreed upon. There are some products in the world with proven anti-inflammatory effectiveness in the prevention and treatment phase. In practice, each cancer centre has its own methods of preventing and treating skin radiodermatitis.

General skin care recommendation

1. Everyday cleansing is recommended. The use of a delicate washing gel, with a unique composition and a pH close to 5, delays the appearance of symptoms associated with radiation reactions. It helps to remove epidermal cell fragments formed in the course of radiation therapy, which subsequently has a positive effect on maintaining the natural protective barrier of the skin. It is recommended at the onset of radiotherapy and after its completion. The way irradiated skin is cleaned is very important. It should be done by hand with warm water. The skin should afterwards be dried with a paper towel. Hydration of the skin. Apply an emulsion or emollient cream with a delicate consistency and unique composition including ceramides that can moisturise the skin with hyaluronic acid; due to its strong hygroscopic properties this produces a moisturising effect due to water retention in the stratum corneum. The cream should be applied two to three times per day after radiotherapy and one hour before irradiation. Natural, soft clothes are recommended, synthetic clothes should be avoided.
2. For shaving, an electric razor should be used.
3. All products which contain alcohol should be avoided e.g. *eau de toilette*, perfume.

Protection and treatment

Management of skin care for patients during radiotherapy remains controversial. Recommendations of the so-called "golden standard" for preventing and treating radiodermatitis have not been fully agreed upon. We can find recommendations which are implemented for different countries or even institutions. A study published in the United Kingdom showed that different advice is given to patients by radiotherapy departments. There is no consensus on how to manage radiodermatitis [41]. It remains a problem for all patients who receive radiotherapy throughout the world. Prevention is management of skin which is irradiated to postpone or prolonged a time when radiodermatitis in III EORTC/RTOG grade occurs. Many radiotherapy departments advise cleaning irradiated skin. Roy et al. [45] and Campbell et al. [46] showed that washing irradiated skin during the course of irradiation for breast cancer is not associated with increased skin toxicity and should not be discouraged. In fact, cleaning reduces bacterial load and the risk of secondary infection [8]. Also Wesbury et al. [47] advises to maintain normal hair washing during cranial radiotherapy. The use of delicate washing gels, with a unique composition and with a pH close to 5, delays the appearance of symptoms associated with radiation reactions. It helps to remove epidermal cell fragments formed over the course of the radiation therapy; this has a positive effect on maintaining the natural protective barrier of the skin. It is recommended from the first days of radiotherapy and after its completion. The use of antiperspirants or deodorants remains controversial despite the results of a few trials [48–50] showing no evidence as regards increasing skin reaction. To prevent severe, acute and late skin toxicity that optimises the treatment plan, the use of intensity-modulated radiotherapy (IMRT) has the potential to reduce the severity of skin reaction. Intensity-modulated radiotherapy techniques are a highly conformal therapy that modulates the intensity of the radiotherapy delivered at a high dose of irradiation to the tumour target with significant sparing of the surrounding healthy skin [42, 43]. Some authors suggest that irradiated skin should not be exposed to sun light for many months or even years [44]. The use of sun block with very high SPF 50 protection is recommended for patients.

Topical corticosteroids

There are few products in the world with proven anti-inflammatory effectiveness in the prevention and treatment phase. Topical corticosteroids are known for their anti-inflammatory effectiveness in the way they inhibit the pro inflammatory cytokines IL-6 cascade which is stimulated by free radicals [8]. They play a huge role in prevention and treatment of radiodermatitis with variable results. The results of a study (n = 176) conducted by Miller et al. [51] showed that patients receiving daily 0.1% of mometasone furoate (MF) during radiotherapy notice less acute skin toxicity than the patients receiving placebo. They reported less itching, irritation, burning and discomfort. Another study published by Hindley et al. [52] in a double-blind study demonstrated that 0.1% of mometasone furoate not only reduces radiodermatitis when applied during and after radiotherapy, but it also has a beneficial effect on quality of life. Boström et al. [53] showed that a combination of 0.1% mometasone furoate with emollient cream treatment significantly decreased acute radiodermatitis. The outcome of another trial [54] for just 20 patients showed statistically significantly better

results at preventing radiodermatitis in patients receiving prednisolone with neomycin compared to patients in the control group. Meghrajani et al. [55] in the publication showed benefits of preventive use of 1% hydrocortisone in women with breast cancer (n = 50). Omidvari et al. [56] and Schmuth et al. [57] reported that prophylactic use of topical corticosteroids (betamethasone 0.1% and 0.1% metylprednisolone respectively) during irradiation in patients treated for breast cancer delays the occurrence of acute radiodermatitis.

Other topical agents

There are some products in the world with proven anti-inflammatory effectiveness in the prevention and treatment phase. Turmeric oil – a mixture of turmerones which together with other fats form the protective barrier on the surface of the skin by sealing the outer skin layer, has an antioxidant effect, preventing microbial contamination. The basic mechanism of turmeric oil is associated with its chemopreventive and antimutagenic activity.

Palatty et al. [58] published the outcome of a random study in 50 patients treated for head and neck cancer during 7 weeks. All patients underwent 7 week irradiation. The experimental group receiving turmeric oil based cream from the first day of treatment. The control group received mineral baby oil for irradiated skin. The study showed a statistically significant decrease in the severity of radiodermatitis in the experimental group compared to the baby oil group. Liguori et al. [59] conducted a study on 134 patients undergoing irradiation. Patients were randomized into two groups. The experimental group received 0.2% hyaluronic acid cream. The control group received a placebo. The hyaluronic cream or placebo were applied to the skin twice daily at the start of radiation. The outcome of this study showed a statistically significant improvement in delaying severe skin reaction in the experimental group. The duration of intensity of radiodermatitis was statistically shorter in the group using the hyaluronic cream [59]. It is likely that hyaluronic acid, due to its strong hygroscopic properties, provides a moisturising effect as a result of water retention in the stratum corneum.

Another randomized trial [60] on breast cancer patients, showed a statistically significant higher rate of radiodermatitis grade ≥2 in the group using the hyaluronic gel comparing to the group of patients receiving petrolatum-based cream. This negative outcome is probably the effect of the gel formula of the hyaluronic product. The products used for protection should have an emollient formula. In 2016 Ben-David et al. [61] in his II phase, prospective, double-blind randomized trial showed that patients treated with melatonin-containing emulsion experienced significantly reduced radiodermatitis compared to patients receiving a placebo. Emulsions containing trolamine are sometimes used in clinical practice, because trolamine is believed to have radioprotective properties as a result of macrophage cell stimulation and removing necrotic tissue, promoting fibroblast proliferation, reducing vascular alterations, restoring CD34 expression, promoting epithelial cell proliferation and decreasing IL-1 expression and collagen secretion [8]. However, the radioprotective properties were not yet confirmed in the clinical studies [62–64].

D-panthenol is a substance that is a natural component of the skin, and necessary for its normal functioning. It has a toning effect, strongly moisturises, makes the skin soft and elastic, soothes irritations, supports the regeneration of any damaged to the epidermis and prevents peeling of the skin. In a study [65] on 86 laryngeal and breast cancer patients undergoing radiotherapy, a dexpanthenol cream (Bepanthen – Roche) was applied on irradiated skin. The study did not show any clinically important benefits of using Bepanthen cream for skin reactions [65]. Silver sulfadiazine cream was investigated by Hemati et al. [66] in 102 women receiving RT for breast cancer. Silver sulfadiazine cream reduced the severity of radiation-induced skin injury compared with general skin care alone.

A new double-blind, placebo-controlled study [67] on 47 patients showed the effectiveness of boron-based gel in reduction of radiodermatitis. An interesting preclinical test with vasoconstrictors was performed on rats by Fahl [68]. All tested adrenergic vasoconstrictors (epinephrine, norepinephrine, or phenylephrine) applied before irradiation gave 80–100% prevention from increased risk of radiation dermatitis. Further preclinical and clinical studies assessing their effectiveness and safety are needed. Evidence from a limited number of trials does not support the use of aloe vera [69, 70], sucralfate [13, 71], calendula [72], tocopherol [73]. From the first day of irradiation, the skin loses its natural protective layer. The natural biological barrier is also disturbed, which in turn exposes the skin to bacteria, fungi and viruses causing inflammation and dehydration. Very promising in the prevention and management of radiodermatitis is STRATA-XRT – a silicone based film which forms a gel dressing. This product was under investigation in 197 patients treated with irradiation for head and neck cancer. It was a single blind randomised controlled study comparing the use of silicone film and 10% glycerine cream as a comparator. The outcome of this study showed that STRATA HRT is effective for preventing, delaying and reducing the severity of radiation-induced dermatitis. Another very interesting product is ectoine, which seems to be a natural skin protectant. Ectoine functions as a superior moisturiser with long term efficacy. Some other agents appear promising (e.i. pentoxiphilline [74], sylimarin [75]) but more long-term studies assessing their effect on irritated skin are essential.

Treatment

After the second or third week of radiotherapy, when erythema occurs, a smooth emollient should be used [25]. Some authors suggest the use of non-scented, hydrophilic, lanolin-free cream [9, 76–78]. It is better to use some forms of creams or ointments than lotions for dry desquamation [8]. The emulsion should

include: shea butter. The basic mechanism of shea butter action is similar to all vegetable oils.It creates a protective barrier on the surface of the skin (occlusive layer, the so-called film), which directly reduces water loss through the skin. In addition, it reduces the destabilization of the homeostasis of the stratum corneum, and thus the remaining layers of the skin. Additionally, emulsion which contains glycerin, moisturises and improves the condition of the skin, collecting water and binding it to the epidermis.

The management of more severe skin reactions with moist confluent desquamation (grade 3) requires more intensive treatment to prevent secondary bacterial and fungal infection [37, 39]. The use of micro-silver (micronized silver) helps to protect burned, exfoliated skin against bacterial and fungal infections to which it is exposed. A microsilver is remaining on the surface and accumulating mainly in its micro cavities. Micro-silver is added to cosmetics in order to maintain its proper functioning; secondary microbial contamination (both during storage and use, as well as after application to irradiated skin) may increase the risk of adverse effects related to the excessive growth of microorganisms on the surface of irradiated skin. Micro-silver can be use as a dressing. Dressings may protect irradiated skin from bacterial contamination or absorb fluids from oozing weeping wounds. The use of dressings in the treatment of moist desquamation is based upon the observation that a moist environment promotes the rate of re-epithelization and increases the speed of wound healing [80]. Other benefits include simplifying wound care and pain control [8, 33]. Hydrogel (with or without moisturising cream) and hydrocolloid dressings have been used in the manage-

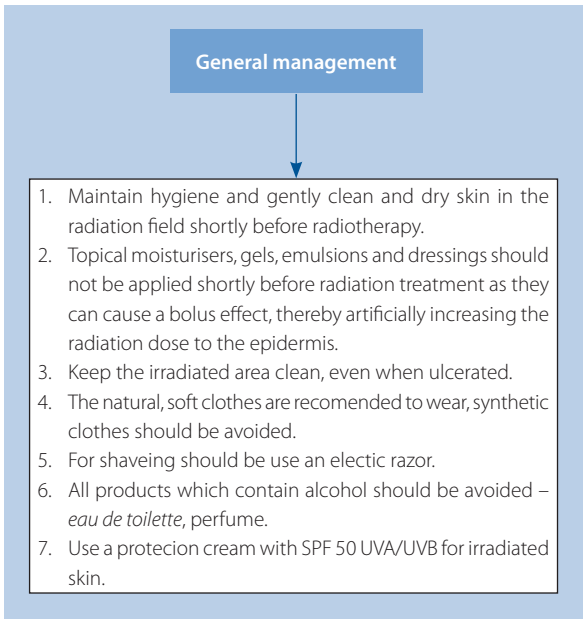

Figure 5. General management approaches

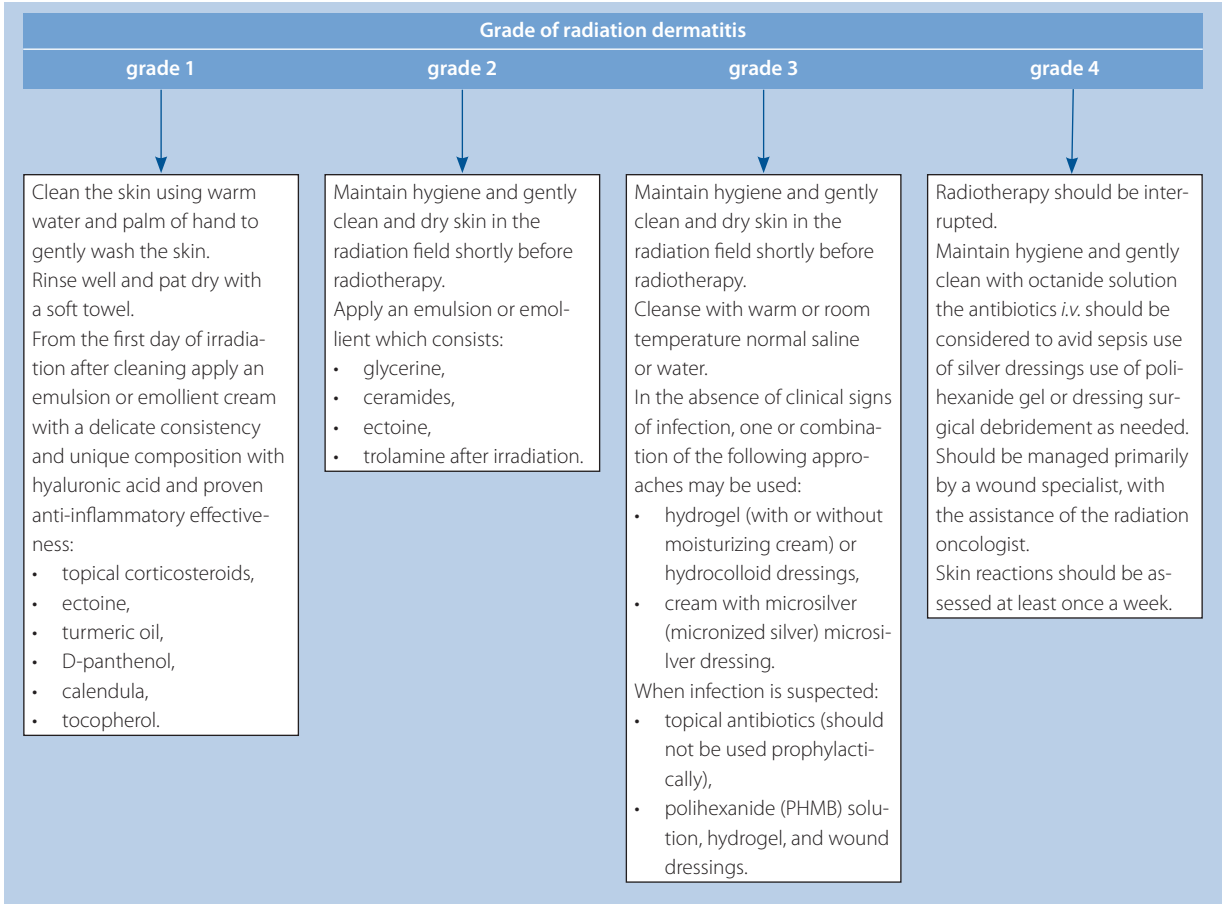

Figure 6. How to manage radiation dermatitis – algorithm

ment of moist desquamation in order to promote a moist environment for reepithelization [8, 33]. Dressings should be changed 1 to 3 times daily or less often, depending on the dressing type and drainage needed [33]. Diggelmann et al. [81] investigated the clinical efficacy of Mepilex Lite dressings in reducing radiation-induced erythema in 24 women with breast cancer. Those dressings significantly reduced the severity of radiation-induced erythema compared with the standard aqueous cream [81]. The results of the study conducted by Vuong et al. [12] suggest that silver leaf nylon dressing is effective in reducing radiodermatitis because of its antibacterial properties. Polihexanide (PHMB) is available as a solution, a hydrogel and in wound dressings [83]. It is well tolerated [84], anti-septically effective against MRSA and VRE (vancomycin-resistant *Enterococcus*) [85–86], can be used for wound irrigation and is suitable as an antiseptic for critically colonized and infected wounds and moist desquamation. The worst skin side effects are radiodermatitis which occurs as a skin necrosis and ulceration. Thanks to new radiotherapy techniques this complication is very rare. When it occurs, radiotherapy should be interrupted [37]. Possible treatment methods include use of silver dressings and surgical debridement sometimes with full-thickness skin grafts [87, 88]. The use of polihexanide PHMB dressing and gel is very promising in the treatment of grade 4 radiodermatitis. The use of Polihexanide gel or dressing is recommended as a therapeutic option for acute wounds, chronic ulcers and second-degree burns due to its analgesic effect and treatment of wound infections, including promoting wound healing [89]. Therefore, PHMB may be considered the first choice agent for infected chronic wounds and burn wounds (gel, dressing). Off-label use of low-intensity heliumlaser (HPLT) has shown to be effective in some patients with chronic ulcerations after RT [90]. There are case reports of patients with IV radiodermatitis in which mesenchymal stem cells injected into and around the wound after the excision of necrotic skin promoted wound healing [91].

Conclusions

Radiodermatitis is a very common side effect of anticancer treatment. This is a huge problem not only for oncologists and dermatologists, but also for GPs. Despite the great commitment and the emergence of new publications every year, a set of unambiguous best practices for the so-called "golden standard" have still not been agreed upon. There are few products in the world with proven anti-inflammatory effectiveness in the prevention and treatment phase. In practice, each cancer centre has its own methods of preventing and treating skin radiodermatitis. There is a need to process recommendations for the management of radiodermatitis.

We can propose an algorithm – "How to manage radiation induce dermatitis" (fig. 5, fig. 6).

Conflict of interest: none declared

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