

Radiation induced bowel injury: a neglected problem



Stigma associated with radiation induced bowel injury (RBI) has restricted interest in its pathogenesis and the pathophysiological processes that occur as a consequence. This neglect has in turn hampered clinical management and led to the widely held belief that RBIs are not amenable to treatment. RBI is more common than Crohn's disease, yet attracts a fraction of the research funding. Furthermore, only a fifth of patients with RBI in the UK see a gastroenterologist, and most who do so are managed ineffectively.¹

In *The Lancet*, Jervoise Andreyev and colleagues¹ report findings from one of the first randomised trials to show that the symptoms of RBI can be improved by a therapeutic intervention. In what will probably be viewed as a landmark trial, Andreyev and colleagues randomised 218 patients to three groups: algorithm-based treatment led by a gastroenterologist or nurse, or usual care. The findings show that in terms of the trial's primary endpoint, the mean difference in change in score on the IBDQ-B instrument between baseline and 6 months, both gastroenterologist-led care (5.47, 95% CI 1.14–9.81; $p=0.01$) and nurse-led care (4.12, 0.04–8.19; $p=0.04$) were superior to usual care; in other words, both men and women with a range of RBIs can have clinical and statistically significant improvements in their symptoms with tailored management programmes determined by an investigative and therapeutic algorithm.

A reasonable question to ask is why a diagnostic and therapeutic algorithm should work in a group of disorders considered refractory to treatment, without the use of new pharmaceutical agents. The answer is surprisingly simple. The investigators recognised that RBI frequently affects several parts of the bowel and almost always affects several normal physiological processes adversely. The identification of these processes (using the diagnostic part of the algorithm) therefore enables adaptive measures, such as dietary modifications and the use of commonly prescribed drugs to reduce the severity of patients' dysfunctional symptoms. The algorithm is provided in the online appendix of the paper, and its development is described elsewhere.²

The investigators showed the algorithm-based intervention to be beneficial for at least 12 months, which is encouraging, but how long these benefits will last is unclear and will need further assessment. It is important

to note, however, that the intervention cannot be expected to heal the bowel injuries that have led to the clinical manifestations.

Future trials should focus on the prophylactic use of pharmaceutical agents, perhaps during and after radiotherapy, given with the intention of limiting severity of injuries. Systematic, evidence-based reviews of interventions to ameliorate gastrointestinal mucositis are available.^{3,4} Moreover, a strategy for how to test new potential pharmacological agents to protect against or mitigate bowel injuries (defined as agents that are given after irradiation, but before the development of symptoms) has been suggested.⁵ Much work has been done in the past 5–10 years to develop medical countermeasures against radiation. Many of these efforts are directed towards reducing gastrointestinal radiation toxicity, and several agents are undergoing advanced development and are en route to US Food and Drug Administration (FDA) approval. Although the primary intent is to enhance preparedness in the event of a radiological or nuclear emergency, many agents that reduce short-term or long-term side-effects of radiation in the emergency setting can probably also benefit cancer survivors, and vice versa.

Andreyev and colleagues' findings¹ have shown that their algorithm can be used just as effectively by specifically trained nurses as by gastroenterologists. The trial results will hopefully promote an improved understanding of pathophysiology of RBI and the adoption of the algorithm into the training programmes of specialist oncology nurses. Such a development would do much to further the translation of the results into clinical practice. Of course, this possibility does not mean that gastroenterologists need no longer bother about radiation injury. Nothing would be better for patients with RBI than if the gastroenterological community was to take ownership of this group of disorders and make sure that the breakthrough achieved by Andreyev and colleagues is just the first of many. The provision of part-time appointments of gastroenterologists at large cancer treatment centres would also do much to reduce the burden of RBI across the world and stimulate treatment advances.

A pertinent question is whether the major technical advances in radiotherapy delivery in the past 15 years



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will lead to reductions in RBI. The answer is both yes and no. Although new technology will allow many radiation oncologists to reduce radiation doses to the bowel, many more will be beguiled into irradiating what they perceive to be new intra-abdominal targets (such as lymph-node drainage regions and organs not commonly treated) or into escalating radiation doses to existing targets. Available data show that limiting dose to the rectum during prostatic radiation without increasing dose to the prostate itself will cause dramatic reductions to symptoms related to rectal injury.⁶ Some data also indicate that increased dosing to the prostate can be achieved without increased rectal injury,⁷ but this finding has not been shown elsewhere.⁸

The results of Andreyev and coworkers' trial should be widely heeded and the algorithm taken into routine clinical practice. This is no more than patients who survive cancer treatment but go on to develop RBI deserve.

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