Non-steroidal topical preparations for treatment of radiation dermatitis: a WHAM evidence summary

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CLINICAL QUESTION

What is the best available evidence for non-steroidal topical preparations for treatment of radiation dermatitis in people undergoing radiation therapy for cancer?

SUMMARY

Radiation dermatitis (RD) is an acute skin reaction that occurs as a result of radiotherapy used to treat a range of different cancers. Severity of symptoms ranges from erythema to dry desquamation (dry flaky skin with itching) to moist desquamation (serous exudate, oedema and blistering). *Level 1* evidence from systematic reviews (SRs)[1, 2] showed no effect for a non-pharmacological topical preparation in treating existing RD compared to a placebo or no treatment. Additional *Level 1* evidence did not support the use of trolamine,[3] sucralfate cream,[4] aqueous cream[4] and was conflicting on the benefit of hyaluronic acid preparations.[3, 5-7] There was insufficient evidence to recommend superoxide dismutase preparations.[8] However, a consensus panel suggested using a topical preparation to treat mild RD,[9] and evidence presented in a companion WHAM evidence summary[10] suggests that prophylactic use of topical preparations might delay progression of RD.

CLINICAL PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional and the clinical context.

There is no strong evidence to support the use of a non-steroidal topical preparation for treating existing radiation dermatitis.

SOURCES OF EVIDENCE

This summary was conducted using methods published by the Joanna Briggs Institute.[11-15] The summary is based on a systematic literature search combining search terms related to radiation dermatitis/radiodermatitis and topical preparations/creams. Searches were conducted in Embase, Medline, Pubmed, the Cochrane Library and Google Scholar for evidence published up to January 2021 in English. Levels of evidence for intervention studies are reported in the table below.

BACKGROUND

Radiation dermatitis is a common side effect of radiotherapy, which is a type of therapy delivered in the management of cancer. Radiation causes damage to epithelial cells and underlying structures of the skin, usually commencing early during radiotherapy and persisting up to six months following radiotherapy.[19, 20] The severity of RD is related to the dose and regimen of radiation and the area of skin over which radiotherapy is administered,[19-21] increasing when cell destruction occurs faster than normal cell reproduction. In early stages of RD the skin becomes warmer, itchy and erythema may present. As cumulative exposure to radiation increases, old skin becomes dry and flaky (referred to as dry desquamation). When the rate of new skin cell production cannot replace shedding cells the epidermis breaks down, becomes oedematous and exudate is present (referred to as moist desquamation).[20] Pain, skin warmth, pruritus, burning sensations are reported by people experiencing RD.[3] Consistent with outcome measures reported in the evidence, when referring to 'grade' of RD this evidence summary uses the Radiation Therapy Oncology Group (RTOG) scale for categorising the severity acute of RD.[22]

Non-steroidal topical preparations are designed to moisturise the skin and/or to maximise the absorption of an active ingredient into the skin. For this evidence summary, the term topical preparation refers to ointment, cream and gel that is applied to the skin to treat RD. Corticosteroid preparations and dressings/barrier films are discussed in other evidence summaries in this series. Other medicated topical preparations (e.g. non-steroidal anti-inflammatory

Level 1 Evidence	Level 2 Evidence	Level 3 Evidence	Level 4 Evidence	Level 5 Evidence
Experimental Designs	**Quasi-experimental Designs**	**Observational – Analytic Designs**	**Observational – Descriptive Studies**	**Expert Opinion/ Bench Research**
1.a Systematic review of RCTs[1-3] 1.c RCT[4-7, 16]		3.e Observational study without a control group[8]		5.b Expert consensus[9, 17, 18]

drug preparations) were eligible, but no individual studies on their use as a treatment for RD were identified.

CLINICAL EVIDENCE

Evidence on using any topical product

A 2013 meta-analysis[1] of six trials found the effectiveness of using any topical preparation in healing RD was not significantly different compared to using no product (75.15% versus 75.19%, p = 0.784, relative risk = 1.01, 95% confidence interval [CI] 0.92 to 1.12). The included studies reported the effectiveness of gentian violet, trolamine and sucralfate, and significant heterogeneity was noted[1] (*Level 1*). A 2010 meta-analysis[2] included six trials reporting topical preparations (wound dressings, corticosteroids, trolamine and sucralfate) for reducing the signs and symptoms of RD. The pooled results showed no significant difference in using a topical treatment compared with control (odds ratio [OR] = 0.43, 95% CI 0.15 to 1.25, p = 0.12). As with the meta-analysis by Zhang et. al. (2013),[1] significant heterogeneity was noted; unsurprising given that four of the six studies were included in both analyses[1, 2] (*Level 1*).

A consensus panel suggested that the use of non-pharmacological topical products could be considered for grade 1 RD. The panel suggested moist desquamation in skin folds (considered to be grade 2 RD) might benefit from use of non-pharmacological product, but for general grade 2 or greater RD the panel suggested different management strategies were preferable[9] (*Level 5*).

Evidence on topical non-pharmacological preparations

Trolamine

A meta-analysis of two RCTs showed no significant effect of trolamine compared to normal care in reducing the maximum severity of RD (mean difference [MD] = 0.00, 95% CI –0.13 to 0.13, p = 0.97). However, people who used trolamine rated it easier to use than a placebo (p < 0.001) and calendula ointment (p < 0.001)[3] (*Level 1*).

Superoxide dismutase

A small observational study[8] (n = 57) reported the use of superoxide dismutase (a preparation with antioxidant effects) to treat RD. At commencement, 75.4% of participants had grade 2 RD and 24.6% had grade 3 RD. After a 12-week treatment period, 91.2% of participants had no RD (the remainder did not attend for follow up). Remission of symptoms took an average of 2.22 weeks[8] (*Level 3*).

Hyaluronic acid

Three studies reported effectiveness of hyaluronic acid cream for treating RD. Compared with a placebo, hyaluronic acid was associated with greater reduction in severity of RD at the completion of radiotherapy (MD = –0.73, 95% CI –1.04 to –0.42, p < 0.0001),[3, 6] greater reduction in severity of RD four weeks after completing radiotherapy (MD = –0.35, 95% CI –0.68 to –0.02, p = 0.04)[3, 6] and less severe maximum grade of RD(MD = –0.95, 95% CI –1.23 to –0.67, p < 0.00001).[3, 5] However, in the third study, hyaluronic acid was not effective in reducing skin pain or improving quality of life[3, 7] (*Level 1*).

Sucralfate cream

An RCT[4] compared sucralfate cream to no treatment for reducing grade of RD, desquamation (measured on a 4-point scale where 0 = no dry or broken skin), erythema, pruritus and pain. The only outcome measure for which statistically significant results were noted was a significantly better scoring for desquamation in the sucralfate group (0.38 versus 0.62, p = 0.04). However, the desquamation scores, which were self-reported by participants, were very low in both groups, and the findings were not considered to be clinically significant[4] (*Level 1*).

Aqueous cream

An RCT[4] compared aqueous cream to no treatment for reducing grade of RD, desquamation (measured on a 4-point scale where 0 = no dry or broken skin), erythema, pruritus and pain. A third arm of the study received sucralfate cream (results reported above). People using aqueous cream had a significantly better self-rated scores for desquamation compared with no treatment (0.45 versus 0.62, p = 0.04). As with the sucralfate cream group, these findings were deemed to be not clinically significant due to the very low desquamation scores seen in this study. None of the other outcome measures were significantly different between aqueous cream and sucralfate cream or no treatment[4] (*Level 1*). Aqueous cream has been associated with signs and symptoms of skin irritation in some people with eczema or dermatitis,[17] related to impairment of the skin barrier function caused by the ingredient sodium lauryl sulphate[18] (*Level 5*).

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CONFLICTS OF INTEREST

The author declares no conflicts of interest in accordance with International Committee of Medical Journal Editors (ICMJE) standards.

ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries are consistent with methodology published in Munn Z, Lockwood C, Moola S. The development and use of evidence summaries for point of care information systems: A streamlined rapid review approach, Worldviews Evid Based Nurs. 2015;12(3):131-8. Methods are provided in detail in resources published by the Joanna Briggs Institute as cited in this evidence summary. WHAM evidence summaries undergo peer-review by an international multidisciplinary Expert Reference Group. More information: https://www.WHAMwounds.com/

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

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