FIBTEM and EXTEM MCF in monitoring deficiencies during liver transplantation.

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Background

- Coagulopathy linked to liver disease is a very complex condition, due to the alteration of the coagulation homeostasis, from the clot's formation to its lysis.
- Chronic liver disease, especially in the most advanced stages (END STAGE LIVERE DISEASE: ESLD), is also characterized by an alteration of the coagulation system due to reduced synthesis of both coagulation and anticoagulant factors.
- The association of ESLD and haemorrhagic disease, based on routine coagulation tests, is also doubtful. In fact, in ELSD PT-INR are often altered without a real increased risk of bleeding. Recent clinical studies show that ESLD patients have an increased thrombotic risk, due to imbalance of coagulation in the procoagulant sense. In the ESLD patient, hemorrhagic events are more often caused by portal hypertension than by a real alteration of coagulation.
- The discussion becomes even more complex in the patient undergoing to orthotopic liver transplantation (OLT).

Background

- Routine coagulation tests have considerable limitations and poor reliability in assessing the degree of coagulopathy (hemorrhagic and thrombogenic risk) in ESLD and in the different phases of OLT.
- Viscoelastic methods (**TEG \ ROTEM**) are considered a good alternative that allow a complete analysis of the coagulation process, they are able to evaluate plasma factors, platelets and their interaction. They are bedside tests therefore point of care; they are performed on whole blood, therefore in a condition closer to in vivo tests. They evaluate the kinetics of the clot from the initial clot formation up to the final clot strength. After this phase it is possible to evaluate the dissolution of the clot, or the fibrinolysis and its severity which cannot be absolutely evaluated with laboratory coagulation tests (6).

Methods

Plasma and platelets transfusion, Prothrombin Complex Concentrate (PCC) and fibrinogen administration occur only in the clinically evident bleeding after ROTEM evaluation according to the following scheme:

- **Plasma transfusion** (from 10-15ml/kg to 30ml/kg depending on the extent of bleeding and hemodynamic monitoring) occurs if:
  - ROTEM INTEM CT> 240 seconds (check HEPTEM to exclude heparin effect);
  - ROTEM EXTEM CT> 80 seconds (if no fluid overload);
- **Fibrinogen infusion** occurs if
  - ROTEM EXTEM MCF <35 mm + ROTEM FIBTEM MCF <8 mm (in absence of diffuse clinical bleeding);
  - ROTEM EXTEM MCF <45 mm + FIBTEM MCF <8 mm (with diffuse clinical bleeding)
  - ROTEM A10 EXTEM <26 or ROTEM A10 EXTEM <30 mm + ROTEM A10 FIBTEM ≤ 8 mm;
- It is also guided on the basis of preoperative laboratory values (cut-off 100mg/dl). The target is a fibrinogenemia of 150-200 mg/dl (with doses of 25-70 mg/kg).
- **PCC administration** (25 mg \ kg) occurs if:
  - INR> 2 in the setting of volume overload (if no VET available)
  - ROTEM EXTEM CT> 80 s in the setting of volume overload;
- **Platelet transfusion** takes place if:
  - Platelet count <50 000 / mm^3 (if no VET available)
  - ROTEM EXTEM A10 <30 mm + A10 FIBTEM> 8 mm
  - ROTEM EXTEM MCF <35 mm + ROTEM FIB

Rotem Fibtem/Extem variation during OLT in 10 pts

Background

- The patient's coagulation setting changes during different phases of transplantation (dissection, anhepatic; reperfusion; neohepatic) compared to the basic setting due to liver disease.
- In the **phase of liver dissection**, the coagulation is influenced by hypothermia, acidosis, and by blood products and fluids management, leading to dilution coagulopathy.
- In the **anhepatic phase**, synthesis of coagulation factor by liver fails and the coagulation setting is determined by the steadiness between exogenous administration and the elimination of coagulation factors.
- During **the reperfusion** of implanted allograft, the coagulation setting is determined by the ability of the graft to synthesize coagulation factors, linked to the degree of perfusion and O2 supply. Furthermore, the graft can release toxins accumulated in the phase of ischemia and establish a reperfusion syndrome. This difficult balance led to a great instability from thrombotic and hemorrhagic risck, that lasts until the graft regains the ability to synthesize coagulation factors fully (4). Moreover, the degree of hyperfibrinolysis, often present in ESLD, increase even more during surgery, especially in the late anhepatic and reperfusion phase

Methods

- In our LT Center, we have been using the ROTEM system for some years, to monitor the degree of coagulopathy from preoperative to immediate postoperative, and to guide the blood products administration.
- In particular, we performed:In particular, we performed:
  - **ROTEM 1**: preoperative evaluation (before crystalloids infusion) + standard laboratory coagulation tests (PT \INR; aPTT; fibrinogen).
  - **ROTEM 2**: anhepatic phase evaluation.
  - **ROTEM 3**: late reperfusion phase evaluation.
  - The presence of clinically evident bleeding outside these phases may require supplementary ROTEM, traditional laboratory tests and EGA.

Particular attention is paid throughout the transplant to maintain the following targets:
1. Body temperature > 36 °C;
2. Ph > 7,3;
3. Hb 7-9 gr\dl
4. Appropriate volume (Pulsion Picco monitoring)

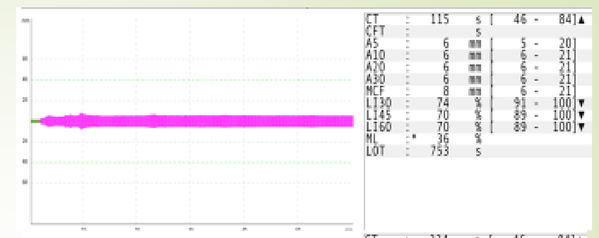
Results

In the period from January 2020 to December 2020, 35 patients underwent LT. We analyzed the first 10 patients to evaluate the effectiveness of ROTEM in detecting hypofibrinogenemia compared to standard laboratory tests. At pre-operative evaluation:
- All patients had normal fibrinogen values (>150 mg/dl).
- ROTEM1 values indicate a fibrinogen deficiency not highlighted by standard coagulation tests.
- ROTEM 2 values showed a constant worsening of FIBTEM MCF and EXTEM MCF.

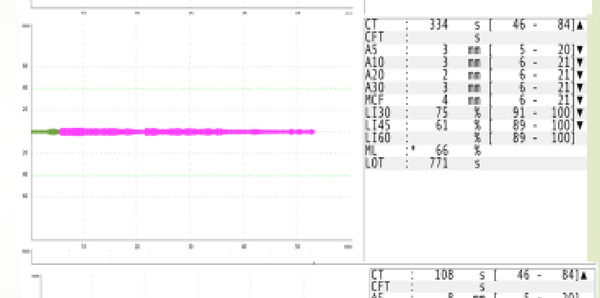
FIBRINOGENEMY mg \ dl	ROTEM 1 FIBTEM MCF	ROTEM 2 FIBTEM MCF	ROTEM 3 FIBTEM MCF	ROTEM1 EXTEM MCF	ROTEM 2 EXTEM MCF	ROTEM 3 EXTEM MCF
210	8	4	11	36	31	37
180	7	6	11	40	30	43
230	9	5	9	30	31	36
290	9	7	10	45	40	51
170	7	8	16	42	32	60
210	8	6	9	38	36	56
190	9	5	13	46	40	47
200	7	4	16	46	42	54
220	8	6	7	42	43	49
260	7	7	9	56	41	48

Example of FIBTEM VARIATION in OLT

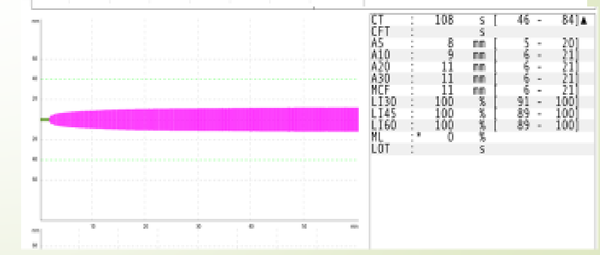
basaline



anhepatic phase



late reperfusion phase



CONCLUSION:

Our study, limited to a small sample, confirms the poor correlation between laboratory fibrinogenemia and ROTEM's FIBTEM MCF and EXTEM MCF.
The ROTEMs are able to monitor the consumption and dilution of fibrinogen in the different phases of OLT, quickly at bedside and with good sensitivity.
The integrations between traditional coagulation and ROTEM algorithms allows an early diagnosis of coagulopathy, a prediction and guidance of transfusion, reducing unnecessary exposure to allogeneic blood products