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Role of TNF-associated cytokines in renal tubular cell apoptosis induced by hyperoxaluria

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Aim: Crystal-cell interaction has been reported as one of the most crucial steps in urinary stone formation. Hyperoxaluria induced apoptotic changes in renal tubular epithelial cells is the end-stage of this interaction.We aimed to evaluate the possible pathways responsible in the induction of apoptosis within the involved cells by assesing the receptoral expression of three different pathways.

Material and Methods: 16 male Spraque-Dowley rats were divided into two groups: While the animals in Group-1 (n:8) received only distilled water;animals in Group-2(n:8) received 0.75 % ethylene glycol (EG) in their daily-water to induce hyperoxaluria for two weeks. Following 24h urine collection, all animals were euthenaised and right kidneys were removed and fixed for immunohistochemical evaluation. Oxalate and creatinine levels (in 24h-urine) and Fas, TNF receptor-1 and Trail receptor-2 expression (in tissue) have been assessed.

Results: In addition to TNF (p= 0.0007) expression; both FAS (p= 0.0129)and FAS-L (p=0.032) expressions significatly increased in animals treated with EG. The expressions of TRAIL (p=0.49) and TRAIL-R2 (p=0.34) receptors did not change statistically after hyperoxaluria induction. Although a positive correlation with cytokine expression density and 24h-urinary oxalate expression (mg oxalate/mg creatinine) has been assessed with TNF (p= 0.04, r=0.82), FAS (p= 0.05, r= 0.80), FAS-L (p=0.04, r= 0.82); no correlation could be demonstrated between TRAIL and TRAIL R2 expressions.

Conclusions: Our results indicate that apoptosis induced by oxalate is possibly mediated via TNF and FAS pathways. But TRAIL and TRAIL-R2 seemed to have no function in the cascade. Correlation with urinary oxalate levels did further strengtlhen the findings.

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