long term complications in stented patients. New antiplatelet agents have been developed and are currently under evaluation as possible alternative to clopidogrel.

POSTERS

COMPARISON OF WHOLE BLOOD COAGULATION ASSESSMENT USING THROMBOELASTOMETRY (ROTEM®) BETWEEN HUMAN AND CYNOMOLGUS MONKEYS

D. Bertini, M. Boldrin,[1] L. Spiezia, C. Radu, C. Bulato, S. Gavasso, E. Cozzi,[1,2] P. Simioni

Department of Medical and Surgical Sciences, 2nd Chair of Internal Medicine, University of Padua, Medical School, Padua; [2]Department of Surgical and Gastrointestinal Sciences, University of Padua, Padua; [1]CORIT, Padua, Italy

Introdction. Microvascular thrombosis, due to activation of clotting cascade, is a key feature of the rejection process that takes place when pig organs are transplanted into primates. To date, little is known about qualitative characteristics of clot formation in primates. The present study is aimed at better understanding the differences in blood coagulation between primate and human using thromboelastometry (ROTEM®). *Matherials and Methods*. We studied ROTEM profiles in 40 naïve cynomolgus monkeys from Mauritius, China and Philippines and in 52 healthy human volunteers. Thromboelastometry (InTEM®, ExTEM®, FibTEM®, NaTEM®) was performed from whole blood with the ROTEM® coagulation analyser (Pentapharm, Munich, Germany).The main parameters obtained were clotting time (CT), clot formation time (CFT), maximum clot firmness (MCF), Area Under Curve (AUC) and Alpha (α) angle. Statistical analysis was performed using unpaired t-student test. *Results.* Data obtained in cynomolgus monkeys were reproducible and consistent with the normal range observed in human healthy subjects. Some important differences were, however, observed in primate blood. In monkeys ROTEM® profiles showed a hypercoagulable profile as compared to humans. Mean CT and mean CFT were significantly lower in primates (–25.7% and –55.5%, respectively) than in humans. MCF, α angle and AUC were significantly higher in primates than in humans (+23%, +21.5% and +32%, respectively). Similar distribution and range in human and monkey platelets were observed. In addition, fibrinogen levels in monkeys were lower than in humans (145.4 mg/dL *vs.* 289.9 mg/dL). *Conclusions*. Primate clot formation studied by ROTEM®, a technology to study whole blood coagulation, is consistent with a higher prothrombotic profile in primates as compared to humans. These differences do not appear to be related to higher platelet counts or fibrinogen levels in monkeys. Together these data suggest that, with regard to coagulation, xenotransplantation in cynos represent a much more difficult situation than xenotransplantation in humans.

INTRA-PLATELET PROTEIN S ANTIGEN LEVELS IN TYPE I PROTEIN S DEFICIENT PATIENTS

C. Radu, C. Bulato, L. Spiezia, D. Tormene, M. Perlati, B. Brandolin, G. Tognin, A. Chiriu, S. Gavasso, P. Simioni

Department of Medical and Surgical Sciences, 2nd Chair of Internal Medicine, University of Padua, Medical School, Padua, Italy

Background. Protein S (PS) is a vitamin K-dependent plasma glycoprotein with a molecular weight of 70 kDa. In human plasma 40% of PS circulates in a free form and the remaining 60% in complex with C4b-binding protein. Moreover, PS is contained inside platelets (Plts). Free PS acts as a cofactor of activated protein C (APC) for the inactivation of coagulation factor Va and factor VIIIa. Intra-Plts PS, released upon Plts stimulation, plays a crucial role in regulating thrombin generation and therefore controlling procoagulant activity. PS deficiency is inherited as an autosomal dominant disorder and is classified as: type I, with reduced plasma levels of total and free PS antigen (PS_{ag}); type II, with normal total and free PS_{ag} but reduced PS activity; type III, with normal total PS_{ag} but reduced free PS_{ag} and PS activity. *Aim of the study.* To evaluate the intra-Plts PS_{ag} levels in 27 carriers of type I PS deficiency. *Patients and methods.* After informed consent, 20 mL of blood was collected in 3.8% sodium citrate solution (1:9 vol/vol) from 27 deficient type I PS subjects and 22 normal individuals. In all subjects, we determined total and free plasma PS_{ag}, PS activity and intra-Plts PS_{ag}. *Results.* In Type I subjects total and free plasma PS_{ag} levels were 62.4±7.0% and 37.04±11.97%, respectively; intra-Plts PS_{ag} levels were 66.00±31.72%. In healthy individuals, total and free plasma PS_{ag} levels were 119.27±17.28% and 110.36±16.60%, respectively. Intra-Plts PS_{ag} levels were 101±29.95%. *Conclusions.* Our study shows a relationship between plasma PS and intra-Plts PS levels in type I PS deficient patients. The reduction of intra-Plts PS mirrors the reduced levels of free and total PS_{ag} present in plasma of carriers of the defect even though PS levels in Plts appears unexpectedly higher than the free PS counterpart. Which of the two plasma components of PS (total or free PS) is the more relevant in determining intra-Plts PS levels is unknown. Whether reduction of intra-Plts PS in inherited PS defects is due to reduce synthesis in megakaryocytes or is the result of PS plasma uptake by megakaryocytes in deficient patients still remains to be clarified.

WHOLE BLOOD COAGULATION THROMBELASTOGRAPHY IN NINE HOMOZYGOUS FACTOR V DEFICIENT SUBJECTS

L. Spiezia, C. Radu, D. Bertini, M. Castelli, E. Campello, M. Fadin, P. Simioni

Department of Medical and Surgical Sciences, 2nd Chair of Internal Medicine, University of Padua, Medical School, Padua, Italy

Background. Rotation thrombelastography, performed by ROTEM® (Pentapharm, Germany), is a useful tool for studying whole blood clot formation. Blood components such as plasma, platelets, leukocytes, and red blood cells are described to influence whole blood (WB) clot formation. Recently, ROTEM® has been reported to hold the capacity to detect a variety of haemostatic disorders including states of hypo- as well as hyper-coagulation. *Aim.* We studied the WB coagulation profile in 9 severe (homozygous) factor FV deficient subjects. *Methods.* Four ROTEM® assays (INTEM, EXTEM, FIBTEM and NATEM) in nine subjects with FV (mean±SD) antigen and activity plasma levels below 2±1% were performed. The following ROTEM® parameters were analyzed: clotting time (CT), clotting formation time (CFT), maximum clot firmness (MCF), alpha (α) angle, maximum velocity (MAXV), maximum velocity time (MAXV-t) and the Area Under Curve (AUC). *Results.* In all subjects enrolled we found a considerable degree of heterogeneity in the coagulation signal. The clot formation profiles ranged from a hypercoagulability (2 subjects), normal findings (4 subjects) to a pattern consistent with hypocoagulability (3 subjects). In our series of parahemophilic cases there were no association between ROTEM® profile and a history of hemorrhagic manifestations referred by patients at the time of sampling. *Conclusions.* WB ROTEM® profiles reveal an unexpected heterogeneity in coagulative pattern among subjects with homozygous FV defects. A possible explanation of our results is that ROTEM® parameters (including MCF and AUC) are mainly influenced by platelet count and fibrinogen plasma levels than by FV plasma levels. Further studies, evaluating the follow-up of bleeding manifestations in homozygous FV deficient subjects, are needed to clarify the potential role of ROTEM® in the management of parahemophilic patients.

TWO YEARS PROSPECTIVE OBSERVATION OF HEPARIN-INDUCED THROMBOCYTOPENIA (HIT) IN MORE THAN THREE THOUSANDS PATIENTS RECEIVING CARDIOVASCULAR SURGERY: EXPERIENCE OF TWO CENTRES

N. Ciavarella, D. Paparella, G. Scroscia, C.P. Ettorre, G. Malcangi, A. Colucci, P. Ranieri

Emostasi e Trombosi, Policlinico di Bari, Italy

Background. the prevalence of HIT is controversial in subjects (s) undergoing cardiovascular surgery and prophylaxis with UFH or LMWH. *Aim.* in order to determine the prevalence of HIT in these patients, we promoteed a two years prospective evaluation in two distinct Centres in the same town. *Methods.* globally 3222 patients were observed. In all patients Platelet (Plt) count, PT, APTT, Fibrinogen, D-dimers were evaluated preoperatively and postoperatively. Presence of Heparin-PF4 (H-PF4) antibodies, detected by ELISA-GTI, were evaluated only in presence of severe thrombocytopenia (less 50×10^9/L or drop of 50% of the Plt count in the first two days after surgery). In one center (1220 patients) postoperative thrombosis prophylaxis was prevalently performed using UFH, in the other (2002 patients) LMWH was used. *Results.* HIT (documented by severe thrombocytopenia and positive anti Heparin-PF4 antibodies) occurred in 18 patients. In 5 cases arterial or venous thrombosis occurred (1 DVT, 1 arterial limb thrombosis requiring amputation, 1 arterial limb thrombosis requiring femoral artery thrombectomy, 1 intra-cardiac thrombosis and massive femoral arterial emboli requiring thrombectomy, 1 arterial and venous thrombosis terminated with death). The remaining 13 patients had no evidence of macro-or micro-thrombosis associated with thrombocytopenia and positive anti Heparin-PF4 antibodies. No difference in incidence of HIT with or without thrombosis was evident based on type of heparin prophylaxis. In all cases heparin treatment was promptly arrested, Lepirudin treatment was succesfully administered in 7 patients. *Conclusions.* thinking and carefull monitoring for HIT has accounted for a low incidence of severe appearance of thromboembolic events associated with this syndrome. Prevalence of HIT was equally ditributed in patients prevalently treated with UFH or LMWH for postoperative prophylaxis.