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Title:

WHAT CAN WE LEARN FROM RESEARCHING IN AN OVERCROWDED RESEARCH AREA? LESSONS LEARNT FROM THE 50 YEARS OF RESEARCH ON RADIATION DERMATITIS

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The author’s institution received research grants from Stratpharma and Moogoo Skin Care to conduct clinical research in the area of radiation dermatitis. None of these companies had any involvement in writing or reviewing this manuscript prior to publication.

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Radiation dermatitis (RD) remains one of the most common side effects, affecting majority of patients receiving radiotherapy.\textsuperscript{1, 2} Despite the advances in radiation treatment techniques, our recent clinical trials indicated as high as 85\% of patients (with mixed-cancer type) undergoing radiotherapy experienced dry desquamation and 15\% of patients experienced moist desquamation, requiring wound dressing.\textsuperscript{1} These proportions were even higher in patients receiving treatment to their head and neck.\textsuperscript{3} Given the high prevalence of RD, much attention and resources have been invested into research to identify the best solution to manage and resolve this treatment side effects.

The first randomized controlled trial (RCT) on RD prevention and management can be traced back to 1962 conducted in the UK, which investigated the effects of steroid and antibiotic ointment versus antibiotic control ointment versus no ointment on the severity of RD.\textsuperscript{4} Since then, the literature on RD prevention and management has been growing and has been “overcrowded”. As our research team embarked on a program of research in this area in 2010, we decided to apply a systematic approach to ensure we were addressing the most pertinent issue, and a true research gap. Therefore, in 2012, we published an overview of systematic reviews, which located, critically appraised, and summarized the findings from six systematic reviews that examined interventions for preventing or managing RD.\textsuperscript{5} This overview reported significant variability in the quality and scope of reviews and suggested that methodological flaws might have resulted in bias in the practice recommendations. Based on these findings, our team subsequently conducted a large systematic review and meta-analysis\textsuperscript{6} of 47 studies including 5,688 participants. In this review, we concluded that, despite the high number of trials in this area, there had been limited high quality, comparative research providing
definitive results suggesting the effectiveness of any single interventions for preventing or managing RD. The negative findings were discouraging to the clinical and research community, and these negative studies included a negative RCT conducted by our team published in 2014. At this time, the research community had to pose a very difficult question to ourselves: what went wrong and how our next steps should be for our future efforts? There was a recognition that perhaps the previous research over the last 50 years was not truly conducted with sufficient novel biological rationale and an extraordinary claim of effectiveness.

Over recent years, there have been breakthroughs in this research area, with several encouraging, positive trials suggesting the efficacy of certain topical corticosteroids, and silicone-based film dressings. These studies included our recently completed RCT that reported significant effectiveness of a silicone-based film forming gel dressing in preventing and reducing both dry desquamation and moist desquamation in patients receiving radiotherapy to their head and neck. To the best of our knowledge, this RCT is the first definitive trial to yield significant, positive effects of non-steroidal topical preparation for RD in patients with head and neck cancer. The distinct difference between these latter, positive trials and the previous, negative trials was that the interventions used in the latter trials clearly addressed underlying a biological mechanism, with sufficient level of anticipated effectiveness.

From the lessons learnt from the 50 years of literature on RD prevention and management, I would like to humbly propose several recommendations for the research community to consider in the conduct of interventional research, especially in any “overcrowded” area of research. First, all researchers should undertake a systematic approach (i.e., a systematic review) to identify the true research gap,
including understanding and postulating why the previous strategies did not work and what holds promise. Second, to ensure the success of our research, our interventions must address promising, underlying relevant mechanisms. Third, considering patient burden and the current stringent research funding climate with a limited research funding pool, the research community has the responsibility to ensure our research investment is put towards the most significant and promising work that will ultimately improve the wellbeing of people affected by cancer.

My very best,

Raymond Javan Chan
References:


