HEMO-TIN TRIAL AND ANTICOAGULATION IN HEMODIALYSIS

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RPN/SQN Joint Education Day, Montreal, May 4th, 2017

Presentation plan

- Introduction
- Current practices
- HEMO-TIN study
- Conclusion

Introduction

- Kidney disease (Facing the Facts 2017)
  - 1 in 10 Canadians
  - Number of patients living with end-stage renal disease has grown 36% since 2006
  - Among the 36,251 people being treated for kidney disease, 58,5% are on dialysis (mostly hemodialysis)
  - 44.8% of patients on dialysis survived at least 5 years

Introduction

- No anticoagulation :
  - 5-10% dialyzer clotting rate during a 3- to 4-hour dialysis session
  - = loss of dialyzer and blood tubings
  - = loss of ~ 100-180 mL of blood

Introduction

- Coagulation
  - Mostly related to the interaction between blood and artificial surfaces
  - Also related to the patient
  - Consequences
    - Reduction of HD efficiency
    - Shortening of circuit lifetime
    - Increase of patient blood loss, nursing workload, disposable consumption, and cost of treatment

Current practices

- At Maisonneuve-Rosemont Hospital:
  - Protocol
  - Tinzaparin
    - Total = 60 un/kg
    - Tight = 30 un/kg
  - Follow-up by nursing
- UFH still used in other hospitals in Quebec
- Other provinces ?

Guidelines and clinical studies

- Heterogeneity
- Lack of clear difference between UFH and LMWH
- Most organisms recommand UFH as standard anticoagulation and LMWH as alternative agent
  - USA = UFH
  - Europe = LMWH since 2002

LMWH

- Renal elimination
- Advantages
  - Higher bioavailability
  - Longer half-life (tinzaparin 1.4-1.9h)
  - Easy to administer
  - Anti-Xa monitoring not required
  - Lower risk of bleeding
  - Less osteoporosis
  - Less hyperkalemia
  - Reduced risk of HIT
  - Long-term studies = safe and effective

HEMO-TIN Trial

- Intermittent HEMOdialysis Anticoagulation With TINzaparin Versus Unfractionated Heparin: A Pilot Multicentre Randomized Controlled Trial (HEMO-TIN trial)
- Lead sponsor : Christine Ribic, MD (nephrologist), MSc, FRCPC, McMaster University / St Joseph's Healthcare Hamilton, Hamilton, Ontario
- Supported by LEO Pharma and McMaster University

HEMO-TIN Trial

- Designed to look at both safety (bleeding risk) and effectiveness (clotting risk) of tinzaparin compared with unfractionated heparin for anticoagulation in hemodialysis patients
- Primary outcome:
  - Rate of major, clinically important non-major or minor bleeding [26 weeks]
- Secondary outcome:
  - Clotting in extracorporeal dialysis circuit [during hemodialysis (weekly for 26 weeks)]

HEMO-TIN Trial

- Phase 4
- Multicenter (four facilities in Ontario)
- Randomized
- Controlled
- Double blind
- Study start date: September 2013
- Study completion date: September 2016

HEMO-TIN Trial

- Crossover
- 95 patients randomized to tinzaparin and 94 patients randomized to unfractionated heparin (n = 189)
- After 3 months, 78 patients remaining in tinzaparin group crossed over to receive unfractionated heparin for 3 months; 79 patients remaining in unfractionated heparin group crossed over to tinzaparin (n = 157)
- 125 patients completed the 3-month crossover phase

HEMO-TIN Trial

- Unfractionated heparin
  - What they were previously receiving (mostly 1000 – 1500 units bolus, and 500 – 1000 units hourly)
- Tinzaparin
  - Adjusted based on a protocol taking into account bleeding and dialyzer clotting
  - Most patients (~ 95%) received one dose of 2500 units at the start of dialysis
    - Up to max 4500 units

HEMO-TIN Trial

Inclusion Criteria	Exclusion Criteria
Age ≥ 18 years	Therapeutic systemic anticoagulation
ESRD maintained on outpatient hemodialysis for ≥ 3 months	Clinically apparent bleeding in the last 2 months
Frequency of hemodialysis: 3 times per week	High risk of bleeding
Anticoagulation with an unfractionated heparin protocol for at least 4 weeks	Planned major surgery in the next 4 months
Patient or legal guardian able to provide written consent	Major surgery in the past 48 hours
Baseline INR ≤ 1.3	Pregnant or lactating
Baseline platelet count ≥ 80,000 x 10^9/L	Child bearing potential
	Allergy/intolerance to heparin or history of heparin induced thrombocytopenia
	Current participation in a related randomized drug trial

HEMO-TIN Trial

- Patients' characteristics
  - Mean age: ~ 65 years
  - 58% male
  - 71% Caucasian
  - ESRD due to diabetic nephropathy: 43%
  - ~ 90% were receiving darbepoetin
  - ~ 60% had a central venous catheter

HEMO-TIN Trial

- 421 bleeding events in the 12,125 hemodialysis sessions studied
  - Evenly distributed between groups : 50,4% with unfractionated heparin *vs* 49,6% with tinzaparin
- Major bleeds (2.1% *vs* 1.6%)
- Clinically important nonmajor bleeds (1.2% *vs* 0.2%)
- Minor bleeds (47.0% *vs* 47.7%)

HEMO-TIN Trial

- Anti-Xa heparin levels
  - Surrogate measure of low molecular weight heparin activity levels and bleeding risk due to bioaccumulation
- In tinzaparin-treated patients, never exceeded 0.2 either before or after dialysis
- Routinely exceeded pre- and post-dialysis in patients receiving unfractionated heparin at baseline and both before and after crossover
  - Several hours after dialysis
  - No more bleeding events

HEMO-TIN Trial

- Grade 4 clotting
  - 0,4% with unfractionated heparin
  - 0.7% with tinzaparin
- Comparable mean dialyzer clotting scores and mean air trap clotting scores

HEMO-TIN Trial

- Conclusion : Tinzaparin was safe and effective as an anticoagulant for hemodialysis patients

HEMO-TIN Trial

- Presented at Kidney Week 2016 (American Society of Nephrology) as a High-Impact Clinical Trial in the Oral Abstract Session
- Oral presentation during the CSN Annual General Meeting on May 5th at the Communications section 16:00 to 17:30
- Should be published soon

Conclusion

- Advantage of LMWH (tinzaparin)
- Cost
- Article coming soon

Thank you!

Questions?

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