

Oral Mucositis in a Patient With Aplastic Anemia Who Underwent Hematopoietic Stem Cell Transplantation: A Case Report

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Abstract

Hematopoietic stem cell transplantation therapy is frequently used to treat aplastic anemia, a rare hematological disease. After hematopoietic stem cell transplantation, most patients may develop oral mucositis as a side effect of treatment. Oral mucositis is a severe condition characterized by erythema, edema, and ulcerations of the oral mucosa. It is stated that the severity of oral mucositis in hematopoietic stem cell transplantation patients directly affects the need for total parenteral nutrition, the incidence of infection, the increase in the use of narcotics, and the prolongation of hospital stay. This case report discussed the healing process of oral mucositis with the effect of treatment and nursing care in a patient who underwent hematopoietic stem cell transplantation. The patient was evaluated comprehensively since his hospitalization, the treatment and care process was managed by taking evidence-based interventions as a guide, and the patient's oral mucositis decreased from Grade III to Grade 0, and he was discharged on the 65th day after transplantation. In conclusion, in the hematopoietic stem cell transplantation process, it is recommended that nurses evaluate the patient with a holistic perspective, use evidence-based guidelines in their practices, record and report the results of the application, take an active role in the research, and increase the analyses.

Keywords: Hematopoietic stem cell transplantation, nursing care, oral mucositis

Introduction

Aplastic anemia is a rare hematological disease. Treatment methods such as radiotherapy, chemotherapy, chemicals (pesticides, arsenic, benzene, etc.), and viruses cause aplastic anemia, but most cases are idiopathic [38]. The incidence of aplastic anemia ranges from 0.6 to 7 points per million population/year and can be seen in all age groups, with a higher incidence during childhood [15]. The main goal of treatment planning in aplastic anemia is to reduce the amount of transfusion and minimize the incidence of infection by correcting the parameters evaluated in peripheral blood [17]. For this purpose, hematopoietic stem cell transplantation (HSCT), immunosuppressive drugs, and supportive care are frequently used as treatment methods [38].

Oral mucositis (OM) is a severe condition characterized by erythema, edema, and ulcerations of the oral mucosa [23]. Head and neck radiation therapy is a complication of chemotherapy, chemoradiotherapy, and HSCT [13]. HSCT affects 75-100 % of patients, and these rates vary depending on stem cell transplantation preparation regimens. Oral intake may be impaired due to pain, leading to the need for parenteral nutrition in some cases [13]. Since oral lesions can weaken the mucosal barrier and cause local or

systemic infection, they may cause prolonged hospital stays and interrupt existing treatment [13,18].

The goal of OM treatment is to prevent or reduce the severity of lesions, manage associated symptoms, and ensure continuity of cancer treatment [26]. Frequent evaluation of oral tissues before and during cancer treatment reduces the risk of infection and helps to determine the initial stages of oral mucositis [29]. In the treatment and care of oral mucositis, it is essential to adopt oral care protocols, follow up on oral and dental health, use various mouthwashes, and provide quality nursing care with frequent evaluation of patients [13,22]. This study examined the effect of treatment and nursing care on patients with oral mucositis who underwent HSCT.

Case Report

I was diagnosed with severe aplastic anemia and married 29, a 29-year-old female patient. With the patient's consent, allogeneic peripheral stem cell transplantation was performed on a 22-year-old male donor who is not a fully compatible relative of Human Leucocyte Antigen (HLA) on **March 6, 2023**. The preparation regimen was cyclophosphamide+fludarabine (RIC regimen). Graft

Versus Host Disease (GVHD) prophylaxis, Antithymocyte Globulin (ATG) 20 mg/kg/day + Methotrexate (+1, +3, +6, +11) + Cyclosporine-a were preferred. Neutrophil engraftment occurred on day +29 (05.05.2023), but platelet engraftment did not happen when discharged on day +65.

The Oral Mucous Membrane Integrity Assessment and Monitoring Form and the World Health Organization Oral Toxicity Scale evaluated the patient's oral mucosa. Oral Mucositis Grade 0 was determined in the first evaluation. On the second day, the epigastric region was followed up with 500 mg sodium alginate, 213 mg sodium bicarbonate, and 325 mg calcium carbonate active suspension to the treatment plan due to complaints of pain and difficulty swallowing. Due to dryness in the lower lip, the patient was given D-alpha tocopheryl acetate (2*1) supplementation on the +7th day. When the patient's oral mucosa was evaluated on the +11th day, the treatment plan was updated with the significant increase in swallowing difficulty, and a swab sample was taken from the lesion in the mouth. A swab from the oral lesion revealed positive HSV-1 DNA and negative HSV-2 DNA. In addition to swallowing difficulties and pain symptoms, the use of analgesics/narcotics was altered due to herpetic dermatitis on the lip on day 21 and was evaluated as OM Grade II (**Table 1**). CMV-DNA, HSV-DNA, and Candida were sent from the oral swab due to the presence of plaques on the patient's oral mucosa on the +26th day. Diffuse lesions in the mouth (punch hole) were seen on day +28 (**Figure 1**). Candida glabrata reproduction and

Cytomegalovirus (CMV) were found negative in the swab sent from the mouth. Due to the increase in lesions in the mouth, the biopsy was performed on +35 days with suspicion of GVHD. OM Grade II was re-evaluated on +42 days with the regression of hemorrhagic lesions on the lip, white fungal plaque, and lip mucosa plaque.

The patient's mucositis showed significant regression on +51 day, and the biopsy result sent with suspicion of GVHD was negative. Although there were white plaques on the back of the tongue, mucositis regressed in other areas on day +58 (**Figure 2**), no pain symptoms were observed, and oral intake continued as fluid-soft. The nutrition team provided nutritional support, and psychosocial support was provided by the consultation-liaison psychiatry. Clinical nurses, Daily oral mucositis assessments were performed regularly. During the period when OM was at Grade II and Grade III level, information was given about the details that the patient should pay attention to in oral care (oral care 4 times a day with 8 hours intervals, mouthwashes to be used, etc.) and nutrition, and the patient was encouraged to perform self-care by cooperating with the patient. To ensure the control and follow-up of the malnutrition process, the patient's weight, waist circumference, and nutrition were also evaluated throughout the hospitalization, and follow-up was performed. Detailed information about the OM treatment process and nursing care is given in (**Table 1**). The patient was discharged with Grade 0 OM on the +65th day at the end of the whole treatment process and nursing care.

Table 1. Findings on Oral Mucositis Process and Management

After Transplant	Degree of Mucositis	Sign/Symptom	Treatment Plan and Nursing Care
+11.day	Grade I	Difficulty swallowing	0.5 g flurbiprofen and 0.24 g chlorhexidine digluconate mouthwash 4*1(1) Nystatin mouthwash 4*1(2) Carbonated mouthwash 4*1(3) D-alpha tocopheryl acetate 2*1(4) Acyclovir 2*10 mgr/kg/day Tramadol 2*50 mgr IV Oral care 4*1(5) Education (nutritional recommendations, acute treatment process, discharge training, etc.) (6)
+21.day	Grade II	Difficulty swallowing, ulceration, bleeding, 1 cm erosive lesion	(1), (2), (3), (4), (5), (6) Tramadol 2*100 mgr IV Valasiklovir tb. 3*1000mg
+22.day	Grade II	Ulceration, bleeding, difficulty swallowing and feeding (regimen 2 nutrition)	(1), (2), (3), (4), (5), (6) Tramadol 2*100 mgr IV Acyclovir 2*10 mgr/kg/day
+28.day	Grade II	Ulceration, bleeding, difficulty swallowing and feeding (regimen 1 feeding), staple hole lesion	(1), (2), (3), (4), (5), (6) Tramadol 1*100 mgr IV Traneksamik asit amp 3*2

			Foscarnet sodium hexahydrate 2*90 mgr (daily dose calculation) Ensure strawberry flavoured food 3*200 ml
+35.day	Grade III	Black drying on the lips, colored plaques on the buccal mucosa in the mouth, white plaques tending to merge with the hard palate, flat 2 cm lesion on the tongue, feeding difficulties (regime 0)	(1), (2), (3), (4), (5), (6) Tramadol 1*100 mgr IV Foscarnet sodium hexahydrate (daily dose calculation) Acyclovir 2*10 mg/kg/day Taking a biopsy from the oral mucosa with suspicion of GVHD Traneksamik amp 3*2
+42.day	Grade II	White fungal plaque in the mouth and upper palate, mucous membrane of the lips, regression in pain and bleeding, decrease in swallowing difficulty (regimen 2 nutrition)	(1), (2), (3), (4), (5), (6) Tramadol 1*50 mgr IV Foscarnet sodium hexahydrate (daily dose calculation) Tramadol amp 3*1
+48.day	Grade I	No pain and difficulty swallowing, marked regression in hemorrhagic areas, oral intake regimen 2 nutrition	(1), (2), (6) Ensure strawberry flavoured food 3*200 ml Borax gargle 4*1



Figure 1. Intraoral pictures of the patient from different points after the development of oral mucositis due to chemotherapy



Figure 2. After the treatment, the patient's intraoral pictures from different points

Discussion

This study examined the effect of treatment and nursing care on OM in patients with aplastic anemia who underwent HSCT. The main goal of OM management is to reduce the infection rate by reducing the effect of oral microbial flora. There are many recommendations for managing oral mucositis according to the evidence level. The classification of the proposals according to the level of proof is made and presented in Table 2 [11,12,30,37].

According to various cancer and treatment methods, OM and other oral complications show different incidences. Their prevalence and severity vary depending on the type of transplantation and the preparation regimen and are seen as an essential complication [1,14]. Evidence-based therapies to ensure effective symptom management and improve quality of life in HSCT patients [11,12,30,37] and the implementation of nursing care is very important [2]. The literature recommends widespread use of oral care protocols to prevent OM

since 2013 and collectively emphasizes oral care during treatment and regular evaluation of OM [7,19,35]. In the prevention and treatment of OM, oral care protocols, mouthwashes (normal saline, sodium bicarbonate, chlorhexidine gluconate), benzydamine, vitamin E, and glutamine use are included in the relevant literature [9,18,28,32]. In addition, it is reported in the research that mouthwashes such as normal saline and carbonated solutions that do not have medical content can be used 4-6 times/day in OM management. Chlorhexidine gluconate mouthwashes are an effective antiseptic, especially against gram-positive and gram-negative organisms, anaerobes, facultative anaerobes, and yeasts, and benzydamine hydrochloride is preferred as an analgesic in the prevention and treatment process of oral mucositis because it is a non-steroidal anti-inflammatory [9,18,28,32]. The effects of new methods and treatment modalities for the management of OM have become one of the areas where healthcare professionals are researching to establish evidence for the treatment of oral mucositis. For example, Silva et al. (2017) mentioned the use of dissolving pain lozenges for the local treatment of oral mucositis in their study, and in addition to cryotherapy, low-level laser therapy, herbal methods and nutritional supplements, apitherapy, essential oils and cognitive behavioral techniques are among these complementary therapies [11,32,34]. In light of all this information, considering the evidence-based care protocols in the OM process management of the case (Table 2), 0.9 % sodium chloride mouthwash, chlorhexidine gluconate, vitamin E, acyclovir use, 2 % morphine mouthwash, and super soft toothbrush were preferred in oral care 4-6 times/day. During the treatment process in HSCT patients, it is essential not to consume foods that will damage the oral mucosa [11]. Especially in

those with painful oral mucosa lesions, it is recommended to avoid acidic fruits, especially citrus fruits, acidic drinks, and spicy, salty, sharp, and rough surface foods [27]. In addition, studies have reported that products such as cold drinks, ice cream, and ice pieces held in the mouth will temporarily relieve pain [6,20,25]. In this case, the use of mucosa-irritating foods was prevented, oral care was done at least 4 times a day, nutrition education was given, and the patient was supported with cold application (ice pieces) and analgesics in severe pain.

Grade III OM is associated with mortality during periods of sepsis and immunosuppression. In the studies conducted on the subject, it has been stated that oral complications due to cancer treatment affect the quality of life and that there are delays in cancer treatment due to these problems affecting the compliance of patients with treatments [4,31,36]. In this case, the OM level progressed to Grade III, and the length of hospital stay was prolonged from +28 days to +65 days after HSCT, causing a delay in the treatment process.

Oncology nurses' use of competent, knowledgeable, evidence-based practices on oral care needs and assuming the role of caregiver, regular patient follow-up, active use of nurse-led patient education and follow-up systems, joint decision of physician and nurse on treatment and care, implementation of individual care plans on a patient basis, application of acute treatment when necessary according to the stage of mucositis contribute to OM management reported [3,5,8,18,21,24]. In this case, treatment and nursing care were applied in line with the literature and guidelines (Tables 1 and 2).

Table 2: Classification of recommendations according to level of evidence in the management of oral mucositis

Evidence	Level of Evidence*	Degree of Recommendation of Evidence**
Use of 0.9 % sodium chloride mouthwash 4-6 times/day in oral care	III	B
Daily toothbrushing with a soft toothbrush, use of super soft toothbrushes in HSCT patients, no flossing	IV	D
Establishment of oral care protocols by a multidisciplinary team, evaluation of pain and oral condition using proven scales	III	B
30 min. oral cryotherapy to prevent oral mucositis in patients receiving high-dose melphalan hydrochloride with or without concomitant total radiotherapy administered HSCT	II	A
Use of low-level laser therapy in patients receiving/not receiving total radiotherapy concomitant with high-dose chemotherapy or undergoing HSCT	II	B
Benzidamin Gargle	I	A
Intravenous use of glutamine in patients receiving high-dose chemotherapy for HSCT and/without concomitant total body radiotherapy	II	B
Klorheksidin gargle	II	B

Use of granulocyte macrophage colony stimulating factor (GM-CSF) mouthwash in patients receiving high-dose chemotherapy for autologous or allogeneic stem cell transplantation	II	C
Use of pentoxifylline in patients undergoing HSCT	II	B
The use of Acyclovir and the like in patients receiving standard-dose chemotherapy	II	B
The use of 2% morphine mouthwash in pain treatment	III	-
Use of morphine-containing patient-controlled analgesia in the treatment of pain in patients undergoing HSCT	I	A

* I: Meta-analyses of well-designed controlled trials, randomized trials (false-positive and false-negative error few), II: At least one well-designed experimental study, randomized studies (false-positive or false-negative error or both high), III: well-designed, semi-experimental studies, (non-randomized, single-group, pretest-posttest comparative, cohort, paired case-control studies), IV: Well-designed, non-experimental studies, (comparative, correlational, descriptive studies and case analyses), V: Case report and clinical examples

**A: Type I evidence or Type II-III-IV evidence shows the same results, B: Type II-II or Type IV evidence shows the same results, C: Type II-II or Type IV evidence does not show continuity, D: There is little or no empirical evidence in this area [11,12,30,37].

Result

O.M., which is one of the common complications of the HSCT process and adversely affects the treatment process, was evaluated comprehensively since the patient's hospitalization, the treatment and care process was managed by taking evidence-based interventions as a guide, and the patient's O.M. decreased from Grade III to Grade 0 and was discharged on the 65th day after transplantation. In line with this result, it is recommended that nurses, who have a primary role in the HSCT process, evaluate the patient with a holistic perspective, use evidence-based guidelines as guidelines in their practices, record and report the results of their methods, take an active role in the researches and increase the analyses.

Informed Consent: Written and verbal consent was obtained from the individual E.K. who participated in the study.

Conflict of Interest Statement: The authors have no conflict of interest to declare this was an unfunded study.

References

- Al-Rudayni AHM, Gopinath D, Maharajan MK, Veettil SK, et al. (2021) Efficacy of Oral Cryotherapy in the Prevention of Oral Mucositis Associated with Cancer Chemotherapy: Systematic Review with Meta-Analysis and Trial Sequential Analysis. *Curr Oncol.* 28(4): 2852-2867.
- Bahar A, Ovayolu Ö, Ovayolu N (2019) Common symptoms in oncology patients and nursing management. *ERU Journal of Faculty of Health Sciences.* 6(1): 42-58.
- Blakaj A, Bonomi M, Gamez ME, Blakaj DM (2019) Oral mucositis in head and neck cancer: Evidence-based management and review of clinical trial data. *Oral oncology.* 95: 29-34.
- Bowen JM, Wardill HR (2017) Advances in the understanding and management of mucositis during stem cell transplantation. *Current opinion in supportive and palliative care.* 11(4): 341-346.
- Bressan V, Stevanin S, Bianchi M, Aleo G, Bagnasco A, et al. (2016) The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: A systematic review. *Cancer treatment reviews.* 45: 105-19.
- Chan X, Tay L, Yap SJ, Wu VX, Klainin-Yobas P (2023) Effectiveness of Photobiomodulation and Oral Cryotherapy on Oral Mucositis Among Patients Undergoing Chemotherapy Conditioning Prior to Hematological Stem Cell Transplantation. *Seminars in oncology nursing.* 39(3): 151405.
- Correa MEP, Cheng KKF, Chiang K, Kandwal A, Loprinzi CL, et al. (2020) Systematic review of oral cryotherapy for the management of oral mucositis in cancer patients and clinical practice guidelines. *Support Care Cancer.* 28(5): 2449-2456.

8. Carneiro-Neto JN, de-Menezes JD, Moura LB, Massucato EM, de-Andrade CR (2017) Protocols for management of oral complications of chemotherapy and/or radiotherapy for oral cancer: Systematic review and meta-analysis current. *Medicina oral, patologia oral y cirugia buccal*. 22(1): e15-e23.
9. Çakır G, Altay N, Törüner EK (2022) Management of Oral Mucositis in Pediatric Oncology Patients Receiving Chemotherapy: Evaluation of Evidence-Based Practices. *Hacettepe University Journal of Faculty of Nursing*. 9(2): 225-232.
10. Çakmak S, Nural N (2020) Oral mucositis in patients receiving chemotherapy and radiotherapy: a review. *Dokuz Eylül University Electronic Journal of Faculty of Nursing*. 13(3): 185-194.
11. Çıtlak K, Kapucu S (2015) Current approaches to the prevention and treatment of oral mucositis in patients undergoing chemotherapy: evidence-based practices. *Hacettepe University Journal of Faculty of Nursing*. 2(1): 70-77.
12. Çavuşoğlu H (2007) Evidence-based nursing in the management of oral mucositis. *Türkiye Klinikleri J Med Sci*. 27(3): 398-406.
13. Elad S, Cheng KKF, Lalla RV, Yarom N, Hong C, et al. (2020) MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 126(19): 4423-4431.
14. Elad S, Yarom N, Zadik Y, Kuten-Shorrer M, Sonis ST (2022) The broadening scope of oral mucositis and oral ulcerative mucosal toxicities of anticancer therapies. *CA Cancer J Clin*. 72(1): 57-77.
15. ElGohary G, El Fakih R, de Latour R, Risitano A, Marsh J, et al. (2020) Haploidentical hematopoietic stem cell transplantation in aplastic anemia: a systematic review and meta-analysis of clinical outcome on behalf of the severe aplastic anemia working party of the European group for blood and marrow transplantation (SAAWP of EBMT). *Bone Marrow Transplant*. 55(10): 1906-1917.
16. Fidan Ö, Arslan S (2021) Development and Validation of the Oral Mucositis Risk Assessment Scale in Hematology Patients. *Semin Oncol Nurs*. 37(3): 151159.
17. Gafter-Gvili A, Ram R, Gurion R, Paul M, Yeshurun M, et al. (2008) ATG plus cyclosporine reduces all-cause mortality in patients with severe aplastic anemia--systematic review and meta-analysis. *Acta Haematol*. 120(4): 237-43.
18. Hong CHL, Gueiros LA, Fulton JS, Cheng KKF, Kandwal A, et al. (2019) Systematic review of basic oral care for the management of oral mucositis in cancer patients and clinical practice guidelines. *Supportive care in cancer*. 27(10): 3949-3967.
19. He M, Zhang B, Shen N, Wu N, Sun J (2018) A systematic review and meta-analysis of the effect of low-level laser therapy (LLLT) on chemotherapy-induced oral mucositis in pediatric and young patients. *Eur J Pediatr*. 177(1): 7-17.
20. Izgu N (2017) Complementary Therapies in the Management of Induced Oral Mucositis during Cancer Treatment. *Journal of Education and Research in Nursing*. 14(4): 304-311.
21. Kara H, Arikan F, Kartoz F, Korcum Sahin AF (2023) A Prospective Study of Nurse-Led Oral Mucositis Management: Impact on Health Outcomes of Patients Receiving Radiotherapy for Head and Neck Cancer and Lung Cancer. *Semin Oncol Nurs*. 39(4): 151440.
22. Koçyiğit H, Karagözoğlu Ş (2021) The Use of Comfort Theory in the Management of Nursing Care of a Patient with Acute Myeloid Leukemia. *Ege University Journal of Faculty of Nursing*. 37(3): 235-243.
23. Kusiak A, Jereczek-Fossa BA, Cichońska D, Alterio D (2020) Oncological-Therapy Related Oral Mucositis as an Interdisciplinary Problem-Literature Review. *Int J Environ Res Public Health*. 17(7): 2464.
24. Kubota K, Kobayashi W, Sakaki H, Nakagawa H, Kon T, et al. (2015) Professional oral health care reduces oral mucositis pain in patients treated by superselective intra-arterial chemotherapy concurrent with radiotherapy for oral cancer. *Supportive care in cancer*. 23(11): 3323-9.
25. Lai CC, Chen SY, Tu YK, Ding YW, Lin JJ (2021) Effectiveness of low level laser therapy versus cryotherapy in cancer patients with oral mucositis: Systematic review and network meta-analysis. *Critical reviews in oncology/hematology*. 160: 103276.
26. López-González Á, García-Quintanilla M, Guerrero-Agenjo CM, Tendero JL, Guisado-Requena IM, et al. (2021) Efficacy of Cryotherapy in the Prevention of Oral Mucositis in Adult Patients with Chemotherapy. *Int J Environ Res Public Health*. 18(3): 994.
27. Muhsiroglu O (2017) Medical nutritional therapy in cancer patients. *Gulhane Medical Journal*. 59(4): 79-88.
28. Miller MM, Donald DV, Hagemann TM (2012) Prevention and treatment of oral mucositis in children with cancer. *J Pediatr Pharmacol Ther*. 17(4): 340-50.
29. Pulito C, Cristaudo A, Porta C, Zapperi S, Blandino G, et al. (2020) Oral mucositis: the hidden side of cancer therapy. *Journal of experimental & clinical cancer research*. 39(1): 210.
30. Potting CM, Blijlevens NA, Donnelly JP, Feuth T, Van Achterberg T (2006) A scoring system for the assessment of oral mucositis in daily nursing practice. *European journal of cancer care*. 15(3): 228-34.
31. Raj D, Yavagal CM, Stanley B, Mathew CM, Yavagal PC (2022) Photobiomodulation: A Novel Treatment Approach for the Management of Radiation Induced Oral Mucositis - A Case Report. *Journal of Advanced Medical and Dental Sciences Research*. 10(4): 21-23.
32. Razmara F, Khayamzadeh M (2019) An investigation into the prevalence and treatment of oral mucositis after cancer treatment. *International Journal of Cancer Management*. 12(11): e88405.

33. Silva FC, Marto JM, Salgado A, Machado P, Silva AN, et al. (2017) Nystatin and lidocaine pastilles for the local treatment of oral mucositis. *Pharm Dev Technol.* 22(2): 266-274.
34. Sonis ST (2011) Oral mucositis. *Anticancer Drugs.* 22(7): 607-612.
35. Thornton CP, Li M, Budhathoki C, Yeh CH, Ruble K (2022) Anti-inflammatory mouthwashes for the prevention of oral mucositis in cancer therapy: an integrative review and meta-analysis. *Support Care Cancer.* 30(9): 7205-7218.
36. Valeh M, Kargar M, Mansouri A, Kamranzadeh H, Gholami K, et al. (2018) Factors affecting the incidence and severity of oral mucositis following hematopoietic stem cell transplantation. *International journal of hematology-oncology and stem cell research.* 12(2): 142-152.
37. Yayla EM (2017) Evidence-Based Applications for Mucosity. *Journal of Education and Research in Nursing.* 223-227.
38. Zhu Y, Gao Q, Hu J, Liu X, Guan D, et al. (2020) Allo-HSCT compared with immunosuppressive therapy for acquired aplastic anemia: a system review and meta-analysis. *BMC Immunol.* 21(1): 10.