

Effect of antisense oligodeoxynucleotides for ICAM-1 on renal ischaemia-reperfusion injury in the anaesthetised rat.

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Abstract:

An antisense oligodeoxynucleotide (As-ODN) to the 3' untranslated region of the mRNA sequence expressing the intracellular adhesion molecule-1 (ICAM-1) was employed to determine ICAM-1's role in renal ischaemia-reperfusion injury in the rat. Wistar-Kyoto rats receiving i.v. either lipofectin-As-ODN (As-ODN group), lipofectin-reverse ODN (Rv-ODN group) or lipofectin (ischaemia control group) 8 h prior to study were anaesthetized and subjected to 30 min of renal artery occlusion. Renal haemodynamic and excretory parameters were monitored before and after renal ischaemia. On termination of the study renal tissue was subjected to histological and Western blot analysis. Renal blood flow decreased in the 3 h post-ischaemia period in the ischaemia control and Rv-ODN groups, but was maintained in the As-ODN group. Glomerular filtration rate was depressed initially but gradually increased to 10% above basal levels in the ischaemia control and Rv-ODN groups, but was below basal levels (20%) in the As-ODN group. There was a three- to fourfold increase in sodium and water excretion following ischaemia in the ischaemia control and reverse-ODN groups but not in the As-ODN treated group. The As-ODN ameliorated the histological evidence of ischaemic damage and reduced ICAM-1 protein levels to a greater extent in the medulla than cortex. These observations suggested that in the post-ischaemic period afferent and efferent arteriolar tone was increased with a loss of reabsorptive capacity which was in part due to ICAM-1. The possibility arises that the action of ICAM-1 at vascular and tubular sites in the deeper regions of the kidney contributes to the ischaemia-reperfusion injury.

Keywords:

intercellular-adhesion molecule-1; oligonucleotides; mechanisms; expression; failure; kidney

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