The Cardiovascular Effects of Tobacco Smoke Exposure in a Rat Model of Chronic Obstructive Pulmonary Disease

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Introduction

Cigarette smoking is the leading cause of preventable disease and death in the United States, accounting for more than 480,000 deaths every year, or 1 in 5 deaths.1 Smoking causes a number of diseases, including cancers, myocardial infarction, stroke, and chronic obstructive pulmonary disease (COPD). COPD is becoming increasingly prevalent globally, and is expected to become the third-leading cause of death worldwide by 2020.2 Pulmonary and systemic hypertension are significant causes of morbidity and mortality in patients with COPD. Factors suspected to influence pulmonary hypertension in COPD patients include lung parenchyma destruction with associated loss of pulmonary microvasculature, and pulmonary artery vasoconstriction induced by alveolar hypoventilation. Pulmonary hypertension in COPD is believed to promote structural vascular changes, which is supported by the failure of oxygen therapy to reverse it.3 However, very little is understood regarding how progressive physiological changes of the cardiovascular system may affect resultant changes in cardiovascular morphology. Cardiovascular changes are commonly associated with COPD. Certain polymorphs found in COPD patients are implicated in increasing risks for other types of diseases, including cancer and cardiovascular disease.4 Cardiovascular symptoms may appear in the form of attherosclerosis, myocardial infarction and/or systemic hypertension. Chronic exposure of the spontaneously hypertensive (SH) rat to tobacco smoke results in COPD, inflammation, arterial obstruction, muscular hypertrophy, and emphysema changes. Little is known regarding the cardiovascular impacts in this animal model, although telemetric measures of cardiovascular physiology are available, along with heart tissue samples. Therefore, this study addresses the critical deficit by analyzing telemetric data in correlation to structural cardiovascular changes.

Hypotheses

1. Exposure to tobacco smoke alters cardiac function and morphology in spontaneously hypertensive rats.
2. Spontaneously hypertensive and normotensive Wistar Kyoto rats show differential sensitivity to tobacco smoke.

Methods

Spontaneously Hypertensive Rats (SHR) and Normotensive Wistar Kyoto Rats (WKY)

Surgical impact of telemetric devices

Filtered Air - 8 weeks

Smoked Air - 8 weeks

Filtered Air - Recovery weeks

Smoked Air - Recovery weeks

Paraffin Sections

Paraformaldehyde Fixation

Immunohistochemistry

Histological Stains

Hematoxylin

Eosin

Pentachrome

Trichrome

Immunohistochemistry and IHC Profiler

Troponin I Immunohistochemistry

Histologic Stains

Figure 5. Sample Trichrome and Pentachrome stained slides

Figure 5. Samples of Trichrome and Pentachrome stained slides captured at 40x from SH- rats exposed to tobacco smoke intermittently for up to 16 weeks. Trichrome stained images were used to analyze the ventricular myocardium. Pentachrome images were used to analyze the coronary microvasculature. There were no qualitative differences between the tobacco-exposed and unexposed groups.

Conclusions

• In both SH and WKY rats, exposure to tobacco smoke was associated with significant transient increases in systolic and diastolic blood pressure.
• In WKY rats, all physiological parameters returned to baseline levels during non-exposure periods.
• In SH rats, all physiological parameters returned to baseline levels during non-exposure periods, except heart rate, which persisted at an elevated level.
• In SH rats, mean pulse pressure was reduced as a result of a greater increase in diastolic compared to systolic pressure. A progressive decrease in mean pulse pressure in SH rats exposed to tobacco smoke was suggestive of potential heart failure.
• In SH rats, exposure to tobacco smoke caused a statistically significant increase in right ventricular wall thickness compared to the unexposed rats.
• Tobacco exposure produced significantly increased heart rate values in SH and WKY rats. However, the SH rats heart rates did not return to baseline during the observation period, which suggests that they are more sensitive to tobacco smoke than WKY rats.
• Telemetric approaches can be implemented to detect and document novel and progressive cardiovascular impacts of tobacco smoke under experimental conditions.

References


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