Modelling severe Staphylococcus aureus sepsis in conscious pigs: are implications for animal welfare justified?

A porcine model of haematogenous Staphylococcus aureus sepsis has previously been established in our research group. In these studies, pigs developed severe sepsis including liver dysfunction during a 48 h study period. As pigs were awake during the study, animal welfare was challenged by the severity of induced disease, which in some cases necessitated humane euthanasia. A pilot study was therefore performed in order to establish the sufficient inoculum concentration and application protocol needed to produce signs of liver dysfunction within limits of our pre-defined humane endpoints. Four pigs received $1 \times 10^8$ cfu/kg BW of S. aureus, and two controls were sham inoculated with saline. A fixed infusion rate of 3 mL/min was used, while the inoculum concentration, i.e., the dose volume, was changed between the pigs. The following dose volumes were used: 10 mL ($n = 1$), 20 mL ($n = 2$), and 30 mL ($n = 1$), corresponding to infusion durations of 3.33, 6.66, and 10 min at dose rates of $3 \times 10^7$, $1.5 \times 10^7$, and $1 \times 10^7$ cfu/min/kg BW, respectively. Blood samples were drawn for complete blood count, clinical chemistry, and inflammatory markers before and every 6 h after inoculation. Prior to euthanasia, a galactose elimination capacity test was performed to assess liver function. Pigs were euthanised 48 h post inoculation for necropsy and histopathological evaluation. While infusion times of 6.66 min, and higher, did not induce liver dysfunction ($n = 3$), the infusion time of 3.33 min ($n = 1$) caused alterations in parameters similar to what had been seen in our previous studies, i.e., increasing bilirubin and aspartate aminotransferase, as well as histopathological occurrence of intravascular fibrin split products in the liver. This pig was however euthanised after 30 h, according to humane endpoints. A usable balance between scientific purpose and animal welfare could not be achieved, and we therefore find it hard to justify further use of this conscious porcine sepsis model. In order to make a model of translational relevance for human sepsis, we suggest that future model versions should use long-term anaesthesia.

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