

Title: Sex-dependent vulnerability for Wistar rats model following intranasal instillation with *Klebsiella pneumoniae* ATCC 43816 causing lobar pneumonia

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ABSTRACT

Background: *Klebsiella pneumoniae* pneumonia causes acute inflammation in the lung, characterized by the recruitment of polymorphonuclear cells, generating free radicals, and decreasing the endogenous antioxidant balance system. Many experimental studies have focused on the induction, progression and resolution of infection up to its peak, but these documented processes remain highly random and their sex dependence un-elicited. These fluctuations of physiopathological parameters would impact disease progression depending on the animal's model and bacterial strain used.

Objective: The present study investigated the sex-dependent vulnerability of Wistar rats to *K. pneumoniae* ATCC 43816 lobar pneumonia induced by the intranasal instillation method.

Methods: Experimental pneumonia was induced by *K. pneumoniae* ATCC 43816 in male and female Wistar rats following intranasal instillation. The physiopathogenesis of the disease was studied by bacteriological, histopathological and histomorphometric analysis of the blood and/or lung tissue, and body weight loss in infected animals. In addition, the overall severity of lesions was determined by the total score obtained by averaging the individual scores from the same group of animals.

Results: The *K. pneumoniae* ATCC 43816 strain showed inoculation dose-, incubation time of the disease- and sex-dependent- differences in its ability to induce lobar pneumonia. Evaluation of different parameters showed that the disease peaked on day 15 post-inoculation, with more pathogenic effects on female rats. This observed sex-dependence difference was mainly highlighted by the determined lethal dose 50 (LD₅₀), bacterial load count in whole blood and lung tissues, body weight loss, inflammatory granulomas forming and diffuse alveolar damages. The pathogenicity was confirmed by scoring the severity of pathologic lesions of lung tissues.

Conclusion The results obtained highlighted the gender-dependency in the physiopathogenesis processes of *K. pneumoniae* ATCC 43816 induced-lobar pneumonia, in Wistar rats. Female Wistar rats' susceptibility is useful in studying pathology and in preclinical studies of new treatments for infectious pneumonia.

Keywords: *Klebsiella pneumoniae*, Intranasal instillation, Lobar pneumonia, Inflammatory granulomas forming, Sex- dependent vulnerability, Wistar rat model

BIOGRAPHY

Dr Betote's research has focused on the discovery of novel natural products from the largely untapped biodiversity of Central and West Africa and their derived biomolecules, and the advancement of fundamental knowledge of

their biological properties to improve their medicinal use. A core research interest is in phytobiochemistry and phytochemistry, oxidative stress and inflammatory diseases and infectious respiratory diseases phytotherapy, i.e. the study of the host-pathogen relationship, phyto-aromatherapy and the pharmacological, physiopathological and immunological responses of the host. He also focused on the development and application of innovative screening methods leading to the discovery of new therapeutic leads and pharmacological biomarkers. This research approach responds to the emergence of microbial resistance and the need to use traditional pharmacopoeia to improve human health worldwide.

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