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Original Research Article

Cost-effectiveness of the introduction of specialized oral care with laser therapy in hematopoietic stem cell transplantation

Letícia Mello Bezinelli[1,2], Fernanda de Paula Eduardo[1], Roberta Marques da Graça Lopes[1], Maria Gabriela Haye Biazevic[2], Carlos de Paula Eduardo[3], Luciana Correa[4], Nelson Hamerschlak[1,5]* and Edgard Michel-Crosato[2]

[1]*Unit of Bone Marrow Transplantation, Hospital Israelita Albert Einstein, São Paulo, Brazil*
[2]*Department of Social Dentistry, Universidade de São Paulo, São Paulo, Brazil*
[3]*Department of Restorative Dentistry (LELO—Special Laboratory of Lasers in Dentistry), School of Dentistry, University of São Paulo, São Paulo, Brazil*
[4]*General Pathology Department, School of Dentistry, Universidade de São Paulo, São Paulo, Brazil*
[5]*Centro de Pesquisa Clínica, Instituto Israelita de Ensino e Pesquisa Albert Einstein, São Paulo, Brazil*

**Correspondence to:*
Nelson Hamerschlak, Centro de Pesquisa Clínica, Instituto Israelita de Ensino e Pesquisa Albert Einstein, Av. Albert Einstein, 627/520, São Paulo, SP, CEP 05651-901, Brazil.
E-mail: hamer@einstein.br

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Abstract

Oral mucositis (OM) is one of the side effects of hematopoietic stem cell transplantation (HSCT), resulting in major morbidity. The aim of this study was to determine the cost-effectiveness of the introduction of a specialized oral care program including laser therapy in the care of patients receiving HSCT with regard to morbidity associated with OM. Clinical information was gathered on 167 patients undergoing HSCT and divided according to the presence ($n = 91$) or absence ($n = 76$) of laser therapy and oral care. Cost analysis included daily hospital fees, parenteral nutrition (PN) and prescription of opioids. It was observed that the group without laser therapy (group II) showed a higher frequency of severe degrees of OM (relative risk = 16.8, 95% confidence interval −5.8 to 48.9, $p < 0.001$), with a significant association between this severity and the use of PN ($p = 0.001$), prescription of opioids ($p < 0.001$), pain in the oral cavity ($p = 0.003$) and fever > 37.8°C ($p = 0.005$). Hospitalization costs in this group were up to 30% higher. The introduction of oral care by a multidisciplinary staff including laser therapy helps reduce morbidity resulting from OM and, consequently, helps minimize hospitalization costs associated with HSCT, even considering therapy costs. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: hematopoietic stem cell transplantation; oral mucositis; oral hygiene; low-level laser therapy

Introduction

Control of infectious foci and maintenance of the mucosal mechanical barrier are essential for the success of hematopoietic stem cell transplantation (HSCT). Oral mucositis (OM) is a common morbid condition during high-dose chemotherapy, with loss of oral mucosal integrity and possible systemic effects [1]. Absence of adequate prevention and treatment of OM may lead to the need to introduce parenteral nutrition (PN) and to an increase in the number of days in use of injectable narcotics, fever, risk of secondary infections, hospitalization times, and hospital costs and mortality, in the period of up to 100 days post-HSCT [2].

Because of the high impact of OM on the success of transplantation and the patient's quality of life, studies related to oral care of the patient submitted to HSCT have focused on the different forms of therapy and prevention of OM [1,3]. It has been shown that oral cleaning alone can lead to a reduction in the severity and duration of OM [4,5], which suggests that OM is caused not only by the cytotoxic effects and aplasia during HSCT but also by unfavourable conditions in the mouth. Nevertheless, neither the clinical benefits of oral care during HSCT nor the costs of this care in the total cost of transplantations have yet been completely established.

Low-level laser therapy (LLLT) is considered one of the most effective forms of therapy for OM in the prevention and repair of oral mucosa lesions [6]. Because of its biomodulator effect, laser works by protecting the mucosal integrity, theoretically decreasing the risk of opportunistic infections in the mouth. Various studies have demonstrated a reduction in severity and duration of OM; however, few have evaluated the link between this efficacy and the wider scope of actions to promote oral health [7–10].

The introduction of an oral care program including laser therapy in the treatment of cancer patients requires specialized staff and equipment. Thus, the aim of this study was to evaluate the cost-effectiveness of a specialized oral care program including laser therapy (laser plus oral care or LOC) in patients undergoing HSCT, on the basis of the hypothesis that the institution of specific protocols for the maintenance of oral mucosal integrity and elimination of infectious foci, associated with specific therapy for OM based on laser therapy, can contribute to a reduction in hospital costs and morbidity.

Methods

Design, patients and data collection

The following methodology for conducting a case–control, retrospective, cost-analysis study was approved by the Research Ethics Committee of our institution (Hospital Israelita Albert Einstein, a private hospital in Brazil).

The medical records of all consecutive patients submitted to autologous and allogeneic HSCT during the period 2000 to 2008 in a private hospital in Brazil were evaluated retrospectively. These were divided into two groups: group I comprised patients who received LOC and were followed up by a dentist during HSCT; and group II comprised patients who did not receive LOC, only a basic self-applied oral care, before the introduction of a specialized team of dentists in our institution.

All the medical records of patients submitted to HSCT during the study period, irrespective of the type of transplant, sex and age, were included. Exclusion criteria were medical records of patients who died early in the process (before the marrow had engrafted) and/or who died before completing 28 days of post-HSCT observation, and records with missing clinical information, or doubtful information, particularly those with inconsistencies between the information described by the nursing staff, doctors and dentists. Incomplete medical records lead also to the exclusion of the case.

The following information was collected: sex, age, primary disease diagnosis, chemotherapy protocol, prophylaxis against graft versus host disease (GVHD), number of days in use of PN, presence of diarrhoea and culture results, fever, infection, pain in the oral cavity and pain when swallowing, analgesic prescription (both opioids and non-opioids) for any reason, degree of OM and number of days of hospitalization. The OM grade was recorded daily, according to the WHO classification [11], starting on the first day of conditioning until the marrow engrafted. Information was gathered on the maximum degrees of OM up to 35 days post-HSCT.

Clinical care

All HSCT patients included in this study received the same protocol of infection prevention: intravenous (IV) administration of acyclovir (GlaxoSmithKline México S.A,, Xochimilco, Mexico) (10 mg/kg body weight, three times per day) or valaciclovir (Glaxo Welcome, Aranda de Duero, Spain) (500 mg/day), fluconazole (Laboratórios Pfizer LTDA, Guarulhos, Brazil) (400 mg/day), antibiotic (sulphametazol plus trimetroprim, brand name Bactrim®, Roche, Rio de Janeiro, Brazil) (400 mg of sulfamethoxazole associated to 80 mg of trimethoprim per day) and levofloxacin (Aventis, Compiégne, France) (500 mg/day).

Patients in group II (control) were those being treated in our hospital before the introduction of a dentist team in the transplant unit. These patients received basic oral hygiene performed by the nursing team while in hospital and had cetylpyridinium chloride mouthwash (Cepacol, Sanofi-Aventis; São Paulo, Brazil) or bicarbonated water or alcohol-free mouthwash with enzymatic action (Oral Rinse, Biotène (GlaxoSmithKline Brasil LTDA, Rio de Janeiro, Brazil)) prescribed for oral washes at home and/or in the hospital. The amount of liquid used each time was not controlled, but it usually consisted of one full bottle cap, which is enough to fill the mouth, three times per day, after teeth brushing. These patients were not seen by a dentist during HSCT or engraftment period: in this group, the oral hygiene was oriented by the attending physicians and nurses only. Oral hygiene procedures were verified by the nurses and doctors, and registered in the medical records.

Group I (the ‘laser plus oral care’) comprised a cohort of patients who received HSCT after the introduction of the dentists team in our transplantation unit (in 2004). Therefore, they had the opportunity to receive specialized oral care, which included oral clinical exams by a dental professional, before and during HSCT, oral hygiene guidance and sessions of LLLT or LLLT only. Only three dentists of the hospital’s staff, working according to the same institutional treatment protocol, evaluated and treated all the patients, in both groups.

The oral procedures that the group I patients received were intra-oral clinical exam, intra-oral and extra-oral radiographs, and guidance on oral hygiene, including the use of a toothbrush, dental floss and an alcohol-free mouthwash with enzymatic action (Oral Rinse); moisturizing the lips with a cocoa butter lip balm (three times a day) when lips were dry, and vitamin E (twice a day); treatment for xerostomia, when present, with a moisturizing gel (Oral Balance, Biotène, three to four times a day); topical application of nystatin (10 ml, swishing for 1 min and then swallowing, three times per day) in the occurrence of opportunist fungal infections; and LLLT, which was started 1 day after the conditioning and continued on a daily basis until the marrow engrafted, even in the absence of OM.

The areas irradiated were the bilateral buccal mucosa, edge of the tongue, palate, floor of the mouth and labial mucosa [12]. Whenever tolerated by the patient, we irradiated the uvula and beyond, and adjacent regions.

The type of laser used was the InGaAIP (indium–gallium–aluminium–phophide) low-level diode laser (MMOptics, São Carlos, Brazil), emitting in the red visible wavelength (660 nm) at 40 mW of power, with an energy density of 8 J/cm^2, with a spot size of 0.036 cm^2. To check potency, calibration was carried out with LaserCheck (Coherent, Santa Clara, CA, USA).

Cost analysis

The cost-effectiveness of LOC in HSCT was evaluated on the basis of some of the variables proposed by Sonis *et al.*, which linked the morbidity of OM to the hospitalization time (days), fever, PN and injecting narcotics, and frequency of patients with significant infection (with risk of sepsis) [2]. Considering that hospital costs increased when there was prescription of opioids or PN, the cost–benefit analysis—that is, the impact of the action on health in terms of monetary values—was calculated on the basis of the type of daily hospital fee (whether this included these complications or not) and the number of days of hospitalization. As a basis for calculation, the following values were adopted:

- daily fees, including the cost of nursing, medications and inputs in general = $US978.89;
- daily fee of transplant without PN or opioids = $US1241.87;
- daily fee of transplant with opioids = $US1575.64; and
- daily fee of transplant with PN = $US1728.98.

In group I (with laser therapy), the cost of dental treatment was added, calculated on the basis of the dentist's fees, frequency of attendance and cost of consumable materials, including maintenance of the laser equipment (the value of the low-level laser equipment was not built-in, considering that only one item of equipment was used for all the patients).

Costs were limited to the time of discharge from hospital; and the costs of HSCT follow-up, which included regular visits to the hospital, complementary exams, home visits and medical procedures/medication prescriptions for late post-HSCT complications, were not included in the calculation. The costs of chemical conditioning and pre-transplant radiotherapy, as well as those inherent to transplant technology (whether bone marrow, umbilical cord or peripheral blood stem cells were used), were also not included.

Statistical analysis

Descriptive analysis based on frequency tables and the chi-square test (or Fischer's exact test, where appropriate) was performed to determine the statistical association between the variables of interest and the presence or absence of oral care. Relative risk estimates, with confidence intervals of 95%, were calculated to evaluate the association between the presence of oral care and maximum degree of OM. For the numerical data, the Mann–Whitney test was performed. To analyse the number of days of hospitalization, the analysis of variance model was used. A level of significance of 5% was adopted. The calculations were performed using the software Statistical Package for Social Sciences (IBM, New York, USA).

Table 1. Clinical characteristics and chemotherapy regimen according to the groups of patients with (group I) and without oral care oral care associated with laser therapy (group II)

	Group I (n = 91)		Group II (n = 76)	
	N	%	*N*	%
Gender (p = 0.175)				
Male	53	58.24	52	68.42
Female	38	41.76	24	31.58
Age (average ± SD) (p = 0.194)		44.87 ± 18.26		42.02 ± 15.63
Base disease (p = 0.321)				
ALL	8	8,79	1	1,32
AML	12	13.19	11	14.47
MM	21	23.08	24	31.58
NHL	24	26.37	17	22.37
HL	8	8.79	8	10.53
Other	18	19.78	15	19.74
Type of transplant (p = 0.002)				
Autologous	62	68.13	68	89.47
Allogeneic HLA-matched related donor	18	19.78	7	9.21
Allogeneic HLA-matched unrelated donor	11	12.09	1	1.32
Chemotherapy drugs (p = 0.019)				
CBV	16	17.58	21	27.63
Mel	38	41.75	40	52.63
BEAM				
Mel/Flu				
Mel/Bu				
Cyclo/TBI	10	11.00	2	2.64
Bu/Flu	8	8.79	0	0.00
Flu/Cyclo	11	12.09	9	11.84
Cyclo				
Other	8	8.79	4	5.26
GVHD prophylaxis (p < 0.0001)				
Without prophylaxis	62	68.13	68	89.47
Cyclosporine	1	1.10	2	2.63
Cyclosporine + MMF	6	6.59	1	1.32
Cyclosporine + Mtx	2	2.20	5	6.58
Cyclosporine + tacrolimus	1	1.10	0	0.00
Mtx + tacrolimus	19	20.88	0	0.00
Hospitalization time in days (mean ± SD) (p = 0.023)				
Autologous		23.3 ± 8.7		24.0 ± 8.8
Allogeneic		34.1 ± 10.1		39.8 ± 7.4
Total		24.0 ± 8.8		35.4 ± 9.8

SD, standard deviation; ALL, acute lymphocytic leukaemia; AML, acute myeloid leukaemia; MM, multiple myeloma; NHL, non-Hodgkin's lymphoma; HL, Hodgkin's lymphoma; Mel, melphalan; Flu, fludarabine; Bu, busulfan; Cyclo, cyclophosphamide; TBI, total body irradiation; MMF, mycophenolate mofetil; Mtx, methotrexate; HLA, human leukocyte antigen; GVHD, graft versus host disease; CBV, cyclophosphamide, carmustine and etoposide.

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Results

In the study period, after applying the inclusion and exclusion criteria, the medical records of 167 patients were reviewed: 91 patients had received laser treatment and were therefore included in group I (with laser), and 76 patients were included in group II (without laser). Table 1 shows the patients demographic and clinical characteristics according to groups. There was a greater frequency of allogeneic transplants in group I (31.87% versus 10.53% for group II, without laser, $p = 0.002$).

There were also statistically significant differences with regard to the chemotherapy regimen ($p = 0.019$) and prophylaxis against GVHD ($p < 0.001$). The majority of patients in both groups were not prescribed any drugs, but in group I (with laser), the association of methotrexate with tacrolimus was more frequent. The use of melphalan (or of associations including this drug) was equally prevalent in both groups. Engraftment time was not statistically different between groups (the period of neutropenia was the same). Hospitalization time was longer for group II ($p = 0.023$).

In this study, there was no case of herpes virus type I infection among patients in any group.

Diarrhoea was present in 70% of patients in both groups (Table 2). However, there was a statistically significant difference only in the period up to D + 5, with higher frequency for group I, receiving laser (58.24% versus 36.84%, $p = 0.006$). In this group, the mean number of days with diarrhoea was slightly higher. Nevertheless, the oral culture was negative in 98% of patients in both groups, showing that mucositis was probably intestinal in origin in all patients.

The frequency of fever ≥ 37.8°C was higher in group II ($p = 0.002$), particularly for the period between D + 6 and D + 11 ($p = 0.010$). In this group, the number of days with fever was also higher. No significant differences were observed regarding frequency of infections.

The figures for frequency of pain in the oral cavity when swallowing, and prescription of analgesics, are shown in Table 3. For all the variables, group II showed significantly higher frequencies.

A significantly higher use of PN (Table 4) was observed in group II in the period between D + 6 and D + 11 ($p = 0.041$). The mean number of days of PN was also higher in this group. The frequency of analgesics prescription was higher only for opioid analgesics ($p < 0.001$).

In both groups, there was significant association ($p < 0.001$) between the maximum degrees of OM and prescription of opioids (Table 4). In group II, 78.3% of the patients who needed opioids manifested grades III and IV of OM, whereas 75% who did not need this prescription exhibited grade II. There was also a significant association between OM and pain in the oral cavity in both groups ($p < 0.001$ and $p = 0.003$).

The presence of fever > 37.8°C and infection was significantly associated with the degree of OM only in group II ($p = 0.005$ and $p = 0.015$), with a higher frequency of these occurrences in grades III and IV of OM (68.2% for fever and 100% for infection).

In group I, receiving laser, there was greater frequency of grades I and II OM in autologous and allogeneic transplants, whereas in group II, there was predominance of grades III and IV (Table 5). This group was 14 times more likely to present these degrees of OM ($p < 0.001$), in the comparison with group I. The corrected relative risk (homogeneity test M-H—$p = 0.817$) continued to be significant, increasing to 16.8.

Figure 1 shows the dispersion of the degrees of OM for the patients in each group during 33 days of post-transplant

Table 2. Frequencies of patients receiving peripheral PN and who manifested diarrhoea, fever and infection, according to the groups with (group I) and without oral care associated with laser therapy (group II)

	Group I (*n* = 91)		Group II (*n* = 76)		
	N	**%**	***N***	**%**	***p***
PN					
Total patients	9	9.89	15	19.74	0.071
Up to D + 5	5	5.49	10	13.16	0.085
From D + 6 to D + 11	8	8.79	15	19.74	0.041
D + 12 or more	6	6.59	12	15.79	0.056
Total days (mean ± SD)	0.87 ± 2.97		2.34 ± 5.32		0.049
Diarrhoea					
Total patients	72	79.12	56	73.68	0.408
Up to D + 5	53	58.24	28	36.84	0.006
From D + 6 to D + 11	49	53.85	33	43.42	0.180
D + 12 or more	18	19.78	21	27.63	0.232
Total days (mean ± SD)	3.15 ± 3.11		2.34 ± 2.06		0.033
Fever (≥37.8°C)					
Total patients	60	65.93	66	86.84	0.002
Up to D + 5	38	41.76	40	52.63	0.161
From D + 6 to D + 11	38	41.76	47	61.84	0.010
D + 12 or more	15	16.48	22	28.95	0.053
Total days (mean ± SD)	1.93 ± 2.36		3.28 ± 2.78		<0.001
Infection					
Total patients	12	13.19	11	14.47	0.810

PN, parenteral nutrition.

Table 3. Frequency of patients who reported pain in the oral cavity and when swallowing, as well as patients who received analgesic prescription for any kind of pain, according to the groups with (group I) and without oral care associated with laser therapy (group II)

	Group I ($n = 91$)		Group II ($n = 76$)		
	N	%	*N*	%	*p*
Pain in the oral cavity					
Total patients	34	37.36	72	94.74	<0.001
Up to D + 5	17	18.68	49	64.47	<0.001
From D + 6 to D + 11	27	29.67	69	90.79	<0.001
D + 12 or more	4	4.40	26	34.21	<0.001
Total days (mean ± SD)	1.24 ± 19.7		6.26 ± 4.04		<0.001
Pain when swallowing					
Total patients	61	67.03	62	81.58	0.034
Up to D + 5	44	48.35	49	64.47	0.037
From D + 6 to D + 11	50	54.95	56	73.68	0.012
D + 12 or more	15	16.48	19	25.00	0.173
Total days (mean ± SD)	3.82 ± 3.65		5.76 ± 4.75		0.005
Analgesic prescription					
Non-opioid	88	96.70	76	100	0.110
Opioid	46	50.55	60	78.95	<0.001
Total days using opioid (mean ± SD)	3.74 ± 2.42		8.82 ± 3.72		<0.001

follow-up: in group II, grades III and IV constitute the maximum values of OM in a large portion of the patients, with regression in these levels to grade I (and few to grade 0) in the period between 11 and 33 days post-transplant. But in group I, some of the patients had grade II as the maximum level of OM, with regression to grade 0 in a shorter period, when compared with group II, without laser (between 10 and 25 days post-transplant).

Cost analysis

A significant association of the costs involved in each type of transplant in the groups with and without laser and hospitalization time and use of PN and opioids was observed (Table 5), and the cost was calculated on the basis of these clinical results alone. It is noted that the cost of autologous transplantation, in which there are no complications with the use of PN and opioids but there is the cost of dental treatment, is slightly higher in group I, with laser (a difference of $US199.93); but the cost of allogeneic transplantation without PN and opioids in this group is lower (a difference of $US5158.22). Totaling the values of PN and opioids, the costs also rise for group II (differences of $US10,557.74 and $US16.297.13, for autologous and allogeneic transplantations, respectively).

Discussion

This study has shown the high impact of a specialized oral care including laser therapy on the reduction in morbidity in the oral cavity of patients submitted to HSCT, without any significant increase in monetary cost. It could be said that the oral care was effective in the control of OM and symptoms of pain.

Various factors are associated with OM risk: female sex, age range of children or elderly persons, chemotherapy regimen based on high doses, presence of total body irradiation (TBI) and prophylaxis against GVHD [13]. In the present study, there was an association only with the chemotherapy regimen, type of transplant and GVHD prophylaxis. The group I, receiving laser, presented a higher frequency of high radio-chemotherapy regimens with risk for OM (such as the use of BEAM (carmustine, etoposide, cytarabine and melphalan), melphalan and cyclophosphamide associated with TBI), of allogeneic transplants (which, as a rule, generate a longer time of neutropenia) and of GVHD prophylaxis. Theoretically, the clinical characteristics of the patients in group I would implicate a higher risk of OM per se, because this group was able to receive more ablative treatments. However, our data have shown that OM prevalence was not different between the groups and that OM was more severe in the group without specialized oral care.

It is noteworthy that group I had a greater frequency of diarrhoea with negative antimicrobial culture. This suggests the presence of high-grade intestinal mucositis, which indicates the patient's susceptibility to the cytotoxic effects of the myeloablative regimen. Despite this, this group receiving laser demonstrated extremely low frequency of grades III and IV of OM, in addition to exhibiting a 14-times lower relative risk (or 16.8 lower when corrected) of being affected by this grade of OM. The frequency of severe degrees of OM among the patients not receiving laser treatment was equivalent to that reported in other studies, in which only oral care was provided (without laser) [4,14]. The frequency is much lower (4.4%) with the use of laser care. This means that the risk for mucositis is the same, but the oral mucosa was protected by the combination of specialized oral hygiene and laser treatment.

The frequency of grades III and IV of OM in patients of group II, without laser (61.8%), was similar to that reported by Wardley *et al.*[15] (67.4%). However, it is above the rates found in more recent studies [14–17]. Despite the innumerable variables interfering in the comparison between the samples of these studies, there appears to be a current trend in the literature to lower frequencies of severe degrees of OM, even without direct therapeutic

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Table 4. Frequency of maximum degrees of oral mucositis, according to clinical variables directly related to this morbidity in the groups with (group I) and without oral care associated with laser therapy (group II)

	Group I ($n = 91$)				**Group II ($n = 76$)**			
	Oral mucositis—maximum degree				**Oral mucositis—maximum degree**			
	I	**II**	**III and IV**	**Total**	**I**	**II**	**III and IV**	**Total**
Parenteral nutrition								
No	46	33	3	82	5	24	32	61
	56.1	40.2	3.7	100%	8.2	39.3	52.5	100%
Yes	5	3	1	9	0	0	15	15
	55.6	33.3	11.1	100%	0.0	0.0	100.0	100%
	$p = 0.446$				$p = 0.001$			
Opioid prescription								
No	36	8	1	45	4	12	0	16
	80.0	17.8	2.2	100%	25.0	75.0	0.0	100%
Yes	15	28	3	46	1	12	47	60
	32.6	60.9	6.5	100%	1.7	20.0	78.3	100%
	$p < 0.001$				$p < 0.001$			
Pain in the oral cavity								
No	48	9	0	57	2	2	0	4
	84.2	15.8	0.0	100%	50.0	50.0	0.0	100%
Yes	3	27	4	34	3	22	47	72
	8.8	79.4	11.8	100%	4.2	30.6	65.3	100%
	$p < 0.001$				$p = 0.003$			
Fever > 37.8°C								
No	18	11	2	31	2	6	2	10
	58.1	35.5	6.5	100%	20.0	60.0	20.0	100%
Yes	33	25	2	60	3	18	45	66
	55.0	41.7	3.3	100%	4.5	27.3	68.2	100%
	$p = 0.690$				$p = 0.005$			
Infection confirmed by culture								
No	45	30	4	79	5	24	36	65
	57.0	38.0	5.1	100%	7.7	36.9	55.4	100%
Yes	6	6	0	12	0	0	11	11
	50.0	50.0	0.0	100%			100.0	100%
	$p = 0.743$				$p = 0.015$			
Total	51	36	4	91	5	24	47	76
	56.0	39.6	4.4	100%	6.6	31.6	61.8	100%
HSCT								
Autologous	37	23	2	62	5	24	39	68
	40.7	25.3	2.22	68.2%	6.6	31.6	51.3	89.5
Allogeneic	14	13	2	29	0	0	8	8
	15.4	14.3	2.2	31.9%	0.0	0.0	10.5	10.5
Total	51	36	4	91	5	24	47	76
	51.0	39.9	4.4	100.00%	6.6	31.6	61.8	100
Relative risk	0.1	0.8	14.1[a]		0.1	0.8	14.1[a]	15
CI 95%	0.1–0.3	0.5–1.2	5.3–37.3		0.1–0.3	0.5–1.2	5.3–37.3	
p	<0.001	0.284	<0.001		<0.001	0.284	<0.001	

p values for Fisher's exact test. Relative risk for 'with oral care' as reference category.
HSCT, hematopoietic stem cell transplantation.
[a]The relative risk was corrected to 16.8 (CI 95%, 5.8–48.9, $p < 0.001$). Homogeneity test M-H—$p = 0.817$.

interference in OM. Prophylactic measures of infection control and advances in transplant technology probably contributed to these results.

Another result of the present study was the difference in distribution of the frequencies of OM, use of PN and fever ≥ 37.8°C in relation to the time post-transplantation. In addition to exhibiting duration of OM, group II, without laser, had peaks of frequency of grades III and IV, particularly after D + 6. Meanwhile, in the group with LOC, the most severe degrees of OM took longer to manifest (around D + 9). This may indicate that besides reducing the duration of the OM, the laser therapy was efficient in maintaining low levels of OM severity for a longer time, particularly in the period of severe neutropenia. This trend in OM distribution over time probably also influenced the period of PN use and presence of fever ≥ 37.8°C. Group II, without laser, exhibited significantly greater PN use and fever in the period between D + 6 and D + 11, which coincided with the peaks of severe OM in this group. It is worth mentioning that the associations between the use of PN and opioids, as well as the occurrence of pain in the oral cavity, fever and infection with different degrees of OM, were significant in group II, probably because of the higher frequency of more severe degrees (III and IV).

Table 5. Description of the cost of transplantations, considering the number of days of hospitalization included in the period evaluated and the additions with reference to the prescription of opioids and peripheral PN

	Values per patient (in $US)			
	Group I		Group II	
	Autologous	Allogeneic	Autologous	Allogeneic
Mean cost of transplantation without need for PN or opioids, according to the mean hospitalization time	27,793.67 (mean of 22.4 days of hospitalization)	42.310,90 (mean of 34.1 days of hospitalization)	29.508,02 (mean of 24.0 days of hospitalization)	49.383,40 (mean of 39.8 days of hospitalization)
Total cost of oral care[a]	1914.28	1.914,28	—	—
Total mean cost of transplantation without need for PN and or opioids	29,707.95	44,225.18	29,508.02	49,383.40
Additional cost of transplantation with need for opioids considering the mean prescription time	6160.75 (mean of 3.91 days of prescription)	8823.58 (mean of 5.60 days of prescription)	14,653.45 (mean of 9.30 days of prescription)	17,142.96 (mean of 10.88 days of prescription)
Additional cost of transplantation with need for peripheral PN considering the mean usage time	1141.12 (considering a mean of 0.66 day of use)	1606.64 (considering a mean of 0.64 day of use)	3406.09 (considering a mean of 1.97 days of use)	4426.18 (considering a mean of 2.56 days of use)
Total mean cost of transplantation with need for peripheral PN and opioids	37,009.82	54,655.40	47,567.56	70,952.53

Basis of calculation: Daily fees including the cost of medicaments and inputs in general, as well as nursing; daily fee of transplant without the need for PN or opioids—$US1241.87; daily fee of transplant with the need for opioids—$US1575.64; daily fee of transplant with the need for PN—$US1728.98. Mean number of days was obtained from the present survey.
PN, parenteral nutrition.
[a]Obtained from the total amount of dentists/transplant fees, which was calculated as a package including a mean hospitalization time of 30 days ($US1300.39), consumable materials and maintenance of laser equipment ($US613.89).

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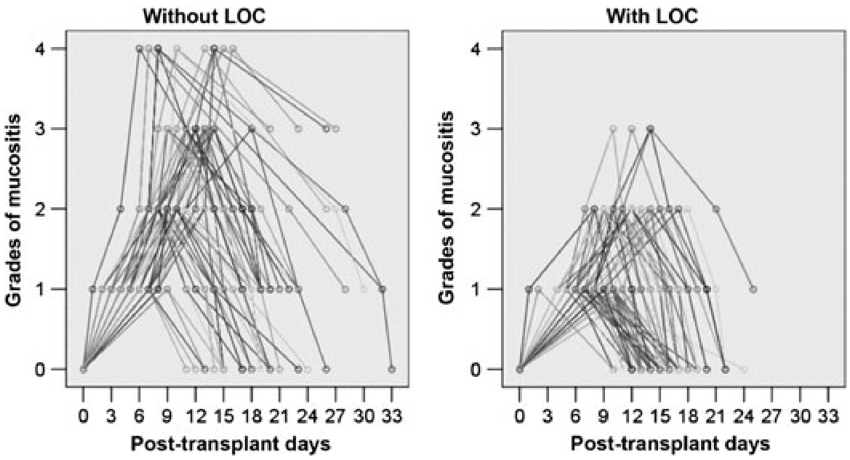

Figure 1. Distribution of oral mucositis grades in accordance with post-transplant days in the groups with or without oral care associated with laser therapy (LOC)

The adoption of laser therapy, as a protocol integrated with other forms of healthcare, was based on studies that demonstrate the high efficiency of low-level laser in the repair of OM lesions and a reduction in painful symptomatology [6,7,10]. The anti-inflammatory and analgesic properties of laser and stimulation of cell proliferation are the main factors associated with its therapeutic effects on OM [6–8,12]. We opted for 8 J/cm^2 at 40-mW power based on our clinical experience, in which we keep analgesia for longer times and reduce inflammation with higher energy laser [12] in this particular type of patients, who often present severe OM. The use of 8 J/cm^2 proved safe. Because it is a topical application that has few or no side effects, laser irradiation is particularly beneficial in situations of immunosuppression, especially for HSCT transplantation patients. It could be admitted that laser therapy was one of the factors that contributed most to the reduction in severity of OM in the present study. An important aspect of the present protocol is that its use was associated with oral hygiene maintenance procedures and daily monitoring of infectious foci and was not restricted to isolated periodic irradiations only.

The monetary cost was analysed on the basis of the severity of OM, as well as its influence of the use of PN and opioids. The significant reduction in the frequency of these prescriptions in group I was the main difference found in comparison with group II, without laser, and had a significant influence on the differences in estimated costs of the two groups. As the minimum unit of monetary calculation was daily hospital fees, without individualization of the innumerable items involved in HSCT, it cannot be confirmed that the reduction in frequency of PN and opioids alone was responsible for the differences in costs. Nevertheless, these variables constitute important economic indicators for contextualizing the hospital realities in each group in a concrete way. These factors were reported in the patients' medical records, with clear indication of their prescription as a result of difficulties with chewing, swallowing and pain in the oral cavity. It was observed that in a situation of HSCT without the need for opioids and PN, laser therapy resulted in a lower additional cost of autologous transplantation. However, in situations where these resources were prescribed, the costs were much higher in the absence of laser therapy (an increase of up to 30%), mainly because of the longer hospitalization times and higher morbidity inherent to the transplant condition. In this study, the cost of the laser device was not included in the therapy cost calculations, but the average cost in Brazil is around $US2500, a value which would probably not have a high impact in the final cost calculation, especially in cases where the device is shared with other specialties in the same hospital. A more in-depth economic study is needed, investigating direct and indirect measurements in greater detail for a more accurate analysis of the influence of laser therapy on reducing the costs of HSCT.

In conclusion, laser therapy and oral care contribute to reducing the morbidity resulting from OM and, consequently, minimizing hospitalization costs during HSCT.

Conflict of interest

The authors have no competing interest.

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