

HYPERBARIC OXYGEN TREATMENT FOR PELVIC RADIATION-INDUCED INJURIES

From a multicenter randomized controlled trial to an experimental
cell model

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien,
Göteborgs universitet kommer att offentligens försvaras i föreläsningssal Karl Kylberg,
sal 2320, Medicinargatan 7B, den 15 maj 2020, klockan 16:00

av Nicklas Oscarsson, Leg Läkare

Fakultetsopponent: Dr Neil B Hampson, Doctor in Medicine, Clinical Professor of
Medicine Emeritus, Division of Pulmonary and Critical Care Medicine, University of
Washington, Seattle, WA, USA

Avhandlingen baseras på följande delarbeten

- I. **Hyperbaric oxygen treatment in radiation-induced cystitis and proctitis: a prospective cohort study on patient-perceived quality of recovery**

Oscarsson N, Arnell P, Lodding P, Ricksten S-E, Seeman-Lodding H, *Int J Radiation Oncol Biol Phys*, 87 (4), 670–675, 2013 doi:10.1016/j.ijrobp.2013.07.039

- II. **Hyperbaric oxygen treatment reverses radiation-induced pro-fibrotic and oxidative stress responses in a rat model**

Oscarsson N, Ny L, Mölne J, Lind F, Ricksten S-E, Seeman-Lodding H, Giglio D *Free Radical Biology and Medicine*, 103, 248–255, 2017 doi: 10.1016/j.freeradbiomed.2016.12.036

- III. **Hyperbaric oxygen reverses radiation-induced cell death in human urothelial and endothelial cells – development of a cell model**

Oscarsson N, Podmolikova L, Seeman-Lodding H, Bergo M, Giglio D (*Manuscript*).

- IV. **Radiation-induced cystitis treated with hyperbaric oxygen therapy (RICH-ART): a randomised, controlled, phase 2-3 trial**

Oscarsson N, Müller B, Rosén A, Lodding Pär, Mölne J, Giglio D, Hjelle KM, Vaagbø G, Hyldegaard O, Vangedal M, Salling L, Kjellberg A, Lind F, Ettala O, Arola O, Seeman-Lodding H *Lancet Onc Epub 2019 Sep 16* doi: 10.1016/S1470-2045(19)30494-2

SAHLGRENKA AKADEMIN
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ABSTRACT

Introduction Cancer is affecting a growing number of persons. Still, the treatment and survival of cancer is improving. Radiation therapy is used in the treatment of cancer. Late radiation-induced injuries afflict 5–15% of irradiated patients. The urinary bladder and bowel may be affected after irradiation of cancer in the pelvic region. Symptoms can be severe, with impaired health related quality of life (HRQoL). Hyperbaric oxygen therapy (HBOT) involves breathing oxygen at high ambient pressure. HBOT can reverse radiation-induced injuries, alleviate patient-perceived symptoms, and improve HRQoL.

We aimed to clarify the effects of HBOT on late radiation-induced injuries in the urinary bladder and bowel, and to clarify some of the underlying mechanisms through which HBOT exerts its effects.

Methods A prospective cohort study assessed effects of HBOT on patient-perceived symptoms (Paper I). A rat study assessed reversal of radiation-induced stress with HBOT (Paper II). A methodological experiment assessed reversal of HBOT on cellular death induced by radiation (Paper III). A multi-center, randomized, controlled trial assessed patient-perceived symptoms, HRQoL, and objective clinical outcomes (Paper IV).

Result HBOT can alleviate patient-perceived symptoms, reduce objective findings, and improve HRQoL in patients affected by late radiation-induced injuries (Paper I, IV). Oxidative stress and downstream effects, induced by the irradiation, can be reversed by HBOT (Paper II). Paper III outlines a method for studies on urothelial cells exposed to radiation and HBOT.

Conclusion HBOT can reduce radiation-induced oxidative stress and inflammatory response. HBOT can reverse injuries induced by radiation therapy to the pelvic region, alleviate patient-perceived symptoms and lead to improved HRQoL.

Keywords: Hyperbaric oxygen treatment, hyperbaric oxygen, late radiation-induced injury, cystitis, proctitis, reactive oxygen species, radiation therapy, quality of life

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