

# ABSTRACT

## Introduction

The purpose of this multicentre observational study was to describe the factors associated with significant and/or persistent dysgeusia symptoms in patients undergoing hematopoietic stem cell transplantation (HSCT).

## Methods

257 autologous and allogeneic HSCT patients at six cancer centers were followed pre-HSCT, regularly during HSCT hospitalization and up to 12 months post-HSCT. Patients with significant and/or persistent dysgeusia were then compared to non-affected patients with respect to factors such as transplant type, previous chemotherapy, HSCT conditioning regimen, oral mucositis, plaque scores, salivary flow, pre-existing periodontal disease and/or untreated dental disease, oral hygiene practices and pre-HSCT dental care.

## Results

Overall, dysgeusia symptoms were reported by 30.4% of patients who had received previous chemotherapy. 81/239 (34%) reported taste change at any time during their hospitalization. Of patients reporting oral symptoms, 17.2% said that taste change was the worst symptom, often preventing the patient from eating solid foods or swallowing liquids. One year following HSCT, only 14 patients reported significant taste change and only 7 patients reported a significant reduction in taste sensitivity. Factors that seemed to predict significant and/or persistent dysgeusia post-HSCT included taste change from previous chemotherapy, allogeneic transplant, full intensity chemotherapy and advanced age.

## Conclusions

Dysgeusia is an important quality of life issue in the HSCT patient population that is reported in a significant percentage of patients pre-HSCT but is rarely reported 12 months post-HSCT. In some patients, it can affect the patient's ability to eat and/or swallow. Severe and/or persistent dysgeusia seems most strongly associated with taste change from prior chemotherapy, full intensity conditioning, allogeneic transplant and advanced age.

# LONGITUDINAL ASSESSMENT AND PREDICTORS OF DYSGEUSIA (TASTE CHANGE) DURING AND AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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## INTRODUCTION

Dysgeusia is a commonly reported side-effect of cancer therapy generally and HSCT specifically. HSCT patients represent a distinct population in which taste is potentially impaired by numerous factors including conditioning regimen-related mucosal injury, prophylactic and supportive medications and changes in the oropharyngeal and gastrointestinal microflora. The contributors to dysgeusia may differ between autologous and allogeneic transplant patients. The purpose of this prospective multicenter study was to describe the factors predictive of dysgeusia, especially significant (grade 3-4) and/or persistent dysgeusia, in a large international cohort of patients undergoing either autologous or allogeneic HSCT for a variety of hematologic malignancies.

## METHODS AND MATERIALS

257 patients completed examinations prior to HSCT and 239 patients (143 allogeneic and 96 autologous) had oral examinations and most completed questionnaires every 3 days during hospitalization. Autologous patients were followed up in person and by questionnaire at Day 100 and one year post-HSCT by questionnaire to identify any long-term side effects. Allogeneic patients were examined in –person and by questionnaire at Day 100, 6 months and 12 months. Dysgeusia patients were compared with asymptomatic patients with respect to factors such as diagnosis, transplant type, previous chemotherapy, conditioning regimen(s), oral mucositis, plaque scores, oral hygiene practices, salivary flow, pre-existing periodontal disease, untreated dental disease, frequency of pre-HSCT dental treatment, age and sex.

## RESULTS

Taste change was commonly reported by patients prior to HSCT and continued to be a factor for a subset of patients during hospitalization. Factors associated with severe dysgeusia during hospitalization included full intensity conditioning (p=.05), melphalan conditioning (p=.04) and taste change from previous chemotherapy (p=.02). Patients with more severe mucositis reported a higher rate of taste change during hospitalization (p=.007) than other patients. At Day 100 follow-up, allogeneic showed higher rates of severe dysgeusia than autologous patients (p=.03) Only 14 patients reported severe taste change at 12 month follow-up and only 7 patients reported their reduction of taste sensitivity as severe. Older age was the only factor associated with severe dysgeusia at 12 month follow-up (p=.01).

Factor	At baseline	During hospitalization	At Day 100	At 12 months
Age	1.0	1.0	1.0	1.0
Gender	1.0	1.0	1.0	1.0
Transplant type	1.0	1.0	1.0	1.0
Regimen	1.0	1.0	1.0	1.0
WHO mucositis	1.0	1.0	1.0	1.0
Plaque score	1.0	1.0	1.0	1.0
Salivary flow	1.0	1.0	1.0	1.0
Periodontal disease	1.0	1.0	1.0	1.0
Untreated dental disease	1.0	1.0	1.0	1.0
Frequency of dental care	1.0	1.0	1.0	1.0

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Salivary flow	1.0	1.0	1.0	1.0
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Untreated dental disease	1.0	1.0	1.0	1.0
Frequency of dental care	1.0	1.0	1.0	1.0

Factor	Odds Ratio (95% CI)	p-value
Age at baseline: 5 year increase	1.0 (0.9, 1.0)	0.3496
Gender: Female vs Male	1.1 (0.7, 1.7)	0.6362
Type of Transplant: Allogeneic vs Autologous	1.0 (0.6, 1.6)	0.8656
Regimen: FIC/Myeloablative vs RIC/NMA	2.1 (1.0, 4.4)	<b>0.0544</b>
Melphalan: Yes vs No	1.4 (0.6, 3.6)	0.4759
WHO mucositis: < Grade 2 vs Grade 2+	0.8 (0.5, 1.3)	0.3421
Plaque score: 0-20% of teeth vs 21+% of teeth	1.4 (0.8, 2.3)	0.2412
Salivary flow: <5 ml/5 min vs 5+ ml/5 min	1.0 (0.6, 1.6)	0.9354
Any teeth with a periodontal pocket >5 mm: Yes vs No	0.8 (0.4, 1.7)	0.6183
Brushing habits: twice/day + vs < twice/day	0.8 (0.5, 1.4)	0.4736
Flossing habits: once/day + vs < once/day	1.0 (0.7, 1.6)	0.9692
Dental Visits: Never/acute problems vs Routinely	1.3 (0.8, 2.1)	0.3629
Prior Chemotherapy: Yes vs No	1.1 (0.4, 2.8)	0.8724
Taste change from prior chemo: Yes vs No	1.7 (1.1, 2.8)	<b>0.0224</b>
Untreated dental disease: Yes vs No	0.8 (0.5, 1.4)	0.4776
Taste change at baseline: Yes vs No	0.7 (0.3, 1.4)	0.3032

Factor	3 months		6 months		12 months	
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Age at baseline: 5 year increase	1.3 (1.1, 1.5)	<b>0.0015</b>	1.3 (1.1, 1.7)	<b>0.0070</b>	1.6 (1.1, 2.4)	<b>0.0145</b>
Gender: Female vs Male	1.3 (0.6, 2.7)	0.4807	1.2 (0.4, 3.6)	0.7479	2.7 (0.8, 9.1)	0.0972
Type of Transplant: Allogeneic vs Autologous	2.2 (1.1, 4.0)	<b>0.0265</b>			1.2 (0.2, 5.5)	0.8393
Regimen: FIC/Myeloablative vs RIC/NMA	1.7 (0.5, 5.9)	0.4028	2.1 (0.5, 8.9)	0.3156	0.6 (0.1, 2.6)	0.5083
WHO mucositis: < Grade 1 vs Grade 2+	1.1 (0.5, 2.4)	0.7570	0.8 (0.2, 2.8)	0.7373	1.0 (0.3, 3.4)	0.9863
Plaque score: 0-30% of teeth vs 31+% of teeth	1.8 (0.7, 4.6)	0.2802	0.9 (0.3, 2.8)	0.8659	1.9 (0.4, 7.7)	0.3970
Salivary flow: <5 ml/5 min vs 5+ ml/5 min	1.3 (0.6, 2.7)	0.3812	0.7 (0.2, 2.1)	0.4925	2.2 (0.7, 6.8)	0.1881
Any teeth with a periodontal pocket >5 mm: Yes vs No	2.1 (0.8, 5.2)	0.1200	1.0 (0.2, 5.9)	0.9576	0.7 (0.1, 4.8)	0.7139
Brushing habits: twice/day + vs < twice/day	1.2 (0.5, 2.7)	0.1493	0.4 (0.1, 1.1)	0.0894	1.9 (0.4, 9.4)	0.4211
Flossing habits: once/day + vs < once/day	1.7 (0.8, 3.8)	0.1744	0.6 (0.2, 1.8)	0.3315	0.9 (0.3, 2.9)	0.8214
Dental Visits: Never/acute problems vs Routinely	0.8 (0.3, 1.8)	0.5289	1.9 (0.6, 6.0)	0.2707	1.4 (0.4, 4.9)	0.5645
Prior Chemotherapy: Yes vs No	1.0 (0.2, 5.3)	0.9762	1.1 (0.1, 8.1)	0.9447	0.7 (0.1, 6.5)	0.7460
Taste change from prior chemo: Yes vs No	1.7 (0.8, 3.4)	0.1677	1.1 (0.4, 3.1)	0.8257	1.4 (0.4, 4.9)	0.5580
Dry mouth from prior chemo: Yes vs No	1.5 (0.7, 3.1)	0.3345	1.2 (0.4, 3.6)	0.7823	1.9 (0.6, 6.2)	0.3021
Microabs from prior chemo: Yes vs No	1.4 (0.5, 4.2)	0.5842	1.8 (0.5, 6.4)	0.3737	1.2 (0.3, 5.0)	0.7885
Untreated dental disease: Yes vs No	1.0 (0.5, 2.1)	0.9973	0.6 (0.2, 2.1)	0.4237	0.4 (0.1, 1.6)	0.2166
Taste change during hospitalization: Yes vs No	1.3 (0.6, 3.0)	0.4768	1.1 (0.3, 3.9)	0.8574	1.7 (0.5, 6.1)	0.4279

## DISCUSSION

In this study, we looked at factors associated with increased dysgeusia symptoms during hospitalization as well as factors associated with more severe dysgeusia over the 12 months of observation.

Patients treated with full intensity conditioning, patients who received melphalan as part of their conditioning chemotherapy and patients who had taste change from previous chemotherapy were more likely to experience severe dysgeusia during hospitalization. Patients with more severe oral mucositis reported dysgeusia symptoms more frequently than other patients.

Overall, allogeneic HSCT patients reported higher rates of significant dysgeusia at Day 100. At 12 month follow-up, only a small number of patients reported significant taste change or reductions in taste sensitivity. Advanced age was associated with higher rates of severe dysgeusia one year post-HSCT

## CONCLUSIONS

Oral side-effects from HSCT are common and can dramatically affect nutrition and overall quality of life. In this large multicenter prospective observational study, dysgeusia was not shown to be associated with factors such as disease type, gender, pre-HSCT dental care, oral hygiene practices, untreated periodontal or dental disease or GVHD status. Oral mucositis, full intensity conditioning and the use of melphalan was associated with increased frequency and/or severity of dysgeusia symptoms during hospitalization. Clinicians may therefore lessen the burden of dysgeusia by more effective management of oral mucositis during hospitalization. In general, dysgeusia symptoms do not persist in most patients one year post-HSCT.