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Title: The effect of hyperglycemia on renal dysfunction associated with altered gene expression profiles in a rat model of mechanical ventilation

Wonil 10117 Choi choi_wi@hanmail.net MD ¹. ¹ Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Republic of Korea, 700-712 .

Body: Background: High blood glucose caused an increase in morbidity and mortality in intensive care unit. The molecular mechanisms of this hyperglycemia effect on kidney are poorly understood. Therefore, we used gene microarrays to profile gene expression patterns involved in hyperglycemia related renal dysfunction. Methods: Serum creatinine was evaluated in control group, hyperglycemia group (HG), euglycemia group (EG) and hyperglycemia with α -lipoic acid (LA) group (HGLA). Dextrose water (D/W) was injected to increase blood glucose above 200 mg/dl in HG group and D/W with insulin was injected in EG group. Control and hyperglycemic rats were studied for microarray (n= 3 each group). The RatRef-12 expression Beadchip (22,226 gene probes per array) was used to analyze the pattern of gene expression in all groups. Results: Microarray analysis showed that 71 genes were differentially expressed in hyperglycemia and control group. The profile revealed that hyperglycemia induced significant alterations of expression of many genes encoding oxidation and antioxidant molecules, apoptosis regulatory protein, metabolic enzyme. Serum creatinine was significantly increased in the HG group compared to EG group (0.96 ± 0.2 vs 0.62 ± 0.1 mg/dl) ($P < 0.01$), which was attenuated by α -LA pretreatment (0.6 ± 0.1 mg/dl) ($P < 0.01$). Either insulin or LA attenuated renal dysfunction with reducing nitrotyrosine accumulation. Conclusions: High glucose caused a renal dysfunction during mechanical ventilation. Either insulin or LA attenuated renal dysfunction. Hyperglycemia also affects gene expression profiles in the kidney tissue mainly through oxidative stress.