INTRODUCTION

- In a rat model of fat embolism (FE) induced by injection of triolein (T), a severe inflammatory reaction leads to vasoconstriction and pulmonary fibrosis (1).
- Lung damage is already evident at 48 hrs, and after partial resolution, a second phase of increasing severity develops up to 10 weeks. (2)
- The renin angiotensin system (RAS) is involved in the process: administration of captopril and losartan prevents the acute inflammatory response and fibrotic process in the lungs (3) and the direct renin inhibitor aliskiren (ALI) also protects the lungs from vasculitis, and fibrotic change in an early phase (48 hrs) (4).
- We extended the study of ALI to the kidneys by evaluating the renal arterial response to T treatment in this model of FE.

METHODS

- 22 Sprague Dawley rats received T (0.2 ml IV, n=18) or saline (n=4).
- The T treated rats were divided into three groups of 6 rats each and injected IP one hour later, with 0.2 ml saline, ALI 50 mg/kg or ALI 100 mg/kg.
- Four controls received saline.
- Rats were killed 48 hrs later; the organs fixed and stained with H&E.
- Trichrome staining showed very little amount of fibers mostly in the adventitia.
- MAR was determined by the ratio of luminal internal diameter of the media vs. its external diameter.
- The vascular evaluation included lumen patency (LP) and media adventitia ratio (MAR), a marker of edema.
- LP was determined by the ratio of luminal internal diameter of the media vs. its external diameter.
- MAR was measured by the external medial diameter vs. external adventitia diameter.
- 10 photos at 400 X were taken by two pathologists unaware of the slide identity.
- Two photos at 100 X were also taken in each slide for evaluation of fibrosis.
- In addition to this evaluation, we also divided the arteries into two groups: small caliber with diameter of <150 mm (mostly located in the cortical section) and the larger caliber >150 mm (mostly present in tubuli).

RESULTS

- No significant difference was observed for the LP in any of the treatments, P=0.8669.
- However there was a significant effect on the MAR when all the arteries were considered, P=0.0007, with a slightly larger ratio for the T+Saline and ALI groups.
- The statistical difference in the MAR was due to effects on the larger arteries >150 mm with P=0.0033 with no differences in the small arteries.
- Renal fibrosis was minimal with either SMA or trichrome stains. Evaluation by image J of SMA stain yield similar values in all the groups. Trichrome staining showed very little amount of fibers mostly in the arterial adventitia.

SUMMARY

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<th>Saline</th>
<th>T+Saline</th>
<th>T+All 50mg</th>
<th>T+All 100mg</th>
<th>P value</th>
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<tr>
<td>LP</td>
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<td>MAR</td>
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<td>36.50</td>
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<td>0.2699</td>
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Table 1: Lumen patencies and media adventitia ratios of all the renal arteries and the difference between small and large caliber arteries.

CONCLUSION

- These findings were different than our observations in the lungs where statistical significance was observed in LP of the T treated rats vs. controls, and the 50 mg ALI treated rats. Fibrosis was severe in the lungs with damage mostly located around the small caliber arteries.
- The study suggests that the influence of the RAS on renal arteries after FE may have different pathological course than that in the lungs and that the course of time changes may be different in the two organs.
- The effect of ALI in the kidneys is different according to the diameter of the arteries (small diameters vs. larger diameters). This finding was also not observed in the lungs.
- ALI treatment did show protection against effects of T on the media adventitia ratio implicating the RAS has some vascular effect in this FE model on the kidney at 48 hrs.

CREDITS/DISCLOSURE/REFERENCES

3. McIff T et al, J of Trauma 2011, 70: 1186-1191
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