



## THE EFFECT OF RAPAMYCIN ON SEVERE PULMONARY LEPTOSPIROSIS IN GUINEA PIGS MODEL

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### Abstract

**Background:** The recent study of experimental leptospirosis in guinea pigs suggested that an auto-immune process may be the etiology of the severe pulmonary hemorrhage in leptospirosis.

**Objectives:** To determine the current immunosuppressive agents could alleviate the inflammation and minimize the organ injury in guinea pigs which infected by pathogenic leptospire

**Methods:** Thirty-six, 3-week-old guinea pigs were divided into six groups (n = 6 in each group) namely. Group 1 (Normal) was a control group. Group 2 (Rapa) was fed with rapamycin. Group 3 (Lepto) was challenged with *Leptospira interrogans* serovar pyrogenes . Group 4, 5 and 6 (Lepto rapa hr-0, Lepto rapa hr-24 and Lepto rapa hr-48) were challenged with *Leptospira interrogans* serovar pyrogenes and started to feed with rapamycin on 0, 24 and 48-hour post inoculation and followed once daily. Two animals of each group were euthanized on 2, 4 and 6 day post inoculation. Pathology, hematology, blood chemistry, Warthin-Starry method and immunofluorescence antibody technique (IFAT) were studied.

**Results:** Lepto rapa hr- 0, Lepto rapa hr-24 and Lepto rapa hr-48 revealed severe thrombocytopenia and severe ecchymotic peritoneal hemorrhage while Lepto revealed moderate thrombocytopenia and mild petechial peritoneal hemorrhage. Histopathology of lung, Lepto rapa hr-4 8 revealed severe multifocal pulmonary hemorrhage while Lepto, Lepto rapa hr-0, Lepto rapa hr-24 revealed moderate multifocal pulmonary hemorrhage. Histopathology of liver, Lepto rapa hr-0 revealed cloudy swelling of hepatic parenchymal cells while Lepto rapa hr-24 and Lepto rapa hr-48 shown multifocal hepatocellular necrosis with the infiltration of neutrophils and lymphocytes around the portal veins and hepatic arteries and Lepto revealed severe hepatic sinusoid congestion. Histopathology of kidney, Lepto rapa hr-0 revealed mild interstitial hemorrhage with renal tubular cell swelling while Lepto rapa hr-24 and Lepto rapa hr-48 revealed moderate interstitial hemorrhage with renal tubular cell swelling and Lepto revealed moderate interstitial hemorrhage and renal tubular necrosis. The IFAT results of the alveolar basement of lung and glomerulus of kidney, Lepto revealed high IgM deposition while Lepto rapa hr-48 revealed few IgM depositions. Whereas Lepto rapa hr-0 and Lepto rapa hr-24 revealed the absence of IgM deposition.

**Conclusions:** The study concluded that rapamycin reduced IgM deposition and alleviated lesions in lung, liver and kidney when rapamycin were concurrently fed. However, rapamycin could not prevent pulmonary hemorrhage and if guinea pigs were fed rapamycin after 48-hour post inoculation, the severity of lesions was increased in those organs.

*2<sup>nd</sup> PMK & AFRIMS Joint Symposium, 7-8 June 2011, Poster presentation*