SP099

EFFECT OF XANTHINE OXIDASE INHIBITORS (XOi) IN RATS SUBMITTED TO LPS.

Ramos MFP; Passos CS, Razvickas CV, Borges F, Schor N.

Nephrology Division, Escola Paulista de Medicina/UNIFESP São Paulo/ Brazil

Introduction: The systemic inflammatory response of sepsis is marked with the production of reactive oxygen species. The antioxidant system is composed among others by glutathione (intracellular) and uric acid (intravascular). Thus, it was studied the role of XOi (allopurinol and febuxostat) in the LPS model of sepsis in rats made hyperuricemic by oxonic acid (OxAc) administration.

Objectives: To evaluate the effect of xanthine oxidase inhibitors in rats submitted to LPS.

Material and Methods: Mean arterial pressure (MAP) was measured by tail method and uric acid (UrAc) by uricase. The LPS was administered i.p. (10 mg/Kg) every 24 hours until the 3rd day. XOi were given by gavage each 24 hours for 3 days. Allopurinol (ALLO,2 mg/ kg) and febuxostat (Febux,1 mg / kg) were used in an equivalent dose as in clinical use . To increase UrAc it was administered OxAc by gavage (750mg/Kg/day) during 5 days. UrAc measurements were done at baseline and at 6Th day. The animals were divided into 9 groups (n = 6): 1-Control, 2-ALLO treated animals, 3-Febux treated, 4-LPS group, 5-LPS+ALLO, 6-LPS+Febux, 7-OxAc treated animals, 8-OxAc+LPS+ALLO and 9-OxAc+LPS+Febux. Data were evaluated by Student's t test and survival curves (Chi square) considering the value of $p < 0.05$. Data were reported as mean and standard deviation.

Results: ALLO administration with LPS treatment caused a significant increases in the mortality , inducing death in 28 of 34 animals (82%) , while the same did not occurred with LPS+ Febux (11/17; 65%) or LPS alone (10 /16; 63%) , $p<0.05$. Figure 1.

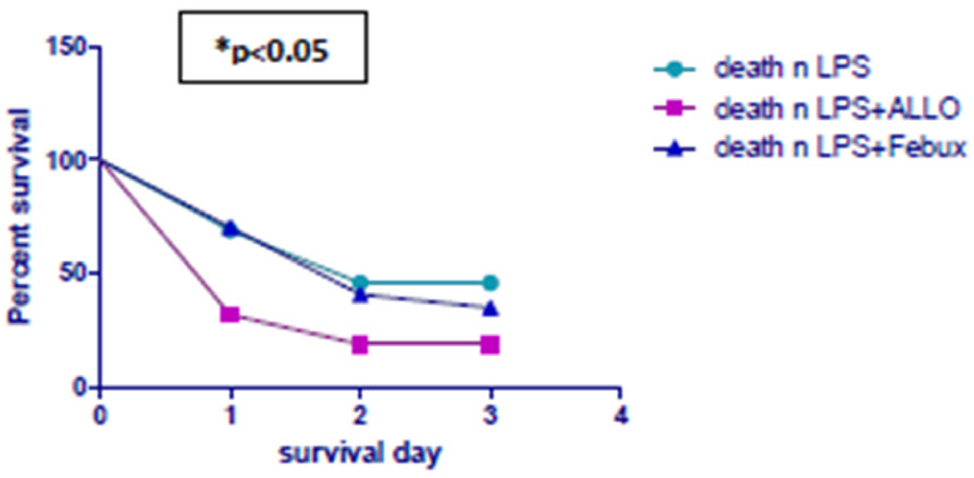

Figure 1. Survival days. **GROUPS:** LPS, LPS+ALLO and LPS+Febux

Administration of OxAc after 5 days increased the UrAc in the plasma from 2.98 ± 0.17 to 3.76 ± 0.59 mg/dL (p=0,015) and also induced MAP to rise from 125 ± 8 to 149 ± 29 mmHg ($p<0.02$). Figure 2 and 3.

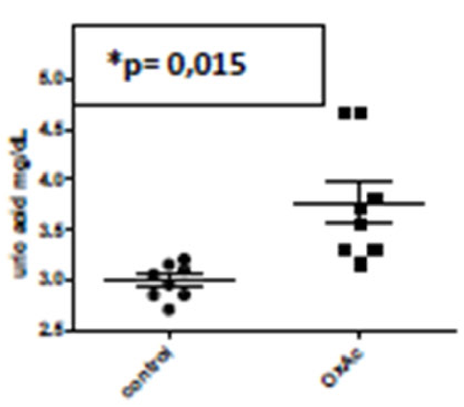

Figure 2. Uric acid after 5 days with OxAc administration.

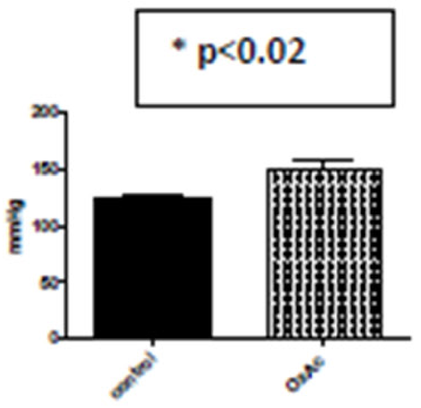

Figure 3. MAP control and after 5days with OxAc administration

Surprisingly no mortality was observed in the groups OxAc+LPS and OxAc+LPS+Febux ($p<0.02$),Figure 4. There was a important lower deaths when it was associated OxAc +LPS+ALLO (12 /18; 67%) compared with LPS+ALLO (28/ 34; 82%), p= 0.08, Figure 5. There was no significant difference between the groups in the mortality, despite the tendency of AcOx to protect against ALLO in this protocol.

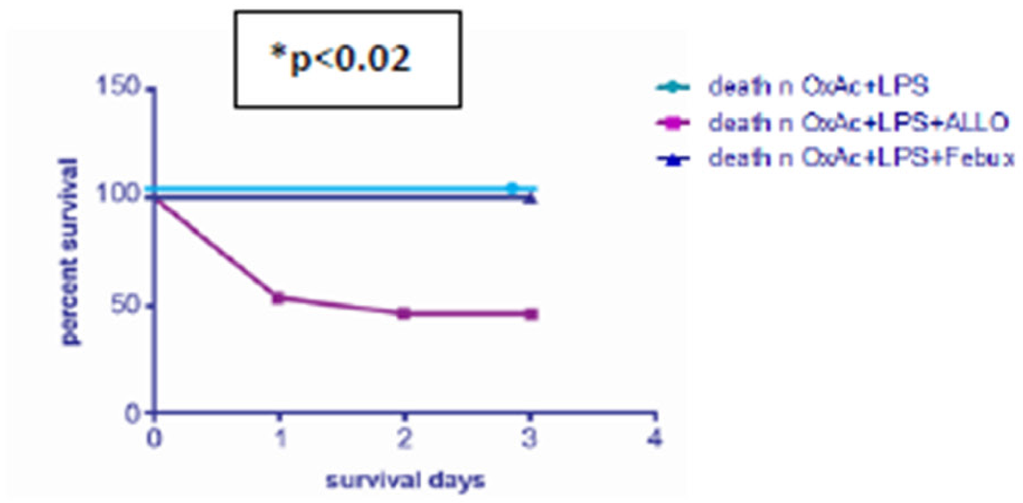

Figure 4. GROUPS: OxAc+LPS, OxAc+LPS+Febux and OxAc +LPS+ALLO

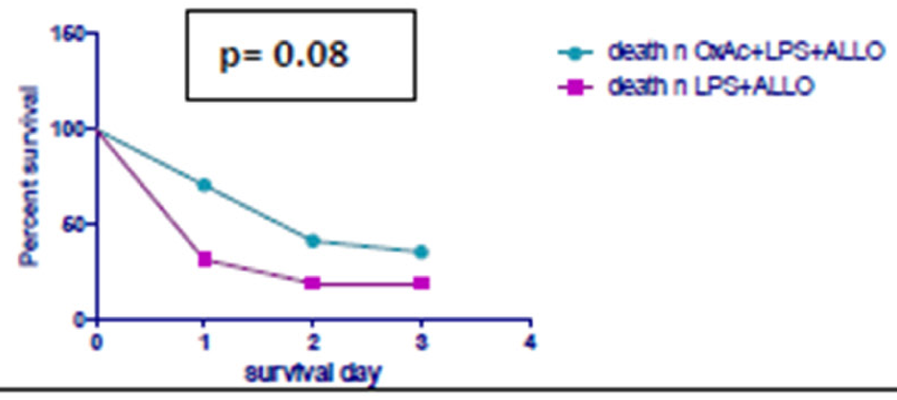

Figure 5. GROUPS: OxAc +LPS+ALLO and LPS+ALLO

Discussion and Conclusion: In this study the administration of ALLO in LPS treated animals, decreased significantly the chance of survival. This effect was not observed with Febux. On the other hand, elevation of plasma UrAc by the OxAc protected the animals from the LPS. Thus, high plasma UrAc, by its potential antioxidant capacity, decreases the effects of LPS and the use of OxAc, increasing blood uric acid, elevate the chance of survival. However, more studies are needed to elucidate if the administration of the xanthine oxidase inhibitors can worsen the evolution of sepsis and also it is necessary to evaluate the potential differences among XOi (ALLO vs. Febux) in this experimental model.

Supported by FAPESP, CAPES, CNPq e FOR

DOI: 10.3252/pso.eu.51era.2014

Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014