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The Management of Mucosıtıs of Pedıatrıc Hematopoıetıc Stem-Cell Transplantatıon

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Hematopoietic stem-cell transplantation (HSCT) is used primarily for hematologic and lymphoid cancers but also for many other disorders [1]. Autologous HSCT (in which stem cells are derived from the patient) is mainly used to treat chemosensitive malignancies. Allogeneic HSCT (in which the stem cells are derived from a donor) is often the preferred treatment option, particularly in patients with acute leukaemia [2]. Oral complications are a significant cause of morbidity and potential mortality for children undergoing HSCT. Oral complications can occur at all stages of HSCT and can interfere significantly with transplant recovery [3]. Oral mucositis is a major complication of HSCT and it is highly distressing to patients, and associated with significant local and systemic complications [2]. In children treated with standard chemotherapy mucositis incidence was between 25-33%, in children who underwent bone marrow transplantation, this rate rises to 100% [4].

Oral mucositis begins approximately 5-10 days following myeloablative conditioning therapy, and resolves within 2-3 weeks in over 90% patients [2]. Oral mucositis is an important clinical problem because of the pain, the requirement for parenteral nutrition and the risk of mucosal infection and subsequent septicaemia [5]. The most severe grade of oral mucositis has been shown to be significantly associated with the number of days of parenteral opioid therapy, the number of days of total parenteral nutrition, the incidence of significant infection, the number of days with fever, the overall time in hospital, and the total inpatient charges [6]. The children suffer oral mucositis-related symptoms during haematopoietic stem cell transplantation and these are: dry lips, taste perception, oral pain, mouth blisters and mouth sores [7].

The management of oral mucositis starts with a pretreatment oral assessment aimed at reducing pre-existent oral infection and trauma-inducing factors. Education on the importance of performing good oral hygiene should be undertaken at this time, and should be reinforced during the HSCT procedure [2]. Basic oral care components are; brushing teeth with a soft toothbrush, cleaning between the teeth with dental floss (if the number of platelets lower than 500.000 mm^3 or there are bleeding gums, not using toothbrush and dental floss) and mouthwashing with sterile water, saline or sodium bicarbonate [8-11] Additionally, in a study is found that laser therapy is well tolerated with remarkable reduction in pain associated with oral mucositis after 1–2 days of laser therapy [12]. The guide of the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society for Oral Oncology (MASCC/ISOO) recommends that:

- Recombinant human keratinocyte growth factor-1 (KGF-1/palifermin) be used to prevent oral mucositis (at a dose of 60 lg/kg per day for 3 days prior to conditioning treatment and for 3 days after transplant) in patients receiving high-dose chemotherapy and total body irradiation, followed by autologous stem cell transplantation, for a hematological malignancy.

- Low-level laser therapy (wavelength at 650 nm, power of 40 mW, and each square centimeter treated with the required time to a tissue energy dose of 2 J/cm2), be used to prevent oral mucositis in patients receiving HSCT conditioned with high-dose chemotherapy, with or without total body irradiation.

- Patient-controlled analgesia with morphine be used to treat pain due to oral mucositis in patients undergoing HSCT.

- Oral cryotherapy be used to prevent oral mucositis in patients receiving high-dose melphalan, with or without total body irradiation, as conditioning for HSCT.

- Intravenous glutamine not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT.

- Granulocyte-macrophage-colony-stimulating factor mouthwash not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, for autologous or allogeneic stem cell transplantation.

- Systemic pentoxifylline, administered orally, not be used to prevent oral mucositis in patients undergoing bone marrow transplantation.

- Systemic pilocarpine, administered orally, not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer, or in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT [13].

These measures are not to prevent mucositis, but to ensure that the oral cavity is maintained as clean and healthy as possible in the event that ulceration does occur. Consequently, efficacy data derived from multi-centre, randomized, placebo-controlled double-blind studies is, for the most part, non-existent for these products. While it is possible that patients might benefit from their use, it is impossible

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to recommend their application (at significant cost) based on the available anecdotal data [14].

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