Lasers in Surgery and Medicine 43:410–420 (2011)

Dual Effect of Low-Level Laser Therapy (LLLT) on the Acute Lung Inflammation Induced by Intestinal Ischemia and Reperfusion: Action on Anti- and Pro-Inflammatory Cytokines

F. Mafra de Lima, MD, MSc,[1*] A.B. Villaverde, MD, PhD,[2] R. Albertini, MD, PhD,[3] J.C. Corrêa, MD, PhD,[3] R.L.P. Carvalho, MD,[4] E. Munin, MD, PhD,[2] T. Araújo, MD, MSc,[3] J.A. Silva, MD, PhD,[3] and F. Aimbire, MD, PhD[5]

[1]*Research and Development Institute, Av. Shishima Hifumi, 2911, São José dos Campos, SP, Brazil*

[2]*Biomedical Engineering Center, Unicastelo, Rod. Pres. Dutra, Km 138, São José dos Campos, SP, Brazil*

[3]*Rehabilitation Sciences Departament, Nove de Julho University - Rua Vergueiro, 235, São Paulo, SP, Brazil*

[4]*Departament of Pharmacology, Biomedical Science Institute, Cidade Universitária, Av. Lineu Prestes, 1524, São Paulo, SP, Brazil*

[5]*Department of Science and Technology, Federal University of São Paulo—Unifesp, São José dos Campos, SP, Brazil*

Background and Objective: It is unknown if pro- and anti-inflammatory mediators in acute lung inflammation induced by intestinal ischemia and reperfusion (i-I/R) can be modulated by low-level laser therapy (LLLT).

Study Design/Material and Methods: A controlled ex vivo study was developed in which rats were irradiated (660 nm, 30 mW, 0.08 cm^2 of spot size) on the skin over the right upper bronchus 1 hour post-mesenteric artery occlusion and euthanized 4 hours later. For pretreatment with anti-tumor necrosis factor (TNF) or IL-10 antibodies, the rats received either one of the agents 15 minutes before the beginning of reperfusion.

Methods: Lung edema was measured by the Evans blue extravasation and pulmonary neutrophils influx was determined by myeloperoxidase (MPO) activity. Both TNF and IL-10 expression and protein in lung were evaluated by RT-PCR and ELISA, respectively.

Results: LLLT reduced the edema (80.1 ± 41.8 $\mu g\ g^{-1}$ dry weight), neutrophils influx ($0.83 \pm 0.02 \times 10^6$ cells ml^{-1}), MPO activity (2.91 ± 0.60), and TNF (153.0 ± 21.0 pg mg^{-1} tissue) in lung when compared with respective control groups. Surprisingly, the LLLT increased the IL-10 (0.65 ± 0.13) in lung from animals subjected to i-I/R. Moreover, LLLT (0.32 ± 0.07 pg ml^{-1}) reduced the TNF-α level in RPAECs when compared with i-I/R group. The presence of anti-TNF or IL-10 antibodies did not alter the LLLT effect on IL-10 (465.1 ± 21.0 pg mg^{-1} tissue) or TNF (223.5 ± 21.0 pg mg^{-1} tissue) in lung from animals submitted to i-I/R.

Conclusion: The results indicate that the LLLT attenuates the i-I/R-induced acute lung inflammation which favor the IL-10 production and reduce TNF generation. Lasers Surg. Med. 43:410–420, 2011.

Key words: phototherapy; cytokines; mesenteric ischemia; reperfusion injury; IL-10; TNF; inflammation

INTRODUCTION

Abdominal trauma causing intestinal ischemia and reperfusion (i-I/R) may induce remote organ injury, being the lung the first one to be affected [1]. The i-I/R is also associated to induction of systemic inflammatory response, a fact that may indicate a casual link between mediators released during systemic inflammation and the pulmonary dysfunction in adult respiratory distress syndrome (ARDS) [2]. ARDS is a critical illness characterized by acute lung injury, leading to pulmonary permeability, edema, and respiratory failure [1,2]. There is no specific therapy for ARDS, and mortality caused by this disease still remains high [3]. Circulating neutrophils play a major role in the development of both clinical settings and experimental animal models of acute lung inflammation [4–6]. Data obtained from experimental models showed that the interaction neutrophil–endothelial cell adhesion may be a rate-limiting step in the pathogenesis of acute lung inflammation induced by i-I/R [3]. The mechanisms that regulate neutrophil accumulation in the lungs and increase of microvascular permeability, as well as those that exert protective effects against the severity of such lung dysfunction, has been reported [4,5]. Many inflammatory mediators are released during i-I/R, such as tumor necrosis factor (TNF) and IL-10 [7,8].

Indeed, treatment of rats with anti-TNF antibodies prevented neutrophil influx, tissue injury, and lethality after i-I/R [7]. In transgenic mice, there is a greater production of TNF and greater lethality as compared to their

*Corresponding to: F. Mafra de Lima, MD, MSc, Research and Development Institute, Univap, Av. Shishima Hifumi, 2911, São José dos Campos, SP, Brazil. E-mail: flaviafisio@hotmail.com

Accepted 3 February 2011
Published online 15 June 2011 in Wiley Online Library (wileyonlinelibrary.com).
DOI 10.1002/lsm.21053