Model of induced fever in pig: Model validation

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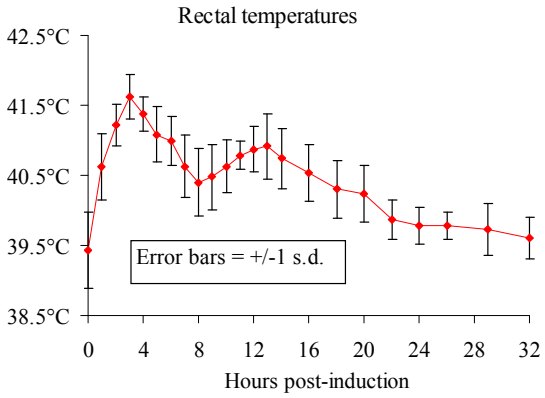
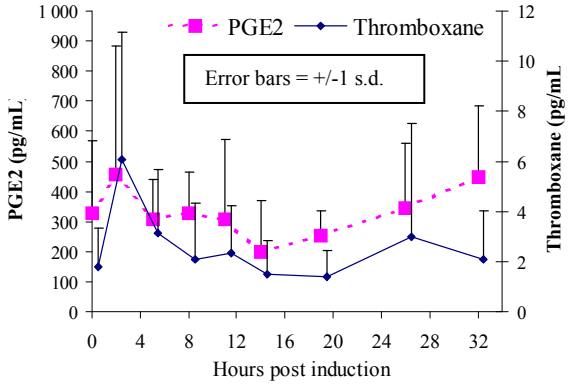
Introduction: In pig models, LPS administrations are known to induce hyperthermia and very often endotoxic shock. Mortalities are also frequently recorded. The aim of the study was therefore to validate a model which induced transitory fever without severe side-effects or fatality.
Materials and Methods: An experimental preparation (no. 110105) based on inactivated Gram +ve bacteria strains was formulated and prepared. Eight pigs (four males and four females), mean bodyweight 33.5 kg, commercial breed, were subjected to an intramuscular administration of experimental preparation 110105. As training, rectal temperatures were measured three times daily during the three days before induction. After induction, animal observations and temperatures were regularly recorded up to 32 hours. Blood sampling was performed just before induction and then on eight occasions up to 32 hours to assess thromboxane B2 (TBX) and prostaglandin E2 (PGE2) patterns. Feed and water consumptions were assessed before induction and during the 26 hours post induction for comparison with the pre induction values. Statistical comparisons between pre- and post-induction rectal temperatures were performed using Repeated Measures Anova and Bonferroni Multiple Comparisons.
Results: During the pre-induction period, two animals presented rectal temperatures higher than 40.0°C at two or more occasions but were nevertheless kept in the experiment. After administration of experimental preparation 110105, rectal temperatures rose quickly to reach a maximum at 3 hours post induction. A biphasic curve was observed in all animals. No significant symptoms, except dullness, were noted.





Rapid increases in TBX levels were recorded. However, these increases were transitory and normal levels were noted from about 5 hours post induction. No specific changes in PGE2 levels were observed. Food intake showed a mean reduction of about 48%, ranging from 37 to 67%. Water consumption was reduced by about 40 %, ranging from 10 to 62%. Statistical comparisons showed that temperatures between T2h and T18h were statistically higher ($p<0.05$) than pre-induction temperatures.
Discussion: After the administration of the experimental preparation, a clear and lasting increase in body temperature was observed in all the animals. Even when pre-induction temperatures were higher than 40°C, post-induction temperatures were raised. If the pigs with pre-induction high temperatures are withdrawn from the statistical analysis, the fever duration is increased to 22 hours. The biphasic curve may have been induced by differences in LPS associated with the different strains of bacteria used in the experimental preparation. Separate preparations with each strain have not been evaluated. TBX levels quickly increased after induction for a short period, consequently although the model clearly induces TBX increases more precise definition would require closer assessments at more frequent intervals. It is surprising that no clear changes in PGE2 were recorded. There are two possible explanations for this: either there is no increase of PGE2 levels or the increase is so transitory that the assay time points used were unable to resolve it.
Conclusion: This model could be used to run PK/PD evaluations of antipyretic compounds. PK/PD evaluation of anti-inflammatory activity of such products would be assessed using the TBX changes.