Chronic Fibrotic Changes in Experimental Pulmonary Embolization in the Rat Model

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INTRODUCTION

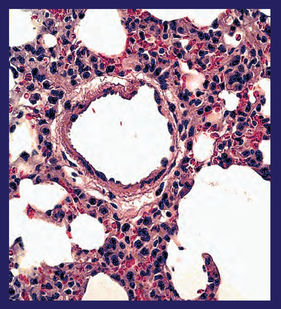
- Fat Embolization Syndrome (FES) occurs in many clinical settings such as long bone fractures, liposuction and CBP.
- Embolized fat is hydrolyzed by lipase into free fatty acids which has been shown to be toxic to the lung.
- Exposure of the lung to free fatty acids can cause the clinical picture of ARDS.
- An animal model for FES has been developed utilizing intravenous triolein as a surrogate for FES exposure.
- We, therefore, hypothesized that intravenous triolein will produce histological changes that are similar to that seen in human FES.

METHODS

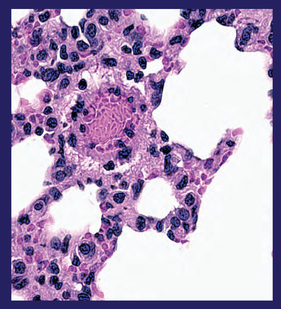
- Pure triolein (0.2 mL) was injected into the caudal vein of unanaesthetized Sprague Dawley rats (n=13), while control animals received 0.2 mL of saline (n=12).
- Weights were recorded until necropsy at 3 wks and 6 weeks.
- Tissues were stained using H&E, trichrome, and Oil Red O.
- Tissues of the lung were examined using 400x magnification.
- Morphometric measurements were made on arterial vessels from both H&E and trichrome-stained lung tissues, triolein and control, at 3 and 6 weeks.
  - Arterial lumen patency = ratio of vessel lumen over external medial diameter
  - Media/adventitia ratio = outer medial diameter over outer adventitia diameter
- Data were analyzed as a function of time and treatment (StatSoft, Tulsa Ok) using analysis of variance and post-tests or t-tests, with $p<0.05$ as statistically significant.

RESULTS

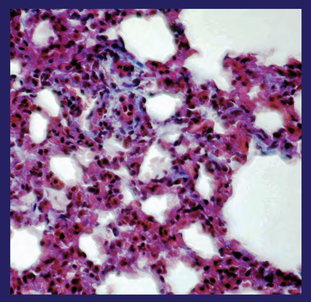
- Gross histopathological changes were seen in the lungs of the triolein group, although heart, liver, kidneys and spleen were normal and weight gain equaled the controls at 3 weeks.
- Pulmonary histological examination revealed diffuse intra-alveolar hemorrhages and edema with peri-bronchial inflammation.
- Vasculitis was more prominent in the peri-bronchial areas.
- Collagen development in the vascular, perivascular, and bronchial regions was evident in both the 3 and 6 week groups treated with triolein.
- Pulmonary arteries revealed significant medial thickening as compared with the control groups with arterial lumen patency significantly reduced in triolein groups vs controls (p=0.004).
- Adventitia/media ratio was not statistically significant.



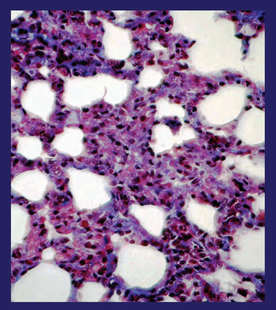
Control H&E



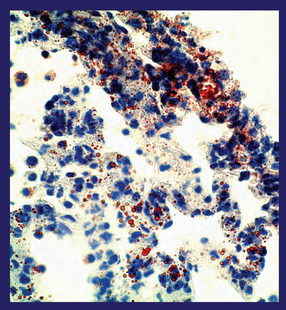
Triolein 3 wk H&E



Triolein 3 wk Trichrome

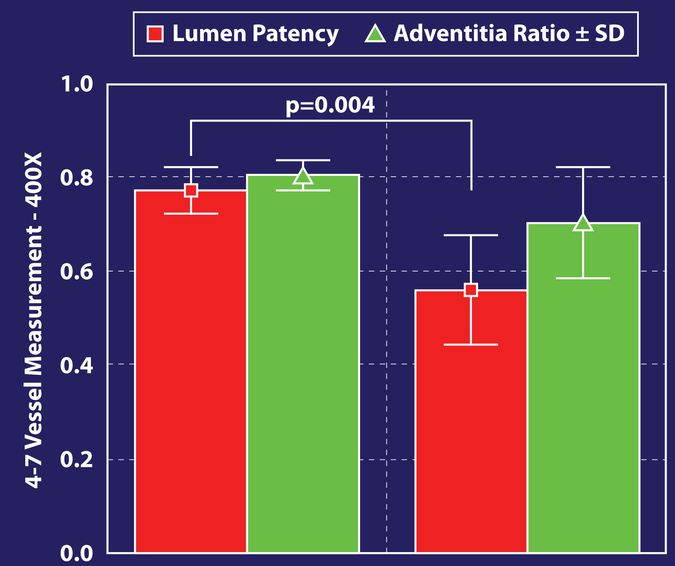


Triolein 6-wk Trichrome



Triolein 6-wk Oil Red O

LUMEN PATENCY AND MEDIA/ADVENTITIA RATIO



CONCLUSION

- Fat staining showed that injected triolein remains in the rat lung after 3 and 6 weeks with associated vascular and septal damage in the lung tissue compared to controls.

DISCUSSION

- This study is a continuation of earlier work that showed severe pulmonary damage within 3-6 hours following triolein induced fat embolism in the rat model, reaching a peak at 96 hours post injection.
- The present work shows that, despite recovery of general condition, body weight and partial reopening of the pulmonary arteries, collagen and vasculitis persisted up to 6 weeks.
- Further studies are needed to verify the eventual recovery or organ evolution toward chronic fibrosis.