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Research Article

Evaluation of the Incidence and Stage of Oral Mucositis in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Retrospective Study

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Abstract

AIM: This study aims to retrospectively evaluate the incidence and stage of oral mucositis in patients undergoing hematopoietic stem cell transplantation.

METHODS: A total of 102 patient records of patients hospitalized between 2014 and 2019 in the adult hematopoietic stem cell transplantation clinic of a tertiary university hospital in Turkey were evaluated. Data were collected through a retrospective evaluation of patient records. Records made according to the WHO Oral Toxicity Scale included in the patient records during hospitalization in the adult hematopoietic stem cell transplantation clinic were evaluated. Oral mucositis data from recordings were analyzed at baseline, and on days 5, 10, 15, and 30).

RESULTS: 96.1% ($n = 98$) of 102 patients developed oral mucositis; only 10.7% had Grade 3, and 2.7% had Grade 4. Oral mucositis development time was 8.28 ± 0.32 days, and recovery time was 14.25 ± 0.78 days. It was determined that smoking, diagnosis, transplantation type, and preparatory regimen affected the oral mucositis healing process.

CONCLUSION: While the incidence of oral mucositis in patients undergoing hematopoietic stem cell transplantation in our study was similar to be similar with the reported findings in the literature, the proportions of Grade 3 and 4 oral mucositis were lower in our study.

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

Introduction

Hematopoietic stem cell transplantation (HSCT) is a high-risk process involving chemotherapy and/or total body irradiation (TBI) and other treatments, as well as prolonged immunosuppressive therapy (Barrach et al., 2015; Osakabe et al., 2017; Staudenmaier et al., 2018). Oral mucositis is the most common complication in HSCT, causing treatment delay and affecting the success of transplantation (Barrach et al., 2015; Bowen & Wardill, 2017; Chaudhry et al., 2016). While oral mucositis is seen in approximately 80-90% of HSCT patients (Osakabe et al., 2017; Vitale et al., 2017; Walladbegi et al., 2018), this rate is 35%–75% in autologous transplants and 75%–100% in allogeneic transplants (Carulli et al., 2013; Mutluay Yayla, 2017).

Mucositis is "inflammatory/ulcerated lesions of the oral and/or gastrointestinal tract" (Mutluay Yayla, 2017; Peterson et al., 2011; Wallhult & Quinn, 2018). The incidence and degree of mucositis vary depending on the patient's risk factors, the type of disease, the treatment characteristics (preparation regimen, transplant procedure), and the disease course (Baysal & Sarı, 2016; Chaudhry et al., 2016). Some treatments suppress the growth and maturation of oral mucosal epithelial cells (Barrach et al., 2015; Bowen & Wardill, 2017), thus leading to mucositis with basal cell loss and the onset of ulceration (Vitale et al., 2017; Baysal & Sarı, 2016). Chemotherapeutic agents such as bleomycin, etoposide, 5-fluorouracil, methotrexate, and doxorubicin, which are known to affect the DNA sequence in particular, often cause mucositis (Awidi et al., 2001; Raber-Durlacher et al., 2000).

Mucositis with significant dose-limiting toxicity causes treatment doses to be reduced or skipped, thereby reducing the effectiveness of treatment (Can et al., 2007; Chaudhry et al., 2016). Previous studies report that changes in the oral cavity in HSCT patients constitute the most worrying risks (Barrach et al., 2015). Oral mucositis prevents patients from eating, drinking liquids, swallowing food, and talking (Berglund et al., 2019; Elad et al., 2015; Staudenmaier et al., 2018). Malnutrition increases the risk of pain and infection (Elad et al., 2015; Mutluay Yayla, 2017; Wallhult & Quinn, 2018), increasing the need for parenteral nutrition, or intravenous administration of nutrition, and the use of narcotic analgesia to control pain (Eduardo et al., 2015; Yıldırım et al., 2018). It has been reported that moderate-to-severe mucositis increases systemic infection, transplant-related

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mortality, and lengthens hospital stay (Bowen & Wardill, 2017; Curra et al., 2018). Consequently, it decreases the quality of life in HSCT patients and causes an increase in health care costs (Elad et al., 2015; Kusiak et al., 2020; Staudenmaier et al., 2018). Therefore, the effectiveness of interventions aimed at preventing and treating OM in order to alleviate symptoms, accelerate tissue repair, and control mucositis infections is of vital importance (Elad et al., 2015; Shouval et al., 2019). The guidelines published by the multinational association of supportive care in cancer (MASCC) and the international society of oral oncology (ISOO) (2019) recommend the use of keratinocyte growth factor in HSCT patients receiving high-dose chemotherapy and TBI (Level of Evidence II) (Multinational Association of Supportive Care in Cancer, 2019). They also recommend oral care protocols in all HSCT patients (Level of Evidence III) and the use of patient-controlled analgesia with morphine in pain due to oral mucositis (Level of Evidence II). The guidelines recommend oral cryotherapy in patients receiving bolus 5-FU and high-dose melphalan (Level of Evidence III) (Bowen & Wardill, 2017; Chen et al., 2017; Lalla et al., 2014).

The implementation of multi-agent combination oral care protocols in the HSCT process is considered the cornerstone of OM management (Level of Evidence III). It is included in the guideline in professional oral care and patient education and plays an important role in OM management (Osakabe et al. 2017). The effectiveness of oral care protocols applied by nurses in preventing OM and their impact on the incidence and degree of OM need to be constantly evaluated (Babic & Murray, 2019). There are prospective studies on this subject in the literature (Blijlevens et al., 2008; Carulli et al., 2013; Göktuna & Arslan, 2023). In this study, unlike the literature, the records and nurse records of patients whose treatment was completed were evaluated retrospectively for HSCT patients. Additionally, because this study had a retrospective design, longer-term data were obtained. This study aims to retrospectively evaluate the incidence and stage of oral mucositis (OM) in patients undergoing hematopoietic stem cell transplantation (HSCT).

Methods

Study Design
This is a single-center retrospective study.

Sample
A total of 102 patient records were examined between 2014 and 2019 in the HSCT clinic of a university hospital in Turkey. The study sample consisted of patients admitted to the clinic for HSCT due to hematological or oncological diseases, and the data from the records of these patients were used. The data regarding mucositis evaluated by the WHO Oral Toxicity Scale were obtained from the Hospital Information Management System (the records of patients aged 18 and above). Records of patients under 18 and whose WHO Oral Toxicity Scale data were not complete were excluded. Research data were retrieved from the patient records.

Data Collection
Research data were collected by the researcher through retrospective evaluation of patient records from a single center, which is a tertiary care university hospital in Turkey. The patients included in the study had received treatment at the HSCT clinic of this hospital between 2014 and 2019. The patient data were retrieved from the patient records in the hospital archive between 01 January 2020, and 30 June 2020. Research data were retrieved from the patient records. Hospital information notes and files were scanned to collect data regarding the results obtained. These records included patient data, WHO Oral Toxicity Scale data, applied OM protocol, and nurse records. OM data from recordings were analyzed at baseline, and on days 5, 10, 15, and 30).

Data Collection Tools
The research data were collected from the "Patient Information Form" and the "WHO Oral Toxicity Scale."

Patient information form
It records information about the patient's sociodemographic characteristics, presence of other chronic diseases, smoking status, previous diagnoses, treatment protocols, and supplements prescribed.

WHO oral toxicity scale
The WHO Oral Toxicity Scale is a tool designed to categorize OM into four grades. Grade 0 indicates that there is no OM, while Grade 1 indicates mild OM, Grade 2 moderate OM, Grade 3 severe OM, and Grade 4 life-threatening OM (Hong et al., 2019; Peterson et al., 2011; Vagliano et al., 2011; Yamagata et al., 2012). Grade 1 is characterized by erythema and soreness, Grade 2 erythema and the ability to swallow solid foods, Grade 3 erythema and the ability to swallow liquid foods only, and Grade 4 erythema and impossible alimentation. The scale is easy to use, suitable for repeated measurements, and can accurately describe the degree of mucositis (Hong et al., 2019; Peterson et al., 2011).

Standard prophylaxis and treatment used for OM in HSCT clinic
All patients were educated about OM before they were admitted to the HSCT clinic. The patients were examined, and other problems such as tooth decay were resolved by the dentist. From the moment the patient was admitted to the HSCT clinic, the patient's oral evaluation (for abscess, erythema, ulcer, mucosal integrity, oral hygiene, and dental prosthesis) was performed and the basic oral care protocol was initiated. Brushing with a soft-tipped toothbrush continued until the platelet count of the patient fell below 50,000 µL. If the platelet count was less than 50,000 µL, the oral care protocol was utilized. Oral cryotherapy application at the clinic was initiated approximately 30 minutes before the patients began receiving Melphalan and applied until 30 minutes after the end of Melphalan therapy.

Basic Oral Care Protocol
It includes the first medical history, oral evaluation, frequent sipping of water, rinsing the mouth with saline, and chewing sugar-free gum. Additional interventions include tooth-brushing with toothpaste, flossing, and cleaning dental prosthesis cleaning (McGuire et al., 2013; Hong et al., 2019; Huang et al., 2018; Vagliano et al., 2011). *Normal saline:* It provides a beneficial, harmless, and gentle cleaning for oral hygiene and patient

comfort (Hong et al., 2019; Huang et al., 2018; McGuire et al., 2013). It was administered as a 10 ml oral gargle 4 times a day. *Resource glutamine:* It has been administered orally at a dose of 5 grams 3 times a day. *The oral care protocol applied in the HSCT clinic according to the OM grades by the WHO Oral Toxicity Scale was as follows:* Grade 1, basic oral care protocol, normal saline gargle. Grade 2, basic oral care protocol, normal saline gargle, resource glutamine (if the patient can tolerate). Grade 3, basic oral care protocol, normal saline gargle, total parenteral nutrition (TPN). Grade 4, basic oral care protocol, normal saline gargle, morphine IV, Fentanyl (Duragesic patch).

Statistical Analysis

The data obtained during the study were evaluated using the Statistical Package for Social Sciences version 23.0 software (IBM Corp.; Armonk, NY, USA). The incidence rates and mean, standard deviation (SD) were used to evaluate the data. For nonparametric data, Mann Whitney U test was used between two groups, the Kruskal-Wallis H test in comparison of three or more groups, and a post hoc test was used to test the relationship between them. $p < .05$ was considered statistically significant.

Ethical Considerations

A written approval for the study was obtained from the Akdeniz University Clinical Research Ethics Committee (Approval no: 70904504/477, Date: Oct 15, 2019), and patient and treatment information regarding the study was obtained from the hospital. In addition, permission was obtained for the use of the data by the relevant adult stem cell transplantation unit (Approval no: 60590709/HEM-2470) and the hospital chief physician (Approval no: 26708535-900 E.151348).

Results

Demographic Characteristics of Patients With OM

OM developed in 96.1% ($n = 98$) of 102 patients, whose records were evaluated within the scope of the study. The mean age of the patients was 49.9 ± 1.2. Autologous transplantation was performed in 73.5% of the patients, and allogeneic transplantation in 26.5%. About 66.3% of the patients were male, and 85.7% of them were married; 59.2% were primary school graduates, and 65.3% were unemployed. While 62.2% of the patients never smoked in their life, 29.6% of them quit smoking at some point. About 45.9% of the patients had comorbid diseases. The mean body mass index (BMI) was 27.2 ± 0.5.

About 33.7% of the patients undergoing HSCT had Multiple Myeloma (MM), 22.4% non-Hodgkin's Lymphoma (NHL), 16.3% Acute Myeloid Leukemia (AML), 12.2% Acute Lymphoblastic Leukemia (ALL), 9.2% Hodgkin Lymphoma (HL), 4.1% Myelodysplastic Syndromes (MDS), 1% testicular cancer, and 1% uterine cancer. All of the patients had previously received chemotherapy and 3.1% had previously received chemotherapy and radiotherapy. HSCT drug protocol time was at least 2 days (34.7%) and at most 6 days (50%), with a mean of 4.35 ± 0.18 days. Before HSCT, the most used chemotherapy drugs in patients were alkylating agents ($n = 96$), antimetabolite agents ($n = 47$), and vinca alkaloids ($n = 30$). The TBI protocol was performed in 9.2% of HSCT patients (Table 1).

Table 1.
Demographic Characteristics of Patients With Oral Mucositis (n = 98)

Characteristics	N	%
Age (Mean ± SD) = 49.95 ± 1.28		
Gender		
Women	33	33.7
Man	65	66.3
Marital status		
Married	84	85,7
Single	14	14.3
Educational status		
İlliterate	2	2.0
Primary school	58	59.2
High school	24	24.5
University	14	14.3
Working status		
Working	34	34.7
Not working	64	65.3
Comorbidity		
Yes	45	45.9
No	53	54.1
Smoking habits		
Yes	8	8.2
Quitted	61	62.2
No	29	29.6
Cancer diagnosis		
Multiple myeloma	33	33.7
Non hodgkin's lymphoma	22	22.4
Acute myeloid leukemia	16	16.3
Acute lymphoblastic leukemia	12	12.2
Hodgkin lymphoma	9	9.2
Myelodysplastic syndromes	4	4.1
Testicular cancer	1	1
Uterine cancer	1	1
HSCT type		
Autologous	72	73.5
Allogeneic	26	26.5
Previously received chemotherapy from HSCT		
Yes	97	99.0
No	1	1
Previously received radiotherapy from HSCT		
Yes	3	3.1
No	95	96.9

(*Continued*)

Table 1.
Demographic Characteristics of Patients With Oral Mucositis (n = 98) (Continued)

Characteristics	N	%
HSCT regimen duration (4.35 ± 0.18)		
TBI regimen		
Yes	9	9.2
No	89	90.8
Chemotherapy treatment regimen*		
Alkylating agents	96	55.17
Antimetabolite	47	27.01
Vinca alkaloids	30	17.24
Monoclonal	1	0.57

*n participated.HSCT= Hematopoietic Stem Cell Transplantation; TBI= Total Body Irradiation.

Characteristics of OM and Grading

The patients were examined for OM on the day chemotherapy was started, one day before the transplant day, and on the days after the transplant. The mean time for developing OM at the HSCT clinic was 9 ± 0.3 days. It developed on average 1.8 ± 0.3 days after transplantation. The average number of days that OM developed after chemotherapy was 8.28 ± 0.32. The most common symptoms observed in patients with OM were impaired taste (93.9%), anorexia (91.8%), difficulty in swallowing (67.3%), and pain (35.7%) (Table 2).

All patients in the HSCT clinic developed Grade 1 OM during the period from admission to discharge. While 62.2% of them developed Grade 2 OM, it was found that 65.57% were autologous transplant patients ($p = .02$). Only 5.1% developed Grade 4 OM, and 80% were allogeneic transplant patients ($p < .001$) (Table 3).

Table 2.
Comorbid Semptoms of Patients With Oral Mucositis

Comorbid Semptoms	n	%	Cumulative (%)
Impaired taste	92	20.6	93.9
Anorexia	90	20.1	91.8
Swallowing	66	14.8	67.3
Pain	35	7.8	35.7
Difficulty eating	24	5.4	24.5
Throat pain	15	3.4	15.3
Dry mouth	9	2.0	9.2
Dry lips	7	1.6	7.1
Ulceration	4	0.9	4.1
Other*	4	0.9	4.1
Burning	4	0.9	4.1
Bleeding	3	0.7	3.1
Difficulty speaking	1	0.2	1.0

*Other= Facial edema, tongue hematoma, hypersalivation

Table 3.
Distribution of Oral Mucositis Stages by Type of Transplantation During HSCT

Oral Mucositis Stage	Type of Transplantation			
	Autologous		Allogeneic	
	n*	%	n*	%
Grade 1 (n = 98)	72	73.46	26	26.54
Grade 2 (n = 61)	40	65.57	21	34.43
Grade 3 (n = 20)	12	60	8	40
Grade 4 (n = 5)	1	20	4	80

*n participated.HSCT= Hematopoietic Stem Cell Transplantation.

At the HSCT clinic, OM grading was regularly performed on the transplant day and on the 5th, 10th, 15th, and 30. days after transplant. The incidence of OM on the transplant day (day 0) was determined as 29.6% (Grade 1-2). It was detected in the first stage of mucositis in 91.8% of the patients. About 49% of patients were found to develop Grade 1 OM on day 5 and 41.8% on day 10. The mean recovery time from OM was found to be 14.2 ± 0.7 days. On the 15th and 30th days, Grade 1 OM was determined in 19.1% and 4.1% of patients, respectively (Table 4) (Figure 1).

OM Recovery Time According to Variables

The difference was found between the mean recovery time from OM and smoking status, which means that patients who were smoking had a longer recovery time than nonsmokers ($p = .03$). When mean recovery time from OM and the type of diagnosis were analyzed together, a statistically significant difference was found between the patients diagnosed with ALL and AML and the patients diagnosed with NHL and MM ($p < .001$). Analysis of chemotherapy protocol by mean recovery time from OM also revealed another statistically significant difference between the patients using alkylating agents and antimetabolite agents ($n = 47$) and the other groups except the group using vinca alkaloids only ($p < .001$). Another difference was detected between mean recovery time from OM and the type of transplant. It was found that patients who received allogeneic transplantation had a longer recovery time than those who received autologous transplants ($p < .001$).

No statistically significant difference was found between mean recovery time from OM and age, gender, presence of comorbid disease, or TBI history (Table 5).

Discussion

Oral mucositis is a condition highly prevalent in HSCT patients and negatively affects the treatment and quality of life (Baysal & Sarı, 2016; Berger et al., 2018; Kusiak et al., 2020; Owlia et al., 2012; Staudenmaier et al., 2018; Yamagata et al., 2012). Factors such as TBI and/or myeloablative preparation regimen and transplant type applied in HSCT patients lead to OM development. In addition, risk factors such as patient characteristics (family history, age, sex, smoking, alcohol use, pre-existing dental problems, previous treatments), condition of oral mucosa (function of the salivation, ...), lack of hydration and nutrition also

Table 4.
Distribution of Oral Mucositis Stages

	Oral Mucositis Stages									
Transplant Day	**Grade 0**		**Grade 1**		**Grade 2**		**Grade 3**		**Grade 4**	
Baseline	69	70.4	27	27.6	2	2	-	-	-	-
5 days	9	9.2	48	49	31	31.6	9	9.2	1	1
10 days	35	35.7	41	41.8	15	15.3	6	6.1	1	1
15 days	69	70.4	19	19.4	4	4.1	2	2.	3	3.1
30 days	92	93.9	4	4.1	1	1	-	-	-	-

*One patient was not included. (He died on the 15th day).**Three patients were not included (Two patients transferred to another clinic, one patient died).Oral Mucositis recovery time** = 14.25 ± 0.78 (days).

accelerate the development of OM (Can et al., 2018; Shouval et al., 2019; 2020). However, the oral care protocol used and patient compliance are also important in the process. Based on evidence from previous research, MASCC and ISOO recommend the use of basic oral care protocol, normal saline, sodium bicarbonate, growth factors (palifermin), low-energy laser, cryotherapy, and morphine treatment in the presence of pain to prevent or alleviate OM during the HSCT process (Elad et al., 2021; Multinational Association of Supportive Care in Cancer, 2019). In this transplant center where the study was conducted, oral diagnosis and treatment of each patient were made by the dentist before transplantation. In the retrospective evaluation, nurses had evaluation records regarding the oral mucosa. In this transplant center, OM was observed 96.1% of the patients, only 10.7% had Grade 3, and 2.7% had Grade 4. Although the incidence of OM in patients undergoing HSCT seems to be concordant with the reported findings in the literature, the proportions of Grade 3 and 4 OM were lower in our study. It is thought that the reason for the low OM stage is due to the oral care protocol applied.

When intraoral changes in HSCT patients with and without OM were compared, dry mouth, taste disturbance, and malnutrition were reported in patients with OM (Osakabe et al. 2017; Shouval et al., 2020). Ferreira and colleagues found changes in taste (88%), changes in sour taste mouth, decreased saliva, atrophy of filiform and fungiform papillae, and decreased papillae in prolonged mucositis in HSCT patients (Ferreira et al., 2020). In our study, in patients with OM, the most common findings were erythema (94.9%), impaired taste (93.9%), loss of appetite (91.8%), difficulty swallowing (67.3%), and pain (35.7%), as well as eating difficulties, sore throat, dry mouth, and dry lips. These symptoms such as, the results are similar to those reported in the literature. Many factors are effective in the healing process of OM. In our study, it was seen that smoking, diagnosis, type of transplantation, and preparation regimen were effective in this process.

Smoking changes the microbial flora and leads to a delay in healing (Berger et al., 2020; Cleverson et al., 2014; Owlia et al., 2012). This study found that smokers had longer recovery times from OM. It has been shown in parallel with the literature that the healing process of mucositis in smokers is long, therefore, an individualized care plan should be made for each patient, keeping in mind that smokers are at a disadvantage.

In addition, in our study, it was found that patients diagnosed with ALL and AML had longer OM recovery times compared to patients who were diagnosed with NHL and MM and treated. In this working group, autologous transplantation was performed on patients with NHL and MM diagnoses, and allogenic transplantation and immunosuppressive therapy were applied to

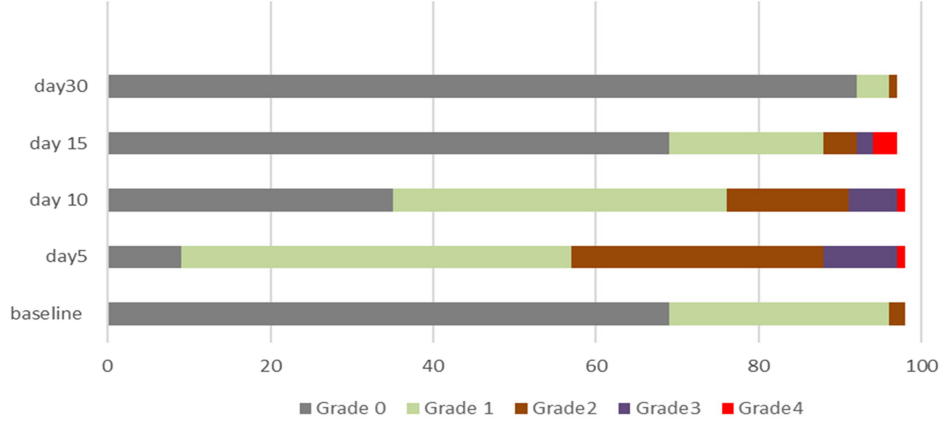

Figure 1.
Distribution of Oral Mucositis Stages

Table 5.
Comparison of Oral Mucositis Recovery Time According to Variables

Variables	Mean ± SD	*p*
Age		
0–54	15.21 ± 8.54	.34
55 and over	13.09 ± 6.33	
Gender		
Women	14.12 ± 7.39	.90
Man	14.31 ± 7.84	
Smoking habits		
Use	18.50 ± 6.78	$p < .03$*
Not use	13.86 ± 7.65	
Comorbidity		
Yes	15.35 ± 7.97	.12
No	13.37 ± 7.36	
Cancer diagnosis		
Acute lymphoblastic leukemia	21.00 ± 7.50[a]	$p < .001$*
Acute myeloid leukemia	19.33 ± 8.37[a]	
Hodgkin lymphoma	13.11 ± 6.17	
Non hodgkin's lymphoma	10.57 ± 3.77[b]	
Multiple myeloma	10.09 ± 2.66[b]	
Myelodysplastic syndromes	30.50 ± 9.32	
HSCT type		
Autologous	11.25 ± 4.46	$p < .001$*
Allogeneic	22.64 ± 8.55	
TBI regimen		
Yes	16.88 ± 6.73	.13
No		
Chemotherapy treatment regimen		
Alkylating agents (n = 40)	10.90 ± 4.37[b]	
Vinca alkaloids (n = 2)	12.50 ± 2.12	$p < .001$*
Alkylating agents + antimetabolite(n = 5)	23.08 ± 7.95[a]	
Alkylating agents + antimetabolite + vinca alkaloids (n = 19)	11.05 ± 5.05[b]	
Alkylating Agents + vinca Alkaloids (n = 7)	11.28 ± 2.98[b]	

*$p < .005$. HSCT= Hematopoietic Stem Cell Transplantation; TBI =Total Body Irradiation.

patients with ALL and AML. It is thought that this difference is due to chemotherapy protocols, transplantation type, and immunosuppressive therapy. There are studies in the literature that support these findings (Shouval et al., 2019; Wysocka-Słowik et al., 2021).

The patients receiving high doses of chemotherapy and TBI have a higher incidence and severity of OM (Berger et al., 2018; Chaudhry et al., 2016;). OM occurs between 5 and 7 days after high-dose chemotherapy (Salvador et al., 2012). In our study, the mean time of OM development was 8.2 ± 0.3 days. Some chemotherapeutic agents (such as bleomycin, etoposide, 5-fluorouracil, methotrexate, and doxorubicin) are known to cause OM more frequently (Baysal & Sarı, 2016; Scully et al., 2006). Previous work in the literature reports that high-dose methotrexate, 5-fluorouracil, and busulfan cause OM (Curra et al., 2018; Elad et al., 2021; Salvador et al., 2012). It has also been found that Melphalan leads to a higher incidence of severe OM than that of BEAM (Blijlevens et al., 2008; Castagna et al., 2007). Additionally, it was found that the patients who used alkylating + antimetabolic agents during the HSCT protocol had more prolonged recovery times (measured in days) compared to the other groups. In this sense, it can be said that the drugs used in the treatment protocol are the main determinant of severe OM risk.

Oral mucositis is more frequent and severe in patients who underwent allogeneic transplant than those receiving autologous transplant (Baysal & Sarı, 2016; Owlia et al., 2012; Vagliano et al., 2011). The follow-up during HSCT showed that the incidence of Grade 1 and Grade 2 OM was higher on day 5 and day 10. While 73.46% of the patients who underwent autologous transplantation had a grade of OM as stage 1, the percentages were found to decrease as the OM stages progressed. In allogeneic transplantation, on the other hand, stage 4 OM is seen in 80% of the patients. Of the patients who progressed to OM Stage 4 (n = 5), allogeneic transplantation was performed in four and autologous transplantation was performed in one patient. Similar to our results, Vagliano and colleagues found that severe OM was 39.7% in allogeneic transplant patients and 16.4% in autologous patients (Vagliano et al., 2011). Shouval et al. (2020) stated in their study that oral microbiota is impaired during allogeneic HSCT (Shouval et al., 2020). In this respect, the results of our study seem to be in agreement with those in the literature. This finding could be explained by the fact that the duration of mucositis is influenced by the phase of bone marrow aplasia following HSCT and the recovery of mucositis generally coincides with marrow reconstitution following stem cell infusion (Vagliano et al., 2011).

Study Limitations

The results of evaluating OM by repeated measurements over a long period of time with a valid and reliable measurement tool are presented; this is the strength of the study. The effect of oral care protocols applied specifically for HSCT in the institution where this research was conducted on the incidence and grade of OM was retrospectively revealed. However, it is a retrospective study, and data on how well patients comply with and maintain these care protocols are limited. A single-center study may limit the generalizability of the results. The inaccessibility of some records and concerns about the reliability of the records are disadvantages of retrospective studies, and these are among the limitations of our study.

Conclusion and Recommendations

As a result, grade 3 and 4 OM rates were lower compared to previous studies. In the retrospective evaluation, it was found that the nurse's application of the oral care protocol in the

management of OM contributed positively to the healing process. Risk factors were found to be effective in the development of OM, increased severity, and recovery. Prevention and treatment of OM, with the understanding of the multidisciplinary team, the importance of implementing the oral care protocol, adding the necessary medical treatments, and cooperating with the team were observed. It is obvious that positive results are obtained from OM applications performed. However, well-designed prospective and randomized controlled trials are needed to obtain more evidence.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the Akdeniz University Clinical Research Ethics Committee (Approval no: 70904504/477, Date: Oct 15, 2019).

Informed Consent: Written informed consent was obtained from the hospital management for data use in this study.

Peer-review: Externally peer-reviewed.

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