INTRODUCTION

• Fat embolism secondary to fractured long bones can result in fat embolism syndrome causing acute respiratory distress syndrome with mortality ranging from 2.5% - 20%.
• In an acute rat model of fat embolism (FE) induced by injection of triolein (T), pulmonary damage includes severe inflammatory reactions leading to vasculitis and fibrosis in 48 hrs (1).
• These alterations are mitigated by agents acting on the renin-angiotensin system (RAS): captopril and losartan (2).
• Previous literature has shown that the pulmonary expression of renin is enhanced after lung injury, particularly in mast cells (3).
• We have extended the study of FE-induced acute lung injury to determine if renin expression is also enhanced and how this might be affected by captopril and losartan.

METHODS

• 23 Sprague Dawley rats (280-300 g) received T (0.2ml IV, n=17) or saline (n=6).
• The T treated rats were divided into three groups and each injected IP one hour later, with .2 ml saline (n = 7), captopril 50 mg/kg (n=5), or losartan 10 mg/kg (n=5).
• Rats given saline initially received IP saline at one hour.
• Rats were killed 48 hrs later; their organs fixed and stained with H&E for morphometry.
• Trichrome stain was used for fibrosis evaluation. Abscam specific antibodies for renin/prorenin cells (R/P).
• 10 photos at 400 X were taken by two pathologists unaware of the of the slide identity. Two photos at 100 X were also taken in each slide for evaluation of fibrosis.

RESULTS

• As previously reported, triolein induced arterial vasculitis, septal inflammation, and severe fibrosis, was markedly reduced by captopril and losartan.
• R/P stained cells showed a significant increase in lungs of the T treated rats compared to controls (p<0.0002) and this effect was enhanced by both captopril and losartan.
• The location, size, and shapes of R/P immunopositive cells were similar in the four groups. However, R/P immunoreactivity was observed in cells with different sizes and shapes.
• Most cells had small, oval intensely stained and compact cytoplasm and nucleus. Others, in a lower number, had a large cytoplasm, less intensively stained with some vacuoles.
• Both types were located mostly in the arteries, adventitia, the thickened septa, and sub-pleura.

CONCLUSION

• The current study has shown that the acute effects of pulmonary FE are associated with an increase in renin staining. This could be related to the known presence of renin in pulmonary mast cells (3) and the increase in mast cells found in a chronic model of FE (4) although other lung cells also contain renin (5).
• The increased number of R/P cells after captopril and losartan, despite the histopathological protective effects of these two drugs, is consistent with their known action on renin production by removing the negative feedback of angiotensin II.
• The results reinforce previous suggestions that interference with the RAS may be useful in treating or preventing FE-induced lung injury (2).

REFERENCES

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