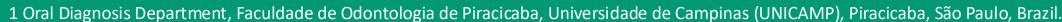


Assessment

Placebo or PBM

HIGH-DOSE METHOTREXATE AND ORAL MUCOSITIS IN ADULTS WITH HEMATOLOGICAL MALIGNANCIES: PHOTOBIOMODULATION, SALIVARY AND SERUM METHOTREXATE CONCENTRATION.

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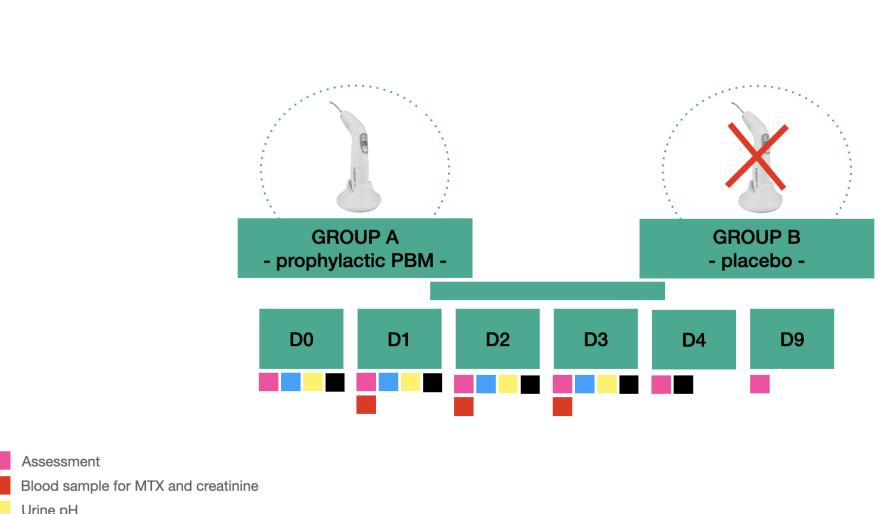


INTRODUCTION

High-dose methotrexate (HD-MTX) is used in cancer treatment, with serum MTX concentration monitoring to minimize toxicities including oral mucositis (OM). This study aimed to evaluate the correlation between serum and salivary MTX concentrations, the relationship between salivary MTX and OM, and photobiomodulation therapy (PBMT) effectiveness in preventing OM.

METHODS

A randomized, double-blind, prospective study was conducted on onco-hematological adult patients receiving their first HD-MTX cycle. Patients were assigned to Group A (prophylactic PBMT 660nm, 100mW, spot size 0.028cm2, 1J per point/10s) or Group B (sham laser). PBMT was applied to the oral mucosa for 5 days after infusion, or until MTX serum concentrations were <5 μmol/L (24h), <1 μmol/L (48h), and <0.1 μmol/L (72h). Serum and salivary MTX concentrations were measured at 24, 48, and 72 hours after infusion. OM severity was classified using WHO criteria. Logistic, multinomial, and robust-error-variance Poisson regression analysis were used.



PBMT	Group A	Group B	
Manufacturer	DMC, São Carlos, SP, Brazil	DMC, São Carlos, SP, Brazil	
Protocols	Intraoral PBMT	Placebo PBMT (using a tip that blocked light emission simulating treatment without delivering active therapy)	
Device information	Therapy XT	Therapy XT	
Number of emitters	Two	Two	
Emitter type	InGaAs	InGaAs	
Beam delivery system	Fiber optic	Fiber optic	
Irradiation parameters			
Wavelength (nm)	660	-	
Spectral bandwidth (nm)	660 ± 10	-	
Operating mode	Continuous wave	-	
Radiant power (W)	100 mW	-	
Beam profile	Gaussian	-	
Treatment parameters			
Beam spot size at target (cm²)	0.028	-	
Irradiance (W/cm²)	3.57	-	
Exposure duration (s)	10	10	
Fluence (J/cm ²)	35	-	
Radiant energy (J)	1	-	
Number of points irradiated	26	26	
Application technique	Contact	Contact	
Frequency	At D0 and D1, and at D2 if plasma MTX concentrations on D1 were ≥5–10 µmol/L; at D3 if D2 concentrations were ≥1 µmol/L; and at D4 if D3 concentrations were ≥0.1 µmol/L. When concentrations were bellow threshold, PMBT was conducted with a blocking tip.	5 consecutive days - D0, D1, D2, D3, and D4.	

centimeters, nm nanometers, s second, W watts.

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RESULTS

Fifty-three patients were included (Group A: n=26, Group B: n=27). Group B had higher chances of developing more severe OM (8.97x more likely, 95% CI, 2.66-30.22; p<0.01) and ulcerated OM (3.85x more likely, 95% CI, 1.48-10.00; p<0.01) [Table 1]. Salivary MTX levels were 29% (24h), 323% (48h), and 589% (72h) of serum levels. In Group A, for every 0.01 increase in salivary MTX at 24h, there was a 12% higher chance of severe OM at 96h (95% CI, 1.0098-1.2424; p=0.03). For Group B, every 0.01 increase in salivary MTX at 48h increased the risk of higher OM grades by 3.4 times (95% CI, 0.9252-1.1713; p=0.02) in 9 days. No correlations were found between serum and salivary MTX (Figure 1) or between serum MTX and OM (Figure 2).

Table 1. Oral mucositis prevalence in Group A and group B, odds ratio, and relative risk.

ОМ	0	1	2	3	OR (CI 95%)*	P* value
Group A	8 (30.77%)	14 (53.85%)	4 (15.38%)	0 (0%)	ref	<0.01
Group B	1 (3.7%)	10 (37.04%)	14 (51.85%)	2 (7.41%)	8.97 (2.66; 30.22)	

ОМ	0 and 1	2 and 3	RR (CI 95%)**	P* value
Group A	22 (84.62%)	4 (15.38%)	ref	_
Group B	11 (40.74%)	16 (59.26%)	3.85 (1.48; 10.0)	<0.01

Abbreviations. OM: oral mucositis. OR: odds ratio. CI: confidence interval. RR: relative risk.

A P-value less than 0.01 was considered significant

* multinomial logistic regression

Figure 2. Oral mucositis grades 0 and 1, grades 2 and 3, and its correlation with serum and salivary MTX concentrations at 24h, 48h, and 72h.

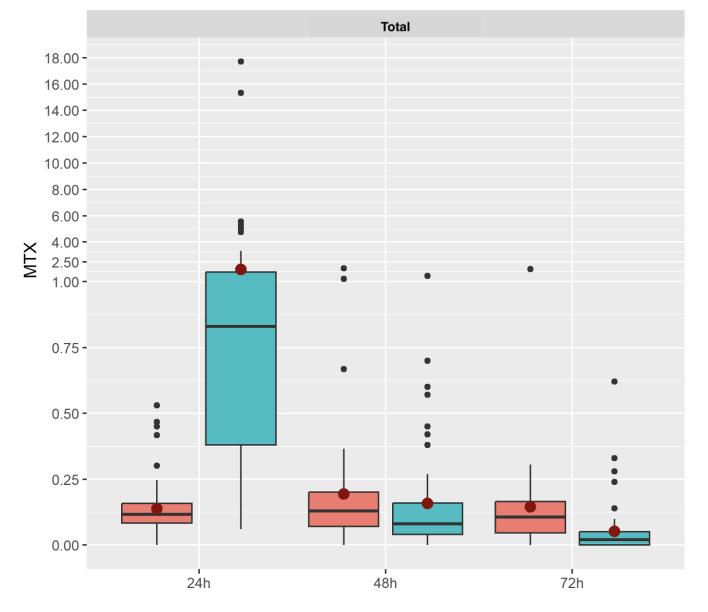
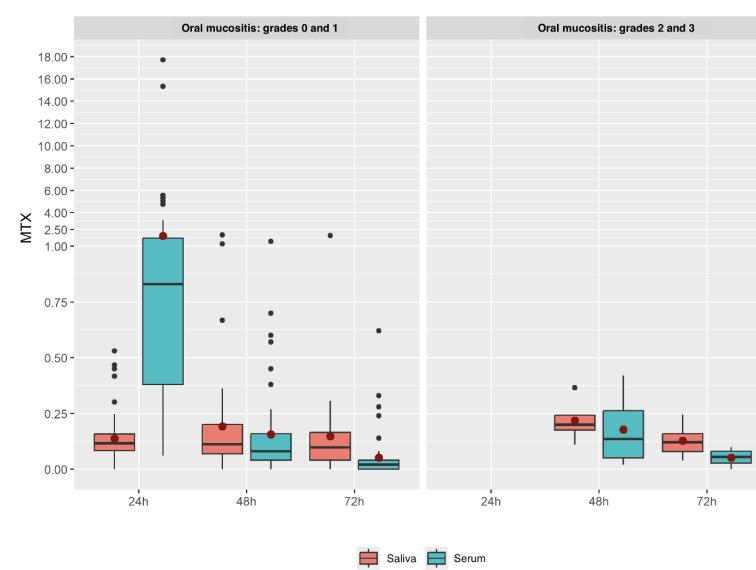


Figure 1. Serum and salivary MTX concentrations at 24h, 48h, and 72h after HD-MTX infusions.



CONCLUSIONS

PBMT effectively reduced the incidence and severity of OM in HD-MTX-treated patients. Additionally, salivary MTX excretion may serve as a predictive marker for OM in HD-MTX treatment protocols.

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^{**} robust-error-variance Poisson regression analysis.