

Cryoprevention of Chemotherapy-Induced Oral Mucositis

Akademisk avhandling

som för avläggande av odontologie doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet, kommer att offentligens försvaras i Europasalen, Konferenscentrum Wallenberg, Medicinaregatan 20, Göteborg, den 6 mars, klockan 9.00

av **Aram Ibrahim**

Fakultetsopponent:

Professor Michael Brennan

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Avhandlingen baseras på följande delarbeten

- I. Walladbegi J., Henriksson R., Tavelin B., Svanberg A., Larfors G., Jadersten M., Schjesvold F., **Mahdi A.**, Garmin Legert K., Peterson E. D., Jontell M. Efficacy of a novel device for cryoprevention of oral mucositis: a randomized, blinded, multicenter, parallel group, phase 3 trial. *Bone Marrow Transplantation* 2022;57:191–7.
- II. **Mahdi A.**, Stubner J., Bergling M., Jontell M., Walladbegi J. Can cryoprevention of oral mucositis be obtained at a higher temperature? *Clinical Oral Investigations* 2021;25:4519–26.
- III. **Ibrahim A.**, Camci E., Khairallah L., Jontell M., Walladbegi J. Cryopreventive temperatures prior to chemotherapy. *Medical Oncology* 2023;40:1–7.
- IV. **Ibrahim A.**, Mahmoud D., Mavandadipur H., Walladbegi J. Interrater Reliability in the Assessment of Oral Mucositis among Patients Receiving High-Dose Chemotherapy: A Multicenter Comparison between Specialized Dentists and Registered Nurses. *BMC Cancer* 2025;25:1874–7.

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR ODONTOLOGI**



Cryoprevention of Chemotherapy-Induced Oral Mucositis

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Abstract

Oral mucositis (OM) is described as one of the most severe side effects of cancer therapy, causing immense pain that may significantly compromise treatment outcomes and increase healthcare costs. Cryoprevention using ice (IC) is a well-substantiated and recommended strategy for the prevention of chemotherapy-induced OM. However, the use of IC is associated with adverse reactions and infection risks from contaminated water. Evidence is also limited regarding optimal cooling temperature, timing and duration, leaving room for further optimization and increased tolerability of this modality. Furthermore, accurate diagnosis is essential for effective management of this condition.

The rationale for this thesis was to provide new insights into cryoprevention for chemotherapy-induced OM to improve the supportive care of cancer patients. The specific aims were to: *(i)* compare the intraoral cooling device (ICD) and IC in the prevention of OM (defined as peak OMAS-total) in a randomized controlled trial involving myeloma and lymphoma patients receiving high-dose chemotherapy in conjunction with hematopoietic stem cell transplantation; *(ii)* evaluate intraoral temperature reduction and tolerability using the ICD set to 8 °C and 15 °C, respectively, during 30 and 60 minutes of cooling; *(iii)* examine the trajectory of the intraoral temperature reduction using IC and ICD set to 8 °C and 15 °C, respectively, during a 30-minute cooling period; and *(iv)* evaluate interrater reliability between nurses and dentists specialized in orofacial medicine regarding OM assessments.

The ICD was equally effective as IC in preventing OM in myeloma patients, and even more effective in the lymphoma group (Study I). The ICD set to 15 °C was inferior to 8 °C in terms of reducing intraoral temperature (Study II). The greatest drop in intraoral temperature was seen after 5 minutes of cooling with IC, the ICD set to 15 °C and 8 °C, respectively (Study III). For OM of any grade, the overall interrater reliability between nurses and dentists specialized in orofacial medicine was found to be fair (Study IV).

This thesis highlights that the ICD is promising in the prevention of OM and that cooling does not necessarily have to be prolonged or extremely cold to achieve clinical effect. This enables more individualized and tolerable cooling protocols. At the same time, the results highlight the need for increased knowledge, training and interprofessional collaboration in the diagnosis and management of OM.

Keywords: Cryotherapy, Intraoral cooling device, Oral mucositis, Multiple myeloma, Lymphoma, Hematopoietic stem cell transplantation, High-dose chemotherapy, Tolerability, Randomized controlled trial

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