What is the Risk of Heparin 5000 Units Q8H as Thromboembolic Prophylaxis in ICU Patients?

Michael Kammermayer, B.Sc., Pharm.D. & Glen Brown, B.Sc. (Pharm), Pharm.D., FCSHP, BCPS

Background

- Patients in critical care areas are at an increased risk for developing venous thromboembolism (VTE) due to the presence of additional risk factors.
- Current guidelines do not make any recommendation on who should receive low-dose unfractionated heparin (UFH) BID versus TID for VTE prophylaxis.
- Literature shows that despite prophylaxis, the rate of VTE is still 9% in ICU patients[1] indicating that these patients may benefit from UFH administered TID.
- **Primary Outcome**: to determine if there is an increase in the activated partial thromboplastin time (aPTT) on the last day of treatment compared to an aPTT measurement prior to heparin therapy.
- **Secondary Outcomes**:
  - the frequency of major bleeding
  - the frequency and number of transfusions required

Methods

- Single center, retrospective chart review involving ICU patients admitted between July 1st, 2011 and June 30th, 2013
- N = 100 (sample size of convenience)
- **Inclusion**: patients $\geq$18 years old who were in the ICU for $\geq$48 hours while receiving either 5,000 or 7,500 units of UFH TID
- **Exclusion**: any criteria that may also prolong aPTT such as end-stage liver failure, acute hepatitis (viral, drug induced or idiopathic), patients on plasma exchange (PLEX), or patients known to have any of the following: hemophilia, Von Willebrand disease, disseminated intravascular coagulation, or a deficiency in any of Factor V, X, or XII
- **Analysis:** aPTT measurements at initiation and termination were compared utilizing a two-tailed *t*-test for normal distribution

Demographics:	#	Mean	SD
Male	71		
Female	29		
Age	19-84	56	16
Wt at initiation (kg)		90	25
Wt at termination (kg)		88	25
Duration (days)		8	6
SCr at initiation (mmol/L)		173	177
SCr at termination (mmol/L)		145	156
Received 5000 units tid	77 (51 Male:26 Female)		
Received 7500 units tid	23 (20 Male:3 Female)		

Table 1: Patient Demographics

A) All Patients (n=100)	Mean	SD
aPTT at initiation	33	6
aPTT at termination	33	7
t-Test	P = 0.61	

B) Dialysis Patients (n=21)	Mean	SD
aPTT at initiation	32	5
aPTT at termination	33	5
t-Test	P = 0.30	

Table 2: A) Mean, and standard deviation (SD) times (in seconds) for aPTTs measured at initiation and termination in all 100 patients. P value determined utilizing a two-tailed *t*-test. B) A subanalysis of patients requiring either CRRT or IHD.

Results

- **Primary Outcome:**
  - UFH TID does not lead to any significant increase in aPTT (Table 2)
  - In the subset of patients on dialysis, there was also no significant increase in aPTT (Table 2)
- **Secondary Outcomes:**
  - Patients experiencing a major bleed – 9%
  - Patients experiencing a bleed of any kind – 12%
  - Patients requiring a transfusion – 22%
  - Patients on dialysis requiring a transfusion – 48%

No. of units of PRBCs	No. of Pts (n = 22/100)	No. of Dialysis Pts (n = 10/21)
1	3	2
2	13	5
3	3	0
5	1	1
6	1	1
8	1	1

Table 3: Number of patients requiring transfusions.

Conclusions

- In adult patients admitted to the ICU, administering UFH TID for VTE prophylaxis does not significantly change aPTT
- Twenty-two percent of patients required transfusions
- Nine percent had a major bleed and 12% had a bleed of any kind compared to 5.6% and 13.2% respectively seen in PROTECT[1]
- 2/9 patients with major bleeds had aPTTs outside of the normal range at termination
- Heparin's role in bleeding and transfusion requirements in this patient population is unknown but estimated to be limited due to a lack of any significant alteration in aPTT

Reference:
(1) Cook D, Meade M, Guyatt G, et al. Dalteparin versus unfractionated heparin in critically ill patients. NEJM 364;14:1305-1314

fraserhealth
Better health. Best in health care.

Vancouver CoastalHealth
Promoting wellness. Ensuring care.

Providence HEALTH CARE
How you want to be treated.

Provincial Health Services Authority
Province-wide solutions. Better health.

UBC