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Introduction

- The renin angiotensin system (RAS) is involved in the control of blood pressure through its action on the kidney, and treatment with the direct renin inhibitor Aliskiren (Ali) reduces RAS activation. (1, 2)
- Pulmonary fat embolism may lead to acute lung injury and its most frequent cause is bone marrow that escapes the intrasosseous system after trauma or surgery. (3)
- We have previously shown in a rat model of fat embolism (FE) that triolein (T) injection leads to a severe inflammatory pulmonary reaction that causes fibrosis in lungs (4) that is rescued by Ali. (5)
- We extended this study to the kidney by evaluating the renin/prorenin (R/P) presence in the kidney with and without Ali in a rat model of fat embolism.

Methodology

- Sprague Dawley rats (280-300 grams) were injected with T (0.2 ml IV, n=12) or saline (n=4) through the tail vein.
- The T injected rats were divided into two groups (N= 6/ group), one hour later rats were injected with 0.2 ml T + saline, or T + Ali 100mg/kg while 4 controls received only saline.
- 48 hours after T injections, rats were euthanized, the kidneys were dissected out and fixed in 10 % formalin, sectioned and later immunostained for R/P specific antibody (from Abcam: ab180608).
- Two pathologists blind to the slide identity took 10 random images.
- R/P immunostained cells were quantified by three independent investigators using ImageJ program on medulla and cortical regions where the tubuli and glomeruli were evident.
- Animals were compared using statistical software (SPSS).

Renin-Prorenin Stained Tubuli

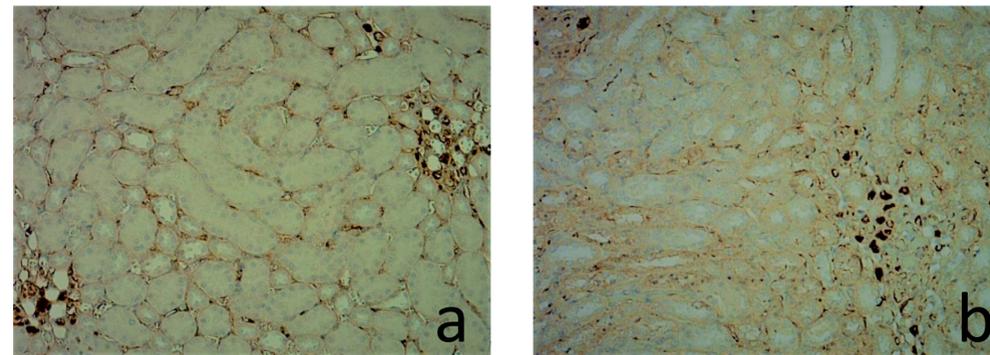


Figure 1. triolein + saline (a) triolein + 100 mg/kg Aliskiren(b)

Renal sections demonstrated no difference in tubuli renin staining either with triolein + saline or triolein + Aliskiren treatment.

Renin-Prorenin Stained Glomeruli

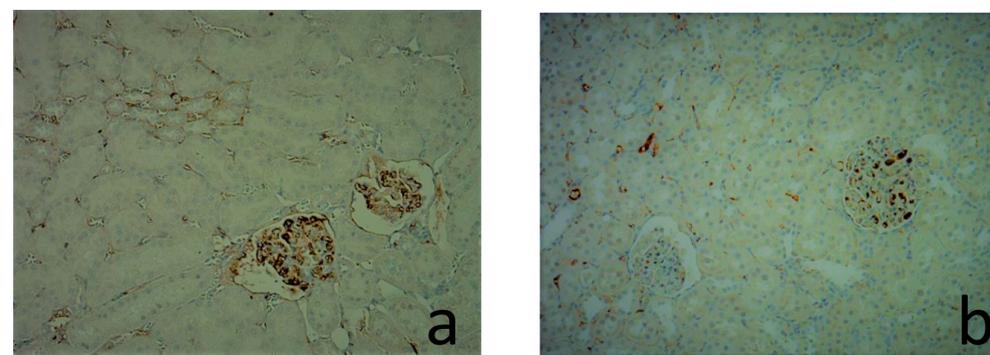


Figure 2. triolein + saline (a) triolein +100 mg/kg Aliskiren(b)

Renal sections demonstrated a decrease in glomeruli renin staining when Aliskiren was administered to triolein treated animals.

Results

- In contrast to our previous results in the lungs of the same animals, the renal sections showed minimal inflammatory damage without significant vasculitis. (6)
- Multiple cells are positive for R/P immunostaining in T+ saline treated animals. It was evident by quantification of these cells by Image J that treatment with T + saline, and T+ Ali resulted in an increase of R/P positive cells versus the saline + saline group but there was no statistically significant difference between the two T treated groups. (fig.1)
- By limiting the R/P staining analysis to the glomeruli, treatment with Ali reduced the renin staining intensity particularly in the juxtaglomerular apparatus, and the difference was statistically significant. (p value=0.0058) (fig.2)

Summary/Conclusion

- As previously reported for lungs and heart, R/P positive cells were also present in the kidneys.
- In the kidney, marked differences in the cortical region (glomeruli) were seen after Ali administration.
- By evaluating the R/P staining of the glomeruli, the study confirms that Ali pharmacological activity is interacting with the RAS system by reducing the secretion of renin in the kidneys and consequently reducing the angiotensin II production in the lungs; therefore, the drug has a potential use for the treatment of the respiratory distress syndrome consequent to the occurrence of fat embolism.

References

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