Low Temperature Atmospheric Pressure Plasma as an Adjunct for the Treatment of Chemotherapy-induced Oral Mucositis

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Abstract: In this contribution, we report an *in vivo* study where rats with oral chemotherapy-induced mucositis were treated with Low Temperature Atmospheric Pressure Plasma (LTAPP) generated with Helium as the working gas. The plasma jet exposure was performed for 5 min at 1.5 cm. Clinical scores and histological evaluation after the treatment indicated that LTAPP tended to promote faster clinical healing.

1. Introduction

LTAPP has been investigated successfully as a possible adjunct for the treatment of oral diseases due to its antimicrobial, anti-inflammatory and tissue repair properties [1,2]. Recently, a study conducted by our group showed that LTAPP may prevent oral mucositis-related candidemia in chemotherapy-treated rats [3]. However, as far as we know, no study has evaluated the tissue repair of oral mucositis after LTAPP treatment. Considering the common occurrence of mucositis in immunosuppressed patients as well as the absence of a well-defined standard protocol for its treatment, the aim of this study was to evaluate the effects of LTAPP in the healing of oral mucositis in chemotherapy-treated rats.

2. Methods

Sixty male rats (*Rathus norvegicus*), aged 90 days, were maintained in usual housing conditions. The animals were randomly divided into control group (no treatment) and treated group (LTAPP). Both groups were subdivided according to the follow up period of 1 day, 5 days and 12 days after LTAPP treatment. Oral mucositis was induced by administration of 5-fluorouracil associated with topical application of 50% acetic acid to delimit an ulcer area in the vestibular fornix.

Plasma source is composed by a dielectric chamber with coaxial DBD geometry connected to a 1.0 m-long flexible plastic tube [4]. The device was driven by a commercial pulsed voltage source. The system was fed with helium gas with 99.9% purity at a flow rate of 2.0 ± 0.1 SLM. The exposure time was 5 minutes, at a distance 1.5 cm and power of 294.1 mW. These parameters were previously determined in preliminary studies [3,4].

3.Results and Discussion

The clinical scores showed a marked reduction of the lesions 12 days after the treatment. In the intergroup analysis no statistically significant difference was observed between the groups (Kruskal-Wallis, $p>0.05$), although the LTAPP group showed a better clinical performance showing a final mean score compatible with mild oral mucositis. The intragroup evaluation showed statistically significant reduction of lesion severity between the periods of 1 and 12 days for control (ANOVA, $p=0.0395$) and LTAPP group (ANOVA, 0.0001), respectively (Fig. 1).

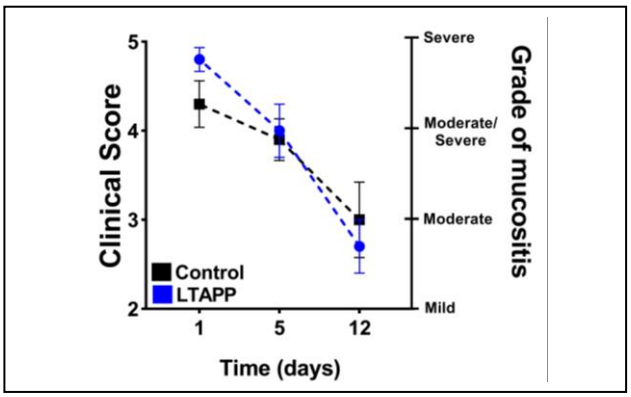

Fig. 1: Mean and standard error of oral mucositis scores of treated (blue) and untreated group (black) on days 1, 5 and 7 after the treatment.

The microscopic analysis showed extensive ulcerations covered by fibrinopurulent pseudomembrane and moderate to high degree of inflammation in both groups 1 day after the treatment. Histologic reepithelization was already observed in different degrees 5 days after the treatment, in addition to the presence of granulation tissue replacing previously ulcerated areas. At 12 days after the treatment, most of the fragments were totally reepithelialized. The connective tissue showed some areas of edema and mild inflammation and some areas of thicker collagen fibers indicating the maturation of the tissue in both groups.

4. Conclusion

Tissue repair occurred almost completely 12 days after the treatment in both groups, with LTAPP group showing a tendency of faster clinical improvement.

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