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Urea-induced ROS caused endothelial dysfunction in chronic renal failure

Maria D'Apolito[1], Anna Laura Colia[2], Massimo Pettoello-Mantovani[1], Michael Brownlee[3], Ida Giardino[2] and Angela Bruna Maffione[2]

[1] Dipartimento di Scienze Mediche e Chirurgiche, Università degli Studi di Foggia, Foggia, Italia
[2] Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Foggia, Foggia, Italia
[3] Department of Medicine, Albert Einstein College of Medicine, New York, Stati Uniti D' America

The pathogenic events responsible for accelerated atherosclerosis in patients with chronic renal failure (CRF) are poorly understood [2] .Here we investigate the hypothesis that concentrations of urea associated with CRF and increased ROS production in adipocytes3 might also increase ROS production directly in arterial endothelial cells, causing the same pathophysiologic changes seen with hyperglycemia [1]. For these purpose, confluent primary human aortic endothelial cells (HAECs) were incubated with either 20mM urea or with 20mM mannitol used as osmotic control, for 48 hours. Urea induces mitochondrial reactive oxygen species in HAEC and cause pro-inflammatory changes in endothelial cells. Breafly, PGI2 Synthase activity, NFκB p65 and NFκB-specific target genes mRNA expression (MCP-1 and VCAM-1) [3] and their protein levels were evaluated. Moreover, we have shown that urea-induced ROS production increases PKC activity, hexosamine pathway activity and intracellular AGE formation in HAEC. In addition, urea-induced ROS decrease GAPDH activity, increase DNA strand breaks and increase PARP activity in HAEC. In summary, urea increases mitochondrial ROS production in arterial endothelial cells, thereby activating pro-atherosclerotic pathways and directly inactivating PGI2 synthase, a critical endothelial-specific antiatherosclerotic enzyme in vitro. The present findings provide further insight into the underlying mechanisms that contribute to the enhanced cardiovascular risk associated with chronic renal failure.

References

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Key words

Urea, endothelial cells, ROS.