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Short communication

Mepitel Film and Mepilex Lite for the prophylaxis and treatment of skin toxicities from breast radiation

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ABSTRACT

Despite the prevalence of radiation dermatitis in breast cancer patients, current practice guidelines for its treatment are limited. We aimed to discuss the quality of evidence for the barrier-forming Mepitel Film for prophylaxis of radiation dermatitis, and argue for further investigation into evidence-based management of skin toxicities. Two studies assessing Mepitel Film were critically evaluated. Both reported that Mepitel Film decreased radiation dermatitis; moreover, patient-reported outcomes significantly favoured Mepitel Film. However, there has not been global adoption of barrier-forming films such as Mepitel, in part due to the absence of multi-centred randomised trials and the heterogeneity of study designs.

1. Introduction

Patients with breast cancer who undergo adjuvant radiotherapy commonly experience radiation-induced skin toxicities that negatively affect their quality of life and self-image. Common toxicities include erythema, dry desquamation, and less frequently, moist desquamation [1,2]. Skin toxicity may be measured by the observer/healthcare provider or be self-reported. In addition to direct photographic evidence, there are also a variety of instruments available, with the Radiation Therapy Oncology Group (RTOG) radiation dermatitis scale being the most commonly utilised tool to report adverse events in large clinical trials in breast radiation [3]. Patients receiving chest wall radiation and patients with large breasts are especially sensitive to developing more severe skin reactions [1]. The current standard of prophylaxis and treatment includes the use of aqueous and corticosteroid creams, which may provide some limited benefit if any at all [4–6]. More recently, attention has been turned towards barrier-forming methods using semi-permeable dressings to treat and prevent radiation-induced skin toxicities [7].

Initially, studies have focused on the efficacy of a silicone-based absorbent dressing Mepilex Lite (Mölnlycke Health Care, Gothenburg, Sweden) for the treatment of erythema and dry or moist desquamation in breast cancer patients [8–10]. Mepilex Lite is applied after the development of skin erythema. While patient-reported outcomes suggested Mepilex Lite improved symptoms associated with skin toxicities, Mepilex Lite did not significantly reduce the incidence of moist or dry desquamation when compared to the usual treatment (aqueous cream) [9,10]. However, recent studies on Mepitel Film (Mölnlycke Health Care, Gothenburg, Sweden) showed its efficacy in prophylaxis of skin toxicities. In this commentary, we aim to discuss the quality of existing evidence of Mepitel Film and explore the barriers against widespread investigation and application of evidence-based management of skin toxicities.

2. Methods

Two studies on the prophylactic use of barrier-forming product Mepitel Film for management of radiation-induced dermatitis in

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breast patients were critically evaluated.

3. Results

In 2014, Herst et al. conducted a phase III intra-patient randomised controlled trial (n = 78) using Mepitel Film, which is applied before the start of radiation and kept on for the entire radiation course, and for several weeks afterwards. The investigators found that Mepitel Film was successful in significantly reducing the incidence of moist desquamation relative to control (26% with aqueous cream to 0% with Mepitel Film) by preventing friction damage to radiation damaged skin [11]. In addition to convincing photographic evidence, observer- and patient-reported outcomes using the Radiation-Induced Skin Reaction Assessment Scale (RISRAS) and observer-rated outcomes using the RTOG significantly favoured Mepitel Film [11]. Furthermore, a recently published Danish study conducted by Moller et al. (n = 79) evaluated Mepitel Film for the prophylaxis of radiation-induced skin toxicities in breast cancer patients. Here, it was found that Mepitel Film significantly reduced patient-reported skin reaction symptoms. Results from the blinded observer-rated skin reactions found significantly lower skin reactions among mastectomy patients (n = 16, p = 0.005) and among patients who received a total radiation dose of 50Gy (n = 20, p = 0.002) [12].

The protective effect of Mepitel Film was less pronounced in a feasibility study of head and neck cancer patients (n = 33), with a decrease in skin reaction severity of 27% in New Zealand patients and 28% in Chinese patients and a decrease in moist desquamation rates of 29% and 37% respectively [13]. These differences in effectiveness could be explained by the significantly higher skin dose received by head and neck cancer patients (average 49Gy in New Zealand patients and 43Gy in Chinese patients) [13] compared with breast cancer patients (average 30Gy) [11].

4. Discussion

Despite the presence of level one evidence on the efficacy of Mepitel Film in breast cancer patients, there is limited global adoption, particularly in North America. Mepitel Film is not included in patient guidelines from major cancer centres and national or provincial/state guidelines such as those from the National Cancer Institute [14–18]. Although there is often a latent period between evidence and translation into clinical practice, there are several factors in this field that may enable more efficient reporting and consolidation of evidence to allow more rapid dissemination of advances in skin symptom management.

4.1. Heterogeneity in measuring skin toxicity

The RTOG scale and RISRAS are two examples of instruments used to score skin toxicity. Furthermore, patients may be assessed at multiple timepoints during radiation or follow-up. The scores obtained may be evaluated as is or combined to identify the maximum, median, mean, or area under the curve. Historically, most studies on radiation-induced skin toxicities utilize the RTOG scale scoring for the maximum level of skin toxicity, which usually occurs around two weeks following completion of radiation [1]. Alternate methods of measuring skin toxicities, such as area under the curve or averages are more representative of the overall patient experience of their side effects across their radiation regimen.

Herst et al. utilised the average score method for reporting RISRAS scores that were evaluated at multiple timepoints (three times weekly during treatment, then once a week for four weeks after treatment completion) during treatment and follow-up, and the maximum toxicity for RTOG [11]. On the other hand, Moller et al. utilised a modified version of the patient-reported component of RISRAS administered at the final day and at 2-weeks after radiation, as well as the maximum toxicity for RTOG [12]. While the patient-reported component of the RISRAS-based scoring system identified significant improvements in skin symptoms using the film in both studies, the RTOG scale showed significant improvements only in the study by Herst et al. ($p < 0.01$). As the photographic evidence provided by Herst et al. convincingly demonstrates superior outcomes in skin areas randomised to Mepitel Film, it suggests that the RTOG scale may be less sensitive in comparison, particularly as it is unable to differentiate between moist desquamation and brisk erythema. This low sensitivity may contribute to the discrepancy in the significance of the two outcomes assessed by Moller et al., although photographic results will provide more definitive evaluation of its efficacy.

4.2. Patient selection and statistical power

In contrast to the positive results from the original study on Mepitel film, Moller et al. found no overall significant effect of Mepitel film on skin toxicity using the RTOG scale [12]. However, this may be due to improper selection of patients, contributing to the low incidences of skin toxicities and resulting in insufficient statistical power to identify any potential difference. For example, the majority of the patient population selected by Moller et al. underwent lumpectomy and received a hypofractionated radiation regimen of 40Gy in 15 fractions. Moreover, it is unknown whether these lumpectomy patients had risk factors for developing skin toxicities such as the physical characteristics of larger breast sizes or greater breast separation. Indeed, there was only one episode of RTOG grade III skin toxicity which resolved 2 weeks after radiation [12]. The drop-out rate was also significant, comprising 22% of all initially randomised patients. As no sample size calculation was completed, it is possible that the study was insufficiently powered for detecting differences among low-risk lumpectomy patients, which comprised the majority of their study population.

Moving forward, it is important for future studies to differentiate between patients with varying risk for developing skin toxicities, performing sub-group analysis in each risk group and ensuring sufficient statistical power using a priori sample size calculation.

4.3. Ongoing studies

A recently published study by Schmeel et al. evaluated Hydrofilm polyurethane film dressings (Hartmann, Heidenheim and der Brenz, Germany) on the prophylaxis of radiation-induced breast skin-toxicities [19]. Although this is a different product from Mepitel Film, it functions through the same principle of being a transparent semi-permeable barrier film applied prophylactically to the skin prior to radiation [19]. In a population of 62 patients, Hydrofilm polyurethane completely reduced the incidence of moist desquamation from 10% in the control arm (n = 6) to 0% in the treatment group, echoing the results from Herst et al. who found a complete reduction of moist desquamation from 26% in control (n = 20) to 0% in treatment [11,19].

Currently, there are two ongoing studies on Mepitel Film in breast radiation, including a phase 3 randomised parallel-assignment study comparing Mepitel Film to control aqueous cream which utilises a primary endpoint of skin toxicity as evaluated by the Common Terminology Criteria for Adverse Events [20]. A second ongoing study is being conducted at the Mayo Clinic and aims to evaluate the severity of radiation dermatitis in high-risk mastectomy patients using Mepitel film [21]. The results of these studies may provide additional evidence with regards to the

optimal care for radiation-induced dermatitis.

4.4. Developing an international consensus

One of the barriers that prevented meta-analysis of the existing two studies on Mepitel Film is the heterogeneity in the study design [11,12]. The two studies had different study populations, measures, and time frames. In assessing results from ongoing and future studies, similar issues may arise which will make it difficult to consolidate the body of evidence. Therefore, the development of an international consensus on reporting skin toxicities may help resolve this issue. RTOG and CTCAE scoring systems may not be sensitive enough to distinguish between small differences in skin reaction severity, such as between moist desquamation and brisk erythema. In addition, patient-reported outcomes have their role in assessing skin reaction severity. Finally, collaboration in conducting international randomised trials using Mepitel Film may provide sufficiently convincing proof to influence changes in practice guidelines across cancer centres globally.

5. Conclusion

Standard of care of topical treatments have shown limited efficacy. Despite robust evidence supporting Mepitel Film for prophylaxis of radiation-induced skin toxicity, clinical adoption has been limited. Well-designed, international, multi-centre trials may influence treatment guidelines and adoption of Mepitel Film. Consensus criteria should be developed to standardize patient populations, reported outcomes, instrument tools, and measurement time points.

Conflicts of interest

None.

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