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INTRODUCTION

We have shown that the histopathological pulmonary effects of inflammation and fibrosis were reduced in a rat model of fat embolism by administration of captopril and losartan (1). More recently we also found that the same affect was induced by administration of the renin inhibitor Aliskiren (2), underscoring the role of the Renin Angiotensin System in the pathogenesis of this condition. Aliskiren treatment also reduced the number of mast cells (MC) (3). We extended our study to the evaluation of the lung macrophages in view of the known interactions of MC with macrophages in the inflammatory process leading to fibrosis.

METHOD

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, aliskiren 50mg/kg or aliskiren 100mg/kg. Rats were killed at 48 hours, lungs collected for histological studies and stained by H & E, SMA1 and Masson trichrome for evaluation of inflammation and fibrosis. Macrophages were stained by CD68. Two pathologists unaware of the slides identity evaluated the lung damage and took 10 photographs of each slide at 400x for the macrophage count.

RESULTS

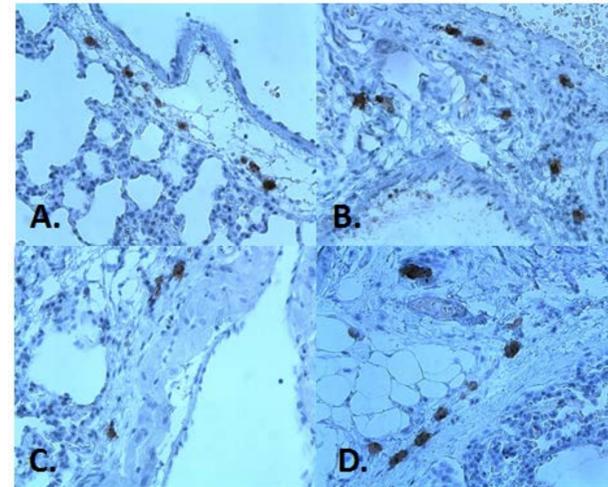


Figure 1. Macrophage distribution with Triolein and Aliskiren administration.

- Control
- Triolein + Saline
- Triolein + Aliskiren 50mg
- Triolein + Aliskiren 100mg

- Severe expected pulmonary inflammation and fibrosis was markedly reduced by both aliskiren doses in the rats injected with T + saline.
- 2 types of macrophages: Compact and Vacuolated
- Compact type was the most frequent and with dimensions similar to those of the MC.
- Vacuolated type was twice as large and showed many droplet-like cytoplasmic vacuoles.
- The compact size macrophages were distributed throughout the lung parenchyma and had no variation in numbers across all 4 groups.
- The T + 50 mg/kg aliskiren group showed a decline in vacuolated macrophage numbers vs the other 3 groups ($p < 0.016$, < 0.025 , and < 0.007) respectively.

CONCLUSIONS

- Two morphological types of macrophages were found: a compact type and a larger vacuolar type.
- Triolein treatment with or without aliskiren did not change the number of compact macrophages compared to saline controls.
- Triolein plus aliskiren 50 mg/kg showed a decrease in the number of vacuolated macrophages compared to the three other groups.
- Although we have previously found profound inflammatory and fibrotic changes in response to triolein that responded to aliskiren, significant changes in macrophages at 48 hours were not found.
- It remains to be seen if macrophage numbers are altered with a different time course than that found with mast cells and if the larger macrophage subtype may be influenced by aliskiren at a different concentration or time.

REFERENCES AND ACKNOWLEDGEMENTS:

1. Mc Iff T, Poisner, A., Herndon B et al: J of Trauma, 70 (5) 118691, 2011.
2. Fletcher A., Molteni A., Ponnareddy R., et al: J of Trauma and Acute Surg Care: in press 2016.
3. Kesh S., Fletcher A., Voelker D. et al. Proc. XIX ICLAF Meeting, Dublin, Ireland Sept 2226, 2016. Q.J.M 109 Suppl.S48, 2016.

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