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Protective Effect of N-acetylcysteine in Lipopolysaccharide-induced Experimental Peritonitis

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Purpose : Our study is aimed to demonstrate the protective effect of N-acetylcysteine (NAC) for the peritoneal membrane through anti-oxidant action in lipopolysaccharide (LPS)-induced acute peritonitis model.

Methods : In our pilot study, three groups of Sprague-Dawley rats received daily intraperitoneal infusion of 1.36% glucose dialysis fluid (80 mL/kg) for 14 days (n=2, each group) through a peritoneal catheter. Group 1 received only dialysis fluid. Group 2 additionally received lipopolysaccharide (LPS) mixed in the dialysis fluid (5 microgram/ml) for 5 days (day 8-12). Group 3 additionally received both LPS and N-acetylcysteine (5 mM in dialysis fluid) for 5 days (day 8-12). At day 14, after peritoneal equilibration test, rats were sacrificed for parietal peritoneal inflammation and fibrosis. We extended our experiment to the primary-cultured rat peritoneal mesothelial cells (RPMCs) in order to demonstrate the protective effect of N-acetylcysteine through anti-oxidant actions. We have tested cell proliferation with both direct cell counting and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) assay. Dichlorofluorescein (DCF)-sensitive cellular reactive oxygen species (ROS) were measured by fluorocytometry.

Results : Rats infused with LPS showed decreased ultrafiltration (UF) volume (-6.5 mL) compared with control rats (+3 mL). The reduction in UF volume by LPS was abrogated by the LPS+NAC infusion (-2.5 mL). 'LPS+NAC' group had less peritoneal inflammation and thickening compared with 'LPS alone' group. In vitro experiment shows exposure of RPMC to LPS impaired cell proliferation ($p<0.01$) and increased DCF-sensitive cellular ROS in comparison with culture media alone. Exposure to NAC+LPS increased cell proliferation ($p<0.001$) and decreased DCF-sensitive cellular ROS in comparison with LPS treatment alone.

Conclusion : In our experimental peritonitis model, repeated infusion of LPS induced peritoneal inflammation and fibrosis. N-acetylcysteine demonstrated protective effect in LPS-induced peritonitis. These protective effect was also demonstrated in the cultured RPMC. NAC might have anti-inflammatory and anti-fibrotic effect through its anti-oxidant action in the LPS-mediated oxidative injury to the peritoneal membrane.