

Adherence to 2020 MASCC/ISOO Clinical Practice Guidelines for the Management of
Mucositis Secondary to Cancer Therapy at a Large Tertiary Academic Hospital

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Abstract

Background: Oral mucositis (OM) is a common side effect of cancer treatment that results in pain, increased morbidity, and increased healthcare costs. The MASCC/ISOO released updated guidelines in 2020 for the management of OM. This project found to what extent the Bone Marrow Transplant service at Academic Hospital was in compliance with clinical practice guidelines.

Methods: The Institute for Healthcare Improvement plan, do, study, act, framework was used. Baseline assessment included review of one month of OM rates. Demographic data, treatment type, transplant type, and documentation of guideline recommendations were tracked.

Intervention: A chart review was performed for patients receiving HSCT or bolus 5-FU on the Bone Marrow Service at Academic Hospital between August 1, 2023 and November 1, 2023. Patients were separated into groups according to the clinical practice guideline recommendation they met criteria for. Data was extracted from patient charts for documentation of recommended interventions as well as data to establish a baseline OM rate at Academic Hospital.

Results: Baseline rates of OM at Academic Hospital were found to be 84.6%, which is at the top of the national range. The largest group (n=37) was recommended PBM for OM prevention after HSCT. Adherence to this guideline for PBM was 0% as the Academic Hospital BMT service does not own equipment to offer PBM. Patients recommended cryotherapy during HD melphalan infusion before autologous HSCT made up a smaller group (n=22) and adhered to guidelines 77% of the time. No patients met inclusion criteria for other examined recommendations.

Conclusions: Use of PBM represents the greatest opportunity to improve OM rates, but will require a significant investment to purchase the equipment. Given the potential for cost savings,

lower morbidity, and lower mortality, Academic Hospital should begin QI efforts to institute guidelines for the use of PBM on the BMT service.

Introduction

Oral mucositis (OM) is a side effect of non-surgical cancer treatment, primarily systemic chemotherapy (CT) and radiotherapy to the head and neck. It is one of the most common side effects of oncology treatment affecting 30-40% of patients treated with CT, 60-85% of patients receiving hematopoietic stem cell transplantation (HSCT), and up to 90% of patients treated with combination radiation and CT for head and neck cancers (Pulito et al., 2020). OM first manifests as erythema and swelling and can progress to complete denuding of the oral membranes and complications leading to death (Bell & Kasi, 2023). The most common complication of OM is pain, often requiring aggressive treatment with opioid medications, as well as compromised nutritional intake and hydration, an impaired ability to speak, secondary infections, and airway compromise (Bell & Kasi, 2023). Patients who experience OM have on average a longer hospital course, higher total costs, and significantly worse outcomes (Lalla et al., 2019).

At present, there is no treatment that is wholly effective for preventing or reversing OM, but extensive research has been conducted over recent years to prevent, treat, and alleviate the symptoms of OM (Elad et al., 2020). In 2020, the Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology (MASCC/ISOO) published updated clinical practice guidelines for the prevention and management of OM (Elad et al., 2020).

These guidelines are directly relevant to the Bone Marrow Transplant (BMT) service at Academic Hospital as this service performs stem cell transplants and administers high dose CT (*Academic Hospital*, n.d.). The specific recommendations with a level one or two Level of

Evidence (LoE) made by the MASCC/ISOO guidelines that were considered in this study include (a) A recommendation for the use of intraoral photobiomodulation (PBM) using low level laser therapy for prevention of OM in adults undergoing HSCT conditioned with high-dose CT (Recommendation 1), (b) A recommendation for the use of oral cryotherapy to prevent OM in patients undergoing autologous HSCT when conditioning includes high-dose melphalan (Recommendation 2 = Group 2), (c) A recommendation to use 30 minutes of oral cryotherapy during infusion of bolus 5-FU CT to prevent OM (Recommendation 3), (d) A recommendation to use keratinocyte growth factor 1 (KGF-1) intravenously for the prevention of OM in patients undergoing autologous HSCT conditioned with a regimen that includes high-dose CT and total body irradiation (Recommendation 4).

Problem description

It was not known to what extent Academic Hospital was compliant with the MASCC/ISOO guidelines. Academic Hospital uses cryotherapy during melphalan infusion for the HSCT population, but it was not known how consistently this occurs. The Academic Hospital BMT service does not use PBM as they don't own the equipment, nor use KGF-1 for the prevention of OM. Possible barriers to implementation included time constraints, cost, planning difficulties, and workforce limitations. Some of the recommended MASCC/ISOO interventions have up front costs that require budget considerations. The incremental cost of PBM ranges from \$935 to \$2120 per patient (Kauark-Fontes et al., 2021). The cost of the growth factor KGF-1 has been reported at \$8250 for a six dose course (Panjwani, 2013).

Time to perform interventions by staff represented another possible barrier. PBM requires approximately 12 minutes per patient per day for 5 to 7 days (Zadik et al., 2019). With set up adding additional time, this could have represented a significant burden on an already

overstretched clinical staff. Planning and implementing change is difficult as many stakeholders would be involved. An exact quantification of Academic Hospital's compliance with the MASCC/ISOO guidelines was necessary to evaluate the rate of OM experienced on the BMT service at Academic Hospital

Available knowledge

THE MASCC/ISOO clinical practice guidelines were created from a summary of the best available evidence and were last updated in 2020. Numerous randomized controlled trials (RCTs) and non-RCTs have been conducted examining the use of PBM in oral mucositis representing the largest new body of evidence for the 2020 guidelines (Elad et al., 2020). The latest evidence for the 2020 guidelines reiterates the recommendation for PBM in HSCT patients and increases the range of PBM protocols that can be used (Zadik et al., 2019). The MASCC/ISOO panel examining the use of cryotherapy found sufficient evidence to increase the LoE to level 2 from level 3 for their recommendation for the use of cryotherapy during high-dose melphalan infusions, strengthening the 2014 guidelines. The guideline for the use of KGF-1 for prevention of OM in the HSCT population as a level 1 recommendation was established in the 2014 guidelines based on five RCTs, and the two new RCTs included in the 2020 guidelines confirm this. Since the 2020 update, research is ongoing and evidence continues to accrue.

Rationale

This project used the Institute for Healthcare Improvement framework using short plan-do-study-act cycles to implement the intervention. This data collection represented a first step to give a baseline for which future interventions can be measured and provide a justification for new interventions. A review of the literature suggested that the MASCC/ISOO guidelines are both evidence-based and cost effective in the prevention and treatment of OM, reducing costs for

both patients and healthcare institutions (Kauark-Fontes et al., 2021). The MASCC/ISOO guidelines are cost effective and clinically effective in the prevention and treatment of OM in the HSCT population and Academic Hospital's BMT service can benefit from the implementation of these treatment modalities.

Specific Aims

The specific aim of this study was to review rates of OM in the HSCT population and determine to what extent the MASCC/ISOO guidelines are adhered to at Academic Hospital. Quantifying this data can guide future decisions and help justify the up-front cost of new beneficial interventions.

Context

Academic Hospital is a large urban academic medical center that has a dedicated bone marrow transplant service with a specialized 30 bed bone marrow transplant unit (*Academic Hospital*, n.d.). In addition to performing stem cell transplants, the BMT service cares for patients receiving chemotherapy, radiotherapy, and immunotherapy for a range of illnesses including hematologic malignancies, aplastic anemia, and myelofibrosis. The BMT service also provides supportive care for the sequela of these treatments such as infections, OM, and graft vs host disease (*Academic Hospital*, n.d.). The adult transplant program has performed more than 3,800 stem cell transplants, including more than 1,200 allogeneic transplants, and is associated with a cancer institute which runs more than 400 clinical trials per year (*Academic Hospital*, n.d.). Changes in policy and procedure are common to accommodate these studies as well as to implement the latest evidence based care. The bone marrow transplant team at Academic Hospital includes Hematologists, medical and radiation oncologists, pharmacists, nurse

practitioners, physician assistants, registered nurses, certified nursing assistants, as well as associated administrative and support staff.

Interventions

A chart review has been performed for patients admitted to the BMT service between the time period of August 1, 2023 and November 1, 2023 who are receiving bolus 5-FU or a HSCT. For the first 30 days, data gathered included the presence of an OM diagnosis to establish a baseline.

For patients admitted between September 1 and November 1, each chart that met the above criteria was reviewed and analyzed for documentation of interventions from recommendations 1 through 4. The presence or absence of a documented intervention associated with a guideline has been recorded.

Cryotherapy has been counted as occurring if there is documentation confirming it was administered during melphalan or 5-FU infusions. The use of KGF-1 has been evaluated on the three days before total body irradiation and on the three days following HSCT and was considered present if it is charted during these times. The use of PBM has been evaluated from the first day of conditioning to two days after conditioning ends and was considered present if it is documented during this time and conforms to one of the protocols recommended by the guidelines as noted in Appendix A.

Patient data gathered included information regarding demographics, diagnosis, and treatment as detailed in Appendix B. Exclusion criteria for this study will include (a) history of previous transplantation of either stem cells or solid organs, (b) planned or previous chimeric antigen receptor (CAR-T) cell therapy, (c) inability to follow a patient through their entire

expected clinical course for the admission, eg. transfer to another institution, leaving AMA, or death.

Study of the interventions

Data was gathered retrospectively from the electronic health record and recorded on a spreadsheet for analysis. No patients were directly contacted.

No unexpected events happened during this project which impacted adherence with guidelines. There were no delays, inconsistencies, or other problems with data collection from the electronic medical record. No modifications or adaptations to the interventions were needed. The absence of unanticipated events, emergencies, or issues with data collection were taken as evidence that the intervention achieved the stated aim.

Measures

The Institute for Healthcare Improvement framework uses outcome measures, process measures, and balancing measures to evaluate quality improvement projects and their impact (Scoville & Little, 2014). The outcome measures for this project are Academic Hospital's adherence with the MASCC/ISOO guidelines.

Process measures ensure the project is performing as planned, in this case accurately reporting Academic Hospital's adherence to recommendations 1 through 4. As detailed in "study of the interventions" above, there were no events or issues requiring reporting.

Balancing measures are meant to look at the system along other dimensions to make sure there are not unanticipated negative effects from the project. Loss of data and any breach of patient confidentiality were monitored for, but no events occurred which required reporting.

Tools used for this project include Academic Hospital's electronic medical record, a spreadsheet for collecting data, and a table to show Academic Hospital's overall compliance with

each investigated guideline. Each of these tools is expected to be valid and reliable within the limits of human error.

Analysis

Patients were grouped into subpopulations according to the guideline they met criteria for, eg. Group 1 are those patients to whom Recommendation 1 applies and so forth. Adherence was evaluated for each group by finding the percentage of patients that had documentation showing compliance with their associated guideline. Each subpopulation was independently evaluated and reported.

Outcome data was organized into a table showing total number of patients, total men, total women, average age, average length of stay, and overall guideline adherence for each subpopulation, see appendix C. Process and balancing measures have been reported individually and analyzed qualitatively, noting their individual impact on the study and outcome measure. The OM diagnosis rate between August 1 and September 1 have been reported for the population as a whole. Data was stored on an encrypted cloud service approved by Academic Hospital.

Ethical considerations

All patient information has been deidentified. This study was approved by the Academic Hospital's Institutional Review Board. I have no conflicts of interest or other ethical conflicts.

Results

This project took place between August 1st, 2023 though October 31st, 2023, and during this time 50 patients met inclusion criteria. The study population included 19 females and 31 males with ages ranging from 27 to 77. The average age was 54. Length of admission ranged from 10 to 60 days with an average of 21 days. No patients received bolus 5-FU or total body

irradiation with high-dose CT for autologous HSCT during the examined time interval. Every patient received a HSCT.

Baseline OM rates were measured from August 1st, 2023 through August 31st, 2023. There were 13 patients who met inclusion criteria during this time. Of these 13 patients, eleven had documentation of the presence of OM for a baseline rate of 84.6%.

Compliance with the MASCC/ISOO guidelines was evaluated from September 1st, 2023 through October 31st, 2023. During this time 37 patients met inclusion criteria. All 37 patients met inclusion criteria for Recommendation 1, and 22 met criteria for Recommendation 2. Of the 37 patients who met inclusion criteria for Recommendation 1, none had documentation of PBM therapy during the examined time period. Of the 22 patients who met inclusion criteria for Recommendation 2, seventeen had documentation of oral cryotherapy. No patients met inclusion criteria for Recommendation 3 or 4.

Summary

The key finding of this study is utilization of PBM represents the greatest opportunity for improvement in preventing OM on the BMT service at Academic Hospital. Group 1 was both the largest group and had the poorest compliance with guidelines at 0%. Alignment with guidelines was much higher in Group 2. This group was slightly smaller at 22 patients and had an overall compliance with guidelines of 77.2%. There is no evidence that Recommendation 3 or 4 are applicable to Academic Hospital as there was no use of bolus 5-FU or high-dose CT with total body irradiation before autologous HSCT on the BMT service during the examined time interval.

Interpretation

National rates of OM range from 60-85% for patients receiving HSCT (Pulito et al., 2020). The rate of OM at Academic Hospital is within this range, but near the top at 84.6%.

Recommendation 1 represents the largest opportunity for improving OM rates at Academic Hospital. Patients for whom recommendation 1 applies comprise the largest group of patients in this study and had the lowest level of compliance with guidelines. Additionally, recommendation 1 has the highest level of evidential support of any of the examined MASCC/ISOO guidelines. Evidence strongly supports both clinical efficacy and cost effectiveness of PBM for preventing OM (Kauark-Fontes et al., 2021).

While Group 2 represented a significant portion of the study population, it was smaller than Group 1 and compliance with guidelines was much higher at over 77%. It is notable that while documentation of the provision of cryotherapy was present more than three quarters of the time, orders to provide cryotherapy were present for every patient in this group. It can be hypothesized that actual rates of completed cryotherapy were likely higher than documented. The smaller size and higher rates of compliance in Group 2, as compared to Group 1, means the potential for improvement in OM rates by improving adherence to cryotherapy guidelines is relatively small, though it may be fairly straightforward to achieve 100% compliance if the issue is mostly due to documentation.

Limitations

This project had several limitations. In examining baseline rates of OM, only the presence of OM was measured while severity was not considered. It is possible the incidence of OM at Academic Hospital could be seen in a more favorable light if the high observed rate was counterbalanced by a correspondingly low severity as compared to the national average. Additionally, the use of PBM by other institutions was not considered in the comparison of OM rates to Academic Hospital.

Adherence to guidelines was evaluated by examining documentation rather than by looking at clinical practice. It is possible that practice does not match documentation, as exemplified by the likely higher rates of cryotherapy in practice than documentation in the chart would suggest.

The limited time scope of this project may have resulted in less accurate findings than otherwise may have resulted from a longer project time frame. In particular, no occurrence of the use of bolus 5-FU or high-dose CT and TBI for autologous HSCT was found. It is unclear if these methodologies are used at Academic Hospital, meaning Recommendations 3 and 4 may not be applicable to Academic Hospital. A longer investigation may have shown these modalities used and thus suggest further avenues for improvement.

Conclusions

Rates of OM at Academic Hospital are at the upper range of what is commonly reported in the literature (Pulito et al., 2020). OM carries both significant financial costs as well as human costs in pain, suffering, morbidity, and mortality (Bell & Kasi, 2023; Lalla et al., 2019). Given the high burdens of OM, efforts should be made to reduce both its incidence and severity. Future efforts should be focused on interventions with the highest potential impact, affect the largest number of people, and are best supported by evidence. While continued effort should be made to research novel treatment modalities to prevent and treat OM, the MASCC/ISOO recommendation for the use of PBM to prevent OM in patients conditioned with high-dose CT for HSCT is currently the clear best opportunity for improvement. Academic Hospital should move forward with quality improvement efforts to institute the MASCC/ISOO recommendation for the use of PBM on the BMT service to adhere to the clinical practice guidelines for the management of OM.

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Appendix A

Cancer Treatment Modality	Wavelength, nm	Power Density (Irradiance), mW/cm ²	Time per Spot, s	Energy Density (Fluence), J/cm ²	Spot Size, cm ²	No. of Sites	Duration
HSCT	632.8	31.25	40	1.0	0.8	18	From the d after cessation of conditioning for 5 d
	650	1000 ^b	2	2.0	0.04	54-70	From the first d of conditioning to d + 2 post-HSCT (for 7-13 d)
RT	632.8	24	125	3.0	1.00	12	Entire RT course
RT-CT	660	417 ^b	10	4.2	0.24	72	Entire RT course
	660	625 ^b	10	6.2	0.04	69	Entire RT course

Abbreviations: CT, chemotherapy; HSCT, hematopoietic stem-cell transplantation; RT, radiotherapy.

^a For details, see Zadik et al, 2019.¹³

^b This involves a potential thermal effect; the clinician is advised to pay attention to the specific parameters.

Table placed here for reference. Originally published by Elad et al., (2020).

Appendix B

Demographic information collected

- Age - See table in appendix D
- Sex - See table in appendix D
- Length of admission in days - See table in appendix D
- Admission diagnosis - acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoid leukemia (ALL), mixed phenotype acute leukemia, primary

myelofibrosis, myelodysplastic syndrome (MDS), lymphoma, mycosis fungoides, and Sezary syndrome

- Chemotherapy and/or radiotherapy treatment - Flu/Mel, Flu/TBI, Bu/Cy, Bu/Flu, Bu/Cy/TT, BEAM, Melphalan, Cy/TBI, Carmustine + TT, Cy/TBI, and Flu/Cy + TBI
- Type of stem cell transplant - 28 autologous transplants, 17 unrelated donor transplants, two matched related donor transplants, and three haploidentical related donor transplants

Appendix C

	Total patients	Men	Women	Average age	Average LOS	Overall adherence
Whole population	50	31	19	54	21	NA
Group 1	37	22	15	57	19	0%
Group 2	22	14	8	57	15	77.2%
Group 3	0	0	0	NA	NA	NA
Group 4	0	0	0	NA	NA	NA

Recommendation 1 applies to Group 1

Recommendation 2 applies to Group 2

Recommendation 3 applies to Group 3

Recommendation 4 applies to Group 4