

PROTECTIVE EFFECT OF ADRENOMEDULLIN ON CONTRAST INDUCED NEPHROPATHY IN RATS

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BACKGROUND and OBJECTIVE:

There is a considerable interest in strategies to prevent contrast-induced nephropathy (CIN) because of the increasing prevalence of renal insufficiency in our aging population and the increasing use of imaging studies using radiocontrast media. Some of the important mechanisms of CIN are renal vasoconstriction and medullary hypoxia. It was shown that adrenomedullin, which has antioxidant, vasodilatory and immunomodulatory effects, attenuated the renal ischemia-reperfusion injury. We aimed to investigate whether adrenomedullin might have a preventive role against the development of CIN.

METHOD and RESULTS:

Wistar albino rats (n = 24) were allocated randomly into four equal groups of 6 each; Control (C), Adrenomedullin (A), contrast media (CM), and adrenomedullin plus contrast media (ACM). CIN was induced by intravenous administration of high-osmolar contrast media, diatrizoat (Urografin % 76, Schering AG, Germany) at dose of 10 ml/kg. Adrenomedullin was administered by intravenous route at dose of 12 mcg/kg. Renal function parameters, kidney histology, and inflammatory markers were determined.

Absolute changes of daily urine output, absolute changes of creatinine clearance and serum cystatin-C levels in ACM group were significantly lower than those in CM group (p<0.05) (Table 1 and figure 1). Additionally proteinuria increased significantly in CM group compared with ACM group (p<0.05) (Table 1). Histopathological lesions in CM group were a little bit more advanced compared to other groups, however there were no significant differences between ACM and CM groups with regard to both histopathologic findings (Table 2) and inflammatory parameters (Table 3).

CONCLUSION:

In conclusion, this study demonstrated the protective role of adrenomedullin against CIN. Adrenomedullin prophylaxis may be useful in the prevention of CIN; further studies are needed to shed more light on this issue.

Table 1. Renal function parameters and weights before and after the experimental procedures in the four treatment groups (n = 6 each)

	C	CM	A	ACM	p
Δ Body Weight (gr)	-22.2±7.6	-26.8±5.4	-22.5±9.4	-31.1±4.5	NS
Δ Daily urine output (ml/100 gr VA)	-0.07±0.5 ^a	-1.46±0.5 ^{a,b,c}	-0.19±0.3 ^b	-0.53±0.1 ^c	0.001
Δ BUN (mg/dl)	1.8±6.9	12.5±6.0	1.4±9.3	8.2±7.4	NS
Δ Serum Cr (mg/dl)	0.06±0.05 ^a	0.17±0.05 ^{a,b}	0.03±0.05 ^b	0.08±0.06	0.003
Δ Cr Clearance (ml/dk/100gr VA)	-0.20±0.12 ^a	-0.39±0.12 ^{a,b,c}	-0.06±0.12 ^b	-0.16±0.12 ^c	0.01
Δ FENa (%)	-0.17±0.09	-0.18±0.09	-0.20±0.08	-0.18±0.06	NS
Δ Proteinuria (mg/gün)	-13±34 ^{a,b}	220±91 ^{a,c}	99±130	88±42 ^{b,c}	0.001
Cystatin - C (ng/ml)	2.54±0.53 ^a	4.12 1.16 ^{a,b,c}	2,39±0.42 ^b	2.77±0.85 ^c	0.005

Table 2. Histology findings in the four treatment groups (n = 6 each)

	C	CM	A	ACM	p
Tubular damage	0.67 0.51 ^a	1.67 0.51 ^{a,b}	0.33±0.51 ^{b,c}	1.17±0.41 ^c	0.001
Medullary congestion	0.33 0.51 ^a	1.17 0.41 ^{a,b}	0.17±0.41 ^{b,c}	1.00±0.00 ^c	0.003

Figure 1. Renal function parameters before and after the experimental procedures in the four treatment groups (Between C and CM p:0.05, between CM and A p:0.001, between CM and ACM p:0.018)

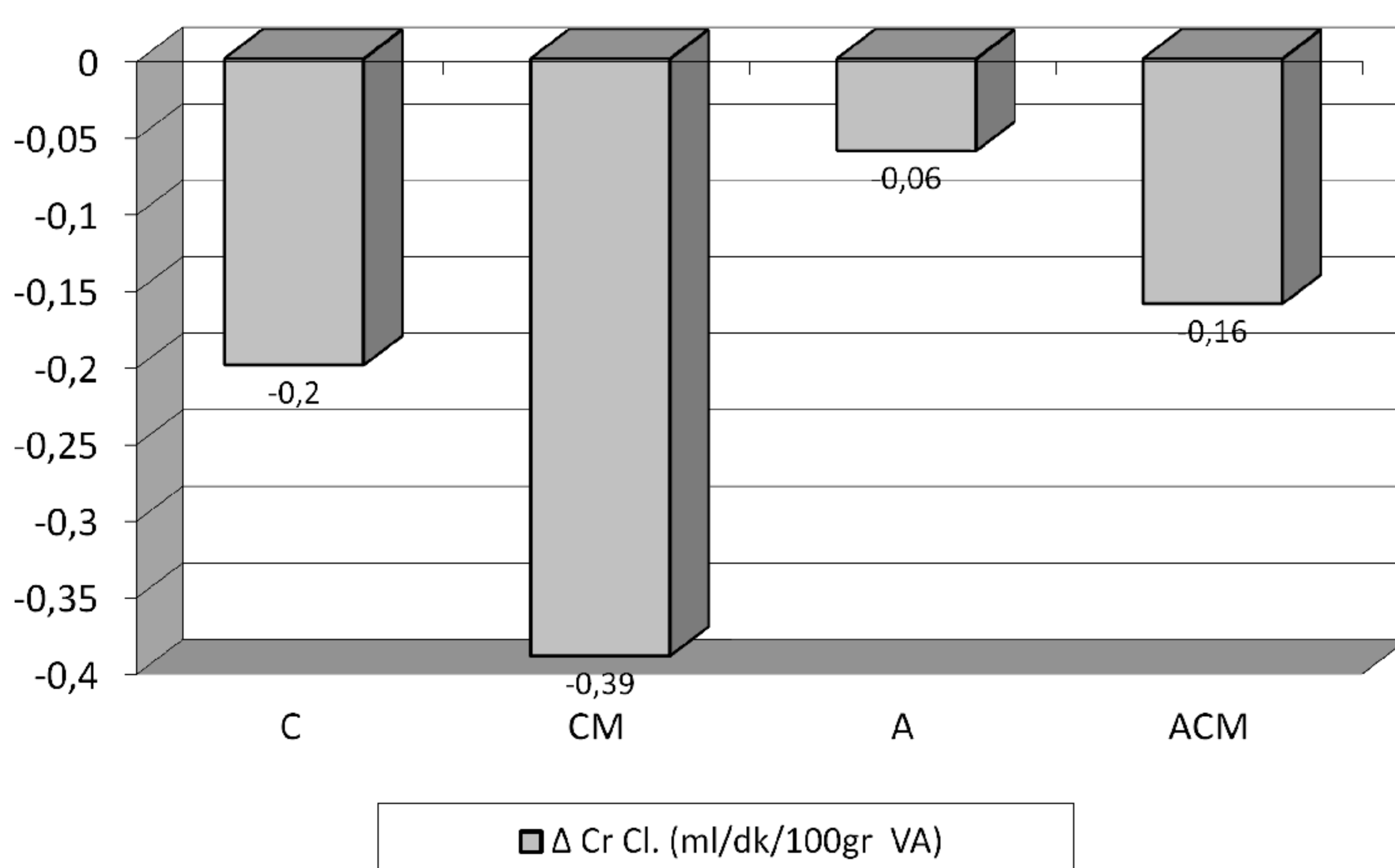


Table 3. Findings of inflammatory markers in the four treatment groups

	C	CM	A	ACM	p
IL-1beta (pg/mL)	66.7±31.3	109.3±36.1	57.6±65.6	85.5±41.9	NS
TNF-alfa (pg/mL)	23.1±5.2 ^a	64.8±22.6 ^a	30.1±6.2	56.4±29.4	0.003
IL-6 (pg/mL)	83.1 36.7 ^{a,b}	242.1 74.5 ^{a,c}	118.1±54.3 ^c	213.1±91.2 ^b	0.001
IL-18 (ng/mL)	0.28±0.06	0.34±0.04	0.29±0.04	0.29±0.09	NS

