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REGULAR ARTICLE

Normal values for thrombelastography (ROTEM®) and selected coagulation parameters in porcine blood

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Abstract The pig is a suitable animal model for researching blood coagulation and fibrinolysis. The present study therefore aimed to investigate in porcine blood the applicability of commercially available tests of coagulation and thrombelastography (ROTEM®) and above all to determine normal values for coagulation parameters (e.g. prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin-antithrombin complexes (TAT), fibrinogen, antithrombin III (AT III), D-dimers, protein C).

Except for the FibTEM® and aPTT tests, all commercially available coagulation tests used were fully applicable for porcine blood. Normal values and reference intervals for porcine blood are given. As compared to the human reference intervals for the coagulation parameters investigated, porcine blood was found to be hypercoagulable.

Introduction

Similarities in the human and the porcine coagulation and fibrinolytic systems increasingly favor the use of porcine models when researching blood

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coagulation [1]. Normal values obtained with commercially available tests of coagulation or thrombelastography (ROTEM®), however, pertain exclusively to human blood. Therefore, the present study aimed to investigate in porcine blood the applicability of such tests and above all to determine normal values for coagulation parameters (e.g. prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin-antithrombin complexes (TAT), fibrinogen, antithrombin III (AT III), D-dimers, protein C) and thrombelastography (TEG) (ROTEM®).

Materials and methods

The present study's data on normal values for coagulation parameters of porcine blood are pooled data from blood samples drawn at baseline from pigs subjected to either of two coagulation research protocols approved by the Austrian Federal Animal Investigation Committee (GZ 66.011/68-BrGT/2003, GZ66.011/118-BrGT/2003).

Animals

All pigs (German/Pietrain; $n=80$; 15—18 weeks old; 36—55 kg body weight) were managed in accordance with the guidelines of the National Institutes of Health. Animals were fasted overnight but had free access to water. Pigs were premedicated with azaperone (4 mg/kg intramuscular) and atropine (0.01 mg/kg intramuscular) 1 h before surgery. Following induction of anesthesia with ketamine (20 mg/kg intramuscular) and propofol (2—4 mg/kg intravenous) and tracheal intubation normoventilation was used (fraction of inspired oxygen (FiO_2), 0.4; endtidal carbon dioxide concentration ($EtCO_2$), 40 mm Hg). Anesthesia was maintained with propofol (6—8 mg/kg/h) and remifentanil (1—2 μg/kg/min). Ringer's solution (10 mL/kg/h) was administered throughout the experiment. No paralyzing agent was used. Body temperature was maintained at normothermia (38—39 °C) by means of a heating blanket.

Monitoring included a standard lead II electrocardiogram and invasive blood pressure measurement in the femoral artery (diameter: 1.2 mm; Leader Cath, Vygon GmbH, Aachen, Germany). An additional catheter (diameter: 1.4 mm; Venenkatheter, B. Braun Melsungen AG, Melsungen, Germany) was inserted into the femoral vein for blood collection.

Experimental protocol

All blood samples ($n=80$) were drawn from the femoral vein, whereby the first ten milliliters of blood were discarded. Blood samples for ROTEM® and coagulation analysis were collected in 3-mL tubes containing 0.3 mL (0.106 mol/L) buffered (pH 5.5) sodium citrate (Sarstedt, Nuermbrecht, Germany). Blood samples for blood cell count were collected in 2.7-mL tubes containing 1.6 mg EDTA/mL (Sarstedt, Nuermbrecht, Germany). All tests were performed by the same investigator (C.R.).

For qualitative and quantitative analysis of coagulation parameters (e.g. PT, aPTT, AT III,

Table 1 Summary of coagulation test parameters, type, name and manufacturer

Parameter	Type of test	Name of test	Manufacturer
PT	clot assay	ThromborelS®	Dade Behring, Marburg, Germany
aPTT	clot assay	Pathrombin SL®	Dade Behring, Marburg, Germany
LA1	clot assay	Screening Reagent LA1®	Dade Behring, Marburg, Germany
PTT-LA	clot assay	PTT-LA®	Stago, Asnieres, France
ATIII	chromogenic	Berichrom AntithrombinIII®	Dade Behring, Marburg, Germany
Fibrinogen	clot assay	Multifibren U®	Dade Behring, Marburg, Germany
D-dimers	immunoassay	D-Dimer Plus®	Dade Behring, Marburg, Germany
TAT	immunoassay	Enzygnost® TAT micro®	Dade Behring, Marburg, Germany
Protein C	chromogenic	Berichrom Protein C®	Dade Behring, Marburg, Germany
White blood cell count	low cytometry by using semi-conductor laser	white blood cell count (XE2100)®	Sysmex, Kobe, Japan
Red blood cell count	low frequency detection with sheath flow technology	red blood cell count (XE 2100)®	Sysmex, Kobe, Japan
Hematocrit	calculated	hematocrit (XE 2100)®	Sysmex, Kobe, Japan
Hemoglobin	photometric measurement	hemoglobin (XE 2100)®	Sysmex, Kobe, Japan
Platelet count	low-frequency detection with sheath flow technology	platelet count (XE 2100)®	Sysmex, Kobe, Japan
ROTEM®	coagulation	InTEM®, ExTEM®, FibTEM®	Pentapharm, Munich, Germany

Prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin-antithrombin complex (TAT), antithrombin III (AT III).