

Researchers discover how to overcome poor response to radiotherapy caused by low haemoglobin levels

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Barcelona, Spain: Patients with head and neck cancer and a low haemoglobin (Hb) level do not respond well to radiotherapy and therefore both control of their tumour and disease-free survival are compromised. Now researchers from The Netherlands have found that the problems caused by low Hb in these patients can be overcome by the use of a treatment known as ARCON therapy, in which accelerated radiotherapy is combined with carbogen (a mixture of carbon dioxide and oxygen) and the water-soluble vitamin nicotinamide [1].

Hans Kaanders, a professor of translational <u>radiation oncology</u> at Radboud University Nijmegen Medical Centre, Nijmegen, will tell the 31st conference of the European Society for Radiotherapy and <u>Oncology</u> [2] today (Friday) that the ARCON regime is the first to show a positive effect in patients with low Hb levels.

The researchers recruited 345 patients with squamous cell laryngeal cancer to a <u>randomised trial</u>: 174 received only accelerated radiotherapy (where two <u>fractions</u> per day are administered during the last week of radiotherapy in order to reduce the overall length of treatment), and 171 ARCON. Patients receiving ARCON inhaled carbogen during radiotherapy and took nicotinamide tablets prior to treatment. Pre-treatment Hb levels in the experimental group were measured and subsequently compared with the treatment outcomes in the accelerated radiotherapy alone arm.



They found that patients treated with accelerated radiotherapy alone who had normal Hb levels before treatment had significantly better control of the cancer at its primary site (76% as opposed to 56%), disease-free survival (72% and 48% respectively), and metastasis-free survival (90% and 70%) than those with low Hb levels.

"However, when we looked at the ARCON group, in cases where the patients had low Hb levels before treatment, we found that ARCON improved control of the cancer at its primary site, and improved disease-free and metastasis-free survival, so that the differences between them and patients with normal Hb levels were no longer significant," says Professor Kaanders' colleague Dr. Geert Janssens. The difference in local control between this low Hb group and the normal Hb accelerated radiotherapy (AR) alone group was only 1% (81% in the ARCON group versus 82% in the AR-only group); for disease-free survival, the difference was 77% (ARCON) as opposed to 70% (AR); and for metastasis-free survival 93% (ARCON) versus 89% (AR).

However, patients in both groups with low Hb levels pre-treatment still had a worse overall survival irrespective of which treatment they received. This is most likely due the fact that many patients with <u>head</u> and neck cancer also have other health problems that cannot be treated by radiotherapy, the researchers say.

"In the past, a number of investigators have tried to improve the outcome for patients with low Hb levels by giving erythropoietin, which stimulates red blood cell production, and red cell blood transfusion before and during treatment, but without success. ARCON is the first treatment to be found to correct for low Hb and therefore to improve prognosis in these patients," says Dr. Janssens. "We know that a decrease in Hb levels is associated with a reduced sensitivity to radiotherapy, and that this can switch the <u>tumour</u> microenvironment into a more aggressive subtype with a higher risk of loco-regional failure and of the



development of distant metastases."

The lack of success with transfusion of red blood cells or erythropoietin suggests underlying adaptive mechanisms. Accelerated radiotherapy to counteract tumour cell repopulation during radiotherapy, combined with carbogen and nicotinamide, administered immediately before irradiation to increase the <u>oxygen</u> level, ensures that adaptive mechanisms cannot erode the effect, and this is probably the key to success of the ARCON regime in patients with low HB levels at presentation, the researchers say.

"We believe that, at a time when healthcare systems are under increasing pressure to introduce expensive targeted treatments, the use of such a low cost, effective therapy should only be encouraged," Professor Kaanders will conclude.

Prof Vincenzo Valentini, radiation oncologist at the Policlinico Universitario A. Gemelli in Rome, Italy, and President of ESTRO, said: "We know that the degree of oxygenation of tumours in laryngeal cancer patients is directly related to the damage that can be caused to them by radiotherapy. This important study shows that, in <u>patients</u> with low haemoglobin <u>levels</u>, it is possible to reoxygenate the tumour by using the simple and cost-effective ARCON regime, and therefore increase the effectiveness of radiation <u>treatment</u>."

More information: [1] When carbogen is inhaled, the increased level of carbon dioxide causes the brain to react to potential suffocation because it interprets the increase in blood carbon dioxide as a decrease in oxygen level, and the body compensates by reducing hypoxia. Nicotinamide also reduces hypoxia by increasing blood flow.

[2] This year the ESTRO conference is held in parallel with the World Congress of Brachytherapy, both taking place in Barcelona from May



9-13.

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