A489 - Does the endotoxin adsorption of pmx column saturate in 2 hours? -preliminary study

C Yamashita 1; K Moriyama 2; D Hasegawa 1; T Kawaji 1; N Kuriyama 1; T Nakamura 1; Y Shimomura 1; S Suzuki 1; Y Kato 1; O Nishida 1
1Fujita Health University School of Medicine, Department of Anesthesiology and Critical Care Medicine, Toyoake, Japan, 2Fujita Health University School of Medicine, Laboratory for Immune Response and Regulatory Medicine, Toyoake, Japan

Introduction:
In the EUPHRATES trial, the polymyxin B-immobilized fiber column (PMX) hemoperfusion (HP) had no significant effect on 28-day mortality. Endotoxin (LPS) burden by endotoxin activity assay >0.90 may exceed 50 μg [1], so the dose and duration of PMX-HP could be insufficient to lower the LPS burden. To confirm this issue, we experimented in a closed-circuit with 24 h continuous LPS addition, and PMX can adsorb > 50μg [2]. Further, LPS concentration became constant within 2 h in the single LPS spike test for determining PMX-HP duration [3]. To prove our hypothesis that the single LPS spike test reflects the adsorption equilibrium, and not saturation, we added LPS intermittently to reaction.

Methods:
LPS (10 ng/mL) was mixed with 125 mL deactivated fetal calf serum as a reflux solution, as previously described [2]; this concentration is much higher than that observed in septic patients. We created a closed circuit that incorporates PMX-01R at 1/14th the amount of an adult PMX and performed PMX-HP at 10 mL/min for 5 h. LPS was added in two shots (post 2 h: 1250 ng, 10 ng/mL; post 4 h: 3750 ng, 30 ng/mL). LPS was measured using the Limulus Amebocyte Lysate test at 0, 0.5, 1, 2, 3, 4 and 5 hr.

Results:
After an initial decrease between 0 and 1 h, LPS concentration did not decrease between 1 and 2 h after PMX-HP initiation. Post LPS pulse addition at 2 h, it increased and then decreased till 3 h. Further, it did not decrease between 3 and 4 h, but it increased and then decreased again after LPS pulse addition post 4 h (Figure 1). LPS adsorption rates were 76.2, 43.4, and 40.7% at 2, 4, and 5 h, respectively.

Conclusion:
LPS adsorption capacity of PMX-01R was maintained even after two additional shots of LPS, suggesting that the constant LPS concentration in the previously reported LPS spike test might be indicative of adsorption equilibrium rather than saturation.

References:
1. Dellinger RP, et al. JAMA 320:1455-1463, 2018
Figure 1. LPS concentration in LPS pulse addition test