The effects of irbesartan and perindopril on clusterin expression and apoptosis in STZ diabetic rats
Matem Tuncdemir, Melek Ozturk
Istanbul University, Cerrahpasa Faculty of Medicine, Department of Medical Biology, Istanbul, Turkey.
mozturk@istanbul.edu.tr

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AIM:
Clusterin are found to be involved in many patho-physiological processes, its biological significance is still controversial, particularly with regard to apoptosis. The aim of this study was to determine the roles of secreted clusterin (s-clu) and nuclear clusterin (n-clu) expressions in experimental diabetic nephropathy, and to investigate the effects of perindopril as an ACE inhibitor and irbesartan as an AT1 receptor blocker on clusterin expression and compare these results with apoptosis.

MATERIAL AND METHOD:
Four groups received streptozotocin injection (STZ, 60mg/kg, single dose, ip). On the 2nd day of STZ injection the rats developing diabetes were divided into 4 groups; (1) STZ-diabetic, (2) irbesartan treated diabetics (15 mg/kg/day, gavage, 30 days), (3) perindopril treated diabetics (6 mg/kg/day, gavage, 30 days), (4) combined treated diabetic group with perindopril and irbesartan (respectively, 3 mg/kg/day, 5 mg/kg/day, gavage, 30 days), (5) control group. During the experimental period blood glucose, microalbuminuria levels, body weights, kidney weight and amount of daily urine were measured. At the end of experiment, renal tissue samples were fixed in formaline and embedded in paraffin. PAS staining, TUNEL method and immunohistochemical staining for clusterin-β (s-clu) and clusterin-α/β (n-clu) antibodies were performed for histological examinations.

RESULTS:
Blood glucose levels and body weight/kidney weight values of all STZ-diabetic groups were higher than the control group. The level of daily urine and microalbuminuria levels were decreased in the all treated diabetic groups (p<0,001). The number of apoptotic cells increased especially in the kidney tubules of STZ-diabetic group (p<0,001), whereas a significant decrease was observed in the combined drug treated group (p<0,05). The expression of clusterin-β was increased in the glomerules and tubules of the untreated diabetic group, although it was decreased in the treated diabetic groups. Immunopositivity of clusterin-α/β in the podocytes and mesangial cells and in the injured tubule cells of untreated diabetic group was found to be increased in their nuclei. The number of n-clu immunopositive cells was decreased in the treated diabetic groups, especially in the combined treated diabetic group (p<0,05).

CONCLUSION:
In the early stages of diabetes, tubular damage was seen in the STZ diabetics. Our results also show that the expression of s-clu was induced in the experimental diabetic nephropathy related to renal tissue damage and that the increase in the n-clu expression in the renal tubules was releated to apoptosis. Although irbesartan, perindopril and combined drug treatment prevented renal injury in the diabetes, low dose application of ACE inhibitor and AT-1 receptor blocker together revealed more efficient results in preventing renal damages.

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