Pharmacological Reports
2011, 63, 494–500
ISSN 1734-1140

Protective effects of endothelin-A receptor antagonist BQ123 against LPS-induced oxidative stress in lungs

Aleksandra Piechota[1], Andrzej Polańczyk[2], Anna Goraca[1]

[1]Chair of Experimental and Clinical Physiology, Department of Cardiovascular Physiology, Medical University of Lodz, Mazowiecka 6/8, PL 92-215 Łódź, Poland

[2]Faculty of Process and Environmental Engineering, Technical University of Lodz, Wólczańska 213/215, PL 90-924 Łódź, Poland

Correspondence: Aleksandra Piechota, e-mail: piechota.aleksandra@wp.pl

Abstract:
The aim of this study was to assess whether endothelin-A receptor (ET_A-R) blocker, BQ123, influences lung edema, lipid peroxidation (TBARS), hydrogen peroxide (H_2O_2), TNF-α concentration or the glutathione redox system in the lung homogenates obtained from LPS-induced endotoxic shock rats. The study was performed on male Wistar rats (n = 6 per group) divided into groups: (1) saline, (2) LPS (15 mg/kg)-saline, (3) BQ123 (0.5 mg/kg)-LPS, (4) BQ123 (1 mg/kg)-LPS. The ET_A-R antagonist was injected intravenously 30 min before LPS administration. Five hours after saline or LPS administration, animals were sacrificed and lungs were isolated for indices of lung edema, oxidative stress and TNF-α concentration. Injection of LPS alone resulted in lung edema development and a marked increase in TNF-α ($p < 0.02$), TBARS ($p < 0.02$), and H_2O_2 ($p < 0.01$) concentrations as well as a depletion of total glutathione ($p < 0.01$). Administration of BQ123 (1 mg/kg), before LPS challenge, led to a significant reduction in TNF-α and H_2O_2 concentrations ($p < 0.05$) and elevation of both total glutathione and the GSH/GSSG ratio ($p < 0.05$). However, it did not prevent LPS-induced TBARS increase and lung edema formation. Interestingly, a lower dose of BQ123 was much more effective in decreasing H_2O_2, TBARS, as well as TNF-α levels ($p < 0.02$, $p < 0.05$, $p < 0.05$, respectively). That dose was also effective in prevention of lung edema development ($p < 0.01$). Taken together, the obtained results indicate that BQ123 is highly effective in decreasing LPS-induced oxidative stress in lungs. Moreover, the dose of 0.5 mg/kg of the antagonist showed to be more effective in decreasing free radical generation and lung edema in endotoxemic rats.

Key words:
BQ 123, oxidative stress, endotoxic shock, lung edema