The postnatal development and growth of the cardio-respiratory system in sprague-dawley rats

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ABSTRACT

The purpose of this study was to investigate the histomorphological changes of the cardio-respiratory system in rat pups over the first month of life. The heart weight and the heart weight relative to body weight ratio were calculated for 51 rats over 13 timepoints, ranging from gestation day 1 (GND) to PND30. For each timepoint, whenever possible, equal number of females and males were used. The aortic wall progressively increased in thickness throughout the duration of our study as a result of an accumulation of extracellular matrix (collagen, elastin and elastic fibers). Postnatally, the cardiac volume essentially increased by cardomyocyte hypertrophy, which showed a more mature appearance around PND21. In the newborn myocardium, mitotic figures and apoptotic bodies were frequently seen, increased on PND4 and showed a diffuse pattern. At birth, the trachea was lined by immature columnar ciliated epithelial cells and submucosal glands became visible around one week after birth. The newborn rat has no alveoli and breathes with smooth, large gas exchange units termed “primary sacculles”. An intensive interstitial cellular proliferation was observed in the lungs between PND6 and PND14, when the majority of alveoli are separated by new secondary septa, formed from the primary walls. These changes were accompanied by few mitoses and/or individual apoptotic cells. The findings described herein suggest that the cardio-respiratory system in rat pups over the first month of life.

INTRODUCTION

In recent years juvenile toxicity studies have been an area of significant concern in preclinical development of drugs and have been targeted of academic interest as well. Added too are concerns about the issues of testing strategies (e.g. route of administration, target organs, age of pups), monitoring of landmarks of postnatal histomorphological development in rodents is a critical component in study design and a fundamental element of such studies. In this study we have investigated the Histomorphological changes of cardio-respiratory system in rat pups over the first month of life.

MATERIALS AND METHODS

The 51 pups in this study were the progeny of 6 time-mated Sprague-Dawley rats dams (citoxlab). For each litter, pups were weighed and sexed at birth, and one pup from each sex and litter was then weighed at each time point. The postnatal development and growth of the cardio-respiratory system in Sprague-Dawley rats was subdivided into many, incompletely closed smaller units (figure 6). These new subdivisions were lined by a simple non ciliated cuboidal epithelium while the mucosa of the large airways is much thinner, has less prominent cross-striations and high mitotic index (arrows). H&E 400x.

RESULTS AND DISCUSSION

During the first month of life, both body and heart weight increased with age, and most significantly after PND21. The heart weight relative to body weight was higher at birth, and progressively decreased until PND30, suggesting that the by the end of first month of life the heart weight increased at a less dramatic rate than body weight. As in human, the cardio-respiratory system of Sprague-Dawley rats is immature at birth. The lungs and airways reached maturity 3 weeks after birth while cardiomyocyte hypertrophy was noticed until PND30. Tissue remodeling by apoptosis and/or mitosis was minimal in the lung, trachea and aorta and marked within the heart, especially at PND4. These results will serve as database of background age-related changes of neonatal and juvenile rats in preclinical toxicological studies.

CONCLUSION

As in human, the cardio-respiratory system of Sprague-Dawley rats is immature at birth. The lungs and airways reached maturity 3 weeks after birth while cardiomyocyte hypertrophy was noticed until PND30. Tissue remodeling by apoptosis and/or mitosis was minimal in the lung, trachea and aorta and marked within the heart, especially at PND4. These results will serve as database of background age-related changes of neonatal and juvenile rats in preclinical toxicological studies.

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