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0733. Impact of endotoxin challenge on disseminated intravascular coagulation in obese minipigs

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Introduction

An early activation of coagulation and fibrinolysis occurs during sepsis and results in a marked increase of thrombin and fibrin formation, leading to the syndrome of disseminated intravascular coagulation (DIC). DIC is a strong predictor of death and multiple organ failure in patients with septic shock [1]. Obesity has been demonstrated to be a hypercoagulable [2] and hypofibrinolytic [3] state but its impact on coagulation and fibrinolysis during sepsis has never been studied.

Objectives

In this study, we aimed to determine if obesity impairs DIC in an acute endotoxic shock using minipigs.

Methods

This was a prospective, comparative and experimental study, approved by the Animal Ethics Committee. Pigs were chosen as a clinically relevant species, resembling to humans in coagulation reactions. Four groups of five "Yucatan" minipigs were studied: lean and obese control groups, lean LPS group receiving Escherichia Coli endotoxin (LPS) and obese LPS group receiving the same endotoxin dose. We measured standard coagulation parameters [prothrombin time (PT), platelet count and fibrinogen levels], thrombin-antithrombin complex (TAT), tissue plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1). All measurements were performed at baseline and at 30, 60, 90, 150 and 300 minutes. Results were given as median with 25-75 interquartile ranges.

Results

At baseline, platelet count (477 [428-532] vs. 381 [307-442] G/l; p=0.005) and fibrinogen levels (4.6 [3.8-5.2] vs. 2 [1.8-2.9] g/l; p< 0.001) were significantly higher whereas prothrombin time (80 [76-92] vs. 96 [89-100] %; p=0.01) was significantly lower in obese pigs compared to lean pigs. Control groups remained stable during the study-period. In LPS groups, administration of endotoxin resulted in a typical hypokinetic shock with DIC. The decrease in coagulation parameters (PT, platelet count and fibrinogen levels) and the increase in TAT complex (581 [382-1057] vs. 247 [125-369] µg/ml at 150 min; p=0.03) were significantly more important in obese LPS group compared to lean LPS group. Concerning the fibrinolytic reaction, we found a more important increase of PAI-1 in obese LPS group at 300 min (481 [365-617] ng/ml vs. 355 [209-660] ng/ml; p=0.66) without reaching statistical significance. Nevertheless, the increase of t-PA was significantly lower in obese LPS group compared to lean LPS group at 90 min (10 [8-17] vs. 5 [2-9] ng/ml; p=0.04).

Conclusions

In our model of endotoxic shock, obese pigs developed a more severe disseminated intravascular coagulation with a more serious procoagulant response.

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