Condensed version and key points from the study:

Protective effect of hydrogen gas inhalation on radiation-induced bone marrow damage in cancer patients: a retrospective observational study

Important Note on Study Status

- This is a preprint — it has not been peer reviewed by a journal. This means the findings have not yet gone through independent scientific scrutiny, and should be interpreted with extra caution.

Study Overview

- A retrospective observational study conducted at Clinic C4 in Tokyo, Japan between May 2015 and November 2016, investigating whether hydrogen gas inhalation mitigates bone marrow damage induced by intensity-modulated radiation therapy (IMRT) in end-stage cancer patients.

- **23 patients with end-stage cancer were included — 7 in the control group** (IMRT + hyperbaric chamber only) and 16 in the hydrogen group (IMRT + hyperbaric chamber + 5% H2 gas inhalation for 30 minutes after each radiation session).

Background — Why Bone Marrow Damage Matters

- Bone marrow damage, such as reductions in white blood cells (leukopenia) and platelets (thrombocytopenia), frequently occurs during cancer radiotherapy including IMRT, and is a limiting factor for continuing treatment. Leukopenia and thrombocytopenia may cause infection and gastrointestinal bleeding, so caution is required.
- Approximately 65% of DNA damage from radiation is caused by indirect effects of free radicals such as hydroxyl radicals (·OH), making selective scavengers of these radicals promising as radioprotective agents.
- The only clinically accepted radioprotective agent, amifostine (Ethyol/WR2721), is not considered a viable option due to its dose-limiting toxicities — highlighting the need for safer alternatives.

How the Intervention Worked

- After each course of IMRT, patients in the H2 group were housed in a mild hyperbaric oxygen health care chamber (HCC) and received 5% H2 gas via a nose cannula at a flow rate of 4L/minute for 30 minutes. The control group received the same HCC conditions without hydrogen.
- Both groups received a similar number of radiation courses and total exposure doses, confirming a comparable baseline between groups.

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Key Results — Blood Markers

- IMRT significantly reduced white blood cells (WBC) and platelets (PLT) in the control group, but not red blood cells, hemoglobin, or haematocrit. In contrast, H2 gas treatment significantly alleviated these reductions in WBC (p=0.0011) and PLT (p=0.0275).
- A bone marrow damage index calculated from total radiation exposure dose and WBC ratio also demonstrated the radioprotective effects of H2 gas (p=0.0231).

Anti-Tumour Effects Were Preserved

- Tumour responses to IMRT were similar between the two groups — 57% of control patients and 44% of H2 patients achieved complete or partial response, and an additional 19% of H2 patients achieved stable disease. These results confirmed that H2 gas inhalation did not compromise the anti-tumour effects of IMRT.

Quality of Life

- Quality of life measures such as fatigue, sleep, and gastrointestinal symptoms were similar between the two groups, indicating that H2 gas inhalation did not compromise QOL — though the authors noted that longer-term inhalation may be needed to see QOL improvements.

Proposed Mechanism

- Molecular hydrogen was identified as a preventive and therapeutic antioxidant that selectively scavenges hydroxyl radicals (·OH) and peroxynitrite ($ONOO^-$). Due to its small size and electrically neutral properties, H2 easily reaches target organs.

- The mechanisms underlying the radioprotective effects of H2 gas may involve not only direct effects on hydroxyl radicals, but also indirect effects via the activation of the host antioxidant and anti-inflammation systems.

Conclusions

- H2 gas inhalation therapy alleviated IMRT-induced bone marrow damage without compromising the anti-tumour effects of IMRT, and may represent a clinically applicable, effective, and safe strategy for managing radiation-induced bone marrow damage in cancer patients.

Limitations to Keep in Mind

- The study had limitations related to the small number of patients, the retrospective observational design, and data collection from a single hospital. Further large-scale clinical studies involving many hospitals are required. researchsquare
- Being a preprint, it has not yet been peer-reviewed — a critical step in validating scientific findings.
- The sample sizes were notably unequal (7 vs. 16), and all patients had end-stage cancer, limiting broader applicability.
- Hydrogen was administered after each radiation session rather than before, which is an unusual protocol compared to prior animal studies that used preventive administration.