Journal Reading

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Introduction

- Survivors of sudden cardiac death have improved neurological outcomes and survival when treated with mild **therapeutic hypothermia (TH).**

- Therapeutic hypothermia is endorsed as the standard of post-resuscitation care by the International Liaison Committee on Resuscitation (ILCOR)and the American Heart Association

In some cardiac arrest cases..

- Thromboembolic event…

- Acute myocardial infarction

- Pulmonary embolism

Treatment

- Systemic anticoagulation

- Intravenous unfractionated heparin(IVUH)

- The pharmacokinetic profile of IVUH during TH is not well under-stood, and dosing inadequacy may result in therapeutic failure or increased bleeding risk.

- The safety of systemic anticoagulation therapy during TH is an area of controversy. Coagulopathy itself is often viewed as a relative contraindication for TH.
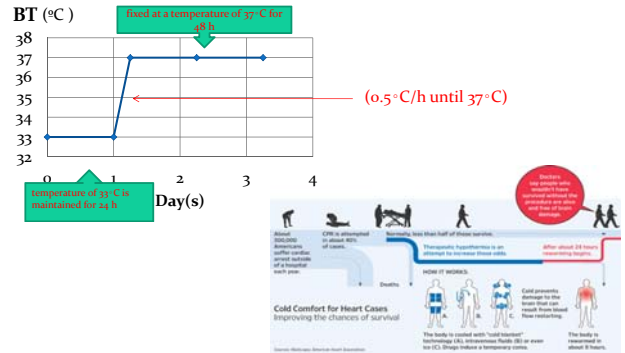
The aim of the study

- The primary aim of this study was to assess the efficacy of our current IVUH dosing protocol in achieving therapeutic aPTT values during TH.
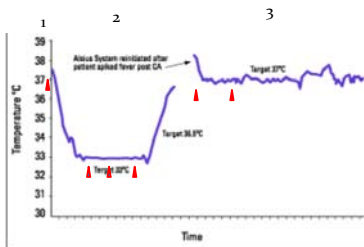
Method---Matrix

- Location: Harper University Hospital andDetroit Receiving Hospital

- Time span:September 2006 through August 2012.

- Inclusive criteria: 1.TH and 2.IVUH

Hypothermia protocol

Data Collection

- Check aPTT at least every 6 hrs during IVUH use
- 1 :baseline   2:TH(up to 3 aPTT) 3:post-rewarming
- aPTT >200s were rounded to 200s


Heparin Dosing

- Heparin dosing requirements were documented as units/kg/h based on total body weight, unless the body mass index was >30
- In these cases, an adjusted body weight ([actual weight – ideal body weight][0.4] + IBW) was used for dosing.
- Target aPTT: 1.5~2 times baseline aPTT

aPTT (sec)	Dose
Initial dose	80 units/kg bolus + 18 units/kg/hr infusion
aPTT <35 sec	80 units/kg bolus + increase infusion rate by 4 units/hr
aPTT 35-45 sec	40 units/kg bolus + increase infusion rate by 2 units/kg/hr
aPTT >45-60	Increase infusion rate by 2 units/kg/hr
aPTT >60-80	No change
aPTT >80-90	Decrease infusion rate by 2 units/kg/hr
aPTT >90	Hold infusion for 1 hour + decrease infusion rate by 3 units/kg/hr

Monitoring Bleeding

- Major bleeding was defined as a drop in hemoglobin of greater than 2 g/dl↓ in 24 h, requiring transfusion on 2 consecutive days, or any major bleed as perceived by the intensivist caring for the patient.

Result ： Data Base
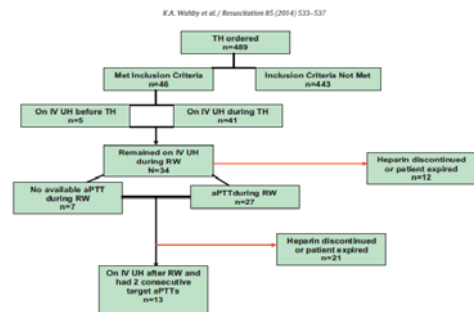
Characteristic of the Matrix

- Indication of IVUH: 1.PE 2.AMI
- IHCA vs OHCA : 47% vs 53%

Table 1
Baseline characteristics and bleeding outcomes.

Characteristic	Results ($n = 46$)
Male sex	44%
Age (years)	61 ± 18
Weight (kg)	83 ± 25
Height (cm)	170 ± 4
BMI	30 ± 7
APACHE II score	31 ± 7
Average down time (min)	14 ± 11
Initial rhythm	
Asystole	7
PEA	10
Bradycardia	5
V tach/VFib	10
Unknown	4
ICU LOS	8 ± 8
Hospital LOS	14 ± 13
Mortality	60%
Baseline PTT	30.9 ± 5.7
Baseline temp	36.5 ± 1.7
Major bleeding	3 (7%)
Minor bleeding	5 (11%)

Heparin rate and response

1. The average baseline aPTT prior to heparinization was 34 ± 5 s
2. The bolus dose was 5200 ± 1500 units
3. Heparin infusion rate was initiated at 13 ± 5 units/kg/h. Initial aPTT during TH was 153 ± 53 s, with an average aPTT of 142 ± 48 s
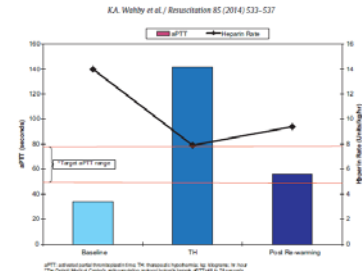
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Fig. 2. Heparin rate and response.

aPTT result

- A significant increase in aPTT from baseline to TH (34 ± 5 vs 142 ± 48 s, $p < 0.001$), and from TH to post-re-warming (142 ± 48 vs 56 ± 17 s, $p = 0.005$)
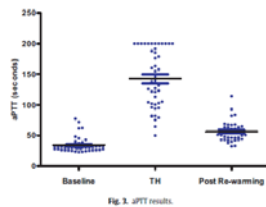

Fig. 3. aPTT results.

Heparin dosing requirement

- Heparin requirements were significantly lower during TH than re-warming (7.9 ± 3 vs 9 ± 4 unit/kg/h, $p = 0.048$), even after adjusting for age, sex, BMI, heparin rate and APACHE score
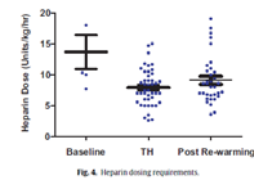

Fig. 4. Heparin dosing requirements.

Dose reduction

- By the end of TH, only 10 patients (22%) achieved target aPTT, with an average IVUH dose of 5.7 ± 1 unit/kg/h to achieve their target.

- This change represents over a 50% reduction in heparin rate, or an absolute change of 7 units/kg/h compared to our mean starting rate, $p < 0.001$.

Dose reduction in patient with IVUH prior to TH

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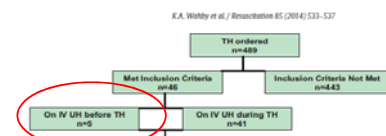
- Ave.14 ± 6 units/kg/h → 4.6 ± 1 units/kg/h
- All 5 patients (100%) required dramatic reductions and interruptions in their heparin rates during
- A 3-fold reduction from their stable heparin rate pre-TH.

Major bleeding

- Three patients with 4 episodes met our definition for major bleeding.
- The bleeding events consisted of one retroperitoneal bleed, two gastrointestinal bleeds and one patient with frank bleeding from the endotracheal tube, rectal tube and multiple vascular access sites.
- The aPTT results for these three patients were all in the supratherapeutic range during TH. Two of the three patients had 2readings during TH >200 s, and the other patient had two consecu-tive readings of >100 s. In all cases, heparin was discontinued.

Discussion : Some exceptions

- 3 (7%) patients achieved target (1.5–2 times baseline) aPTT with initial dosing.

- Their starting IVUH rate was 7 ± 1 units/kg/h.(lower than standard dosing protocols)

Discussion : Some exceptions

- In order to assess the impact of TH on aPTT in patients not on full-dose heparin(subcutaneous heparin 5000 units subcutaneously every 8 h).
- No significant change in aPTT from baseline to TH was witnessed in this sample,33.5 ± 6.4 s versus 34.4 ± 5.9 s, respectively.

Discussion : TH and bleeding

- Whether TH alone increases bleeding risk remains controversial.
- Prolongation of bleeding times and reduced thromboxane concentrations have been seen during TH.
- However, in a recent metaanalysis, bleeding was not significantly different between the cooled patients and normothermic.

Conclusion

- More and more data is available which supports dosage reductions for commonly used medications in the critically ill during TH
- A modified heparin dosing protocol (40 units IV bolus, followed by 7 units/kg/h) for use during TH.

- Thank you!!