

Management of Systemic Unfractionated Heparin Anticoagulation During Therapeutic Plasma Exchange

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Therapeutic Plasma Exchange (TPE)

- **Beneficial effect**
 - Removal of offending agent e.g. antibodies
 - Replacement of a deficient factor e.g. ADAMTS13
- **A single exchange of 1 plasma volume removes ~63% of all solutes in the plasma¹**
- **Removes medications such as anticoagulants, antibiotics, and chemotherapeutics^{2,3}**
- **Limited data on drug removal during TPE, including continuous intravenous infusions such unfractionated heparin (UFH)**

Chopek et al , Therapeutic Hemapheresis. Arlington. VA. American Association of Blood Banks, 1980:13.

Ibrahim et al, Pharmacotherapy. 2007;27(11):1529-1549²

Kale-Pradhan et al, Pharmacotherapy 1997;17(4):684-95³



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Unfractionated Heparin (UFH)

- Binds to antithrombin resulting in increased anticoagulant activity of antithrombin → inhibition of thrombin, factor Xa (activated factor X), and others
- Heparin nomograms are used which incorporate weight, indication, and intensity of anticoagulation
- Has an unpredictable anticoagulant response
- Commonly monitored by aPTT or anti Xa

Dosing During TPE

- **Dose modifications of UFH may be required during TPE**
 - Drug removal
 - TPE-induced changes in coagulation factors levels
- **Experience from literature**
 - Plasmapheresis resulted in 50% decreased in anti Xa level without a dose adjustment of dalteparin in a woman with pulmonary embolus and autoimmune hemolysis¹
 - Membrane filtration plasmapheresis resulted in an average decrease of 40% in anti Xa levels in 11 patients with Guillain Barré syndrome or myasthenia gravis²



Study Design

- **Retrospective review**
- **Therapeutic continuous IV infusion of UFH and TPE from January 1, 2008 to June 30, 2010**
- **Single volume plasma exchanges were performed on the COBE® Spectra Apheresis System**
- **Anticoagulant Citrate Dextrose Solution A (ACD-A) was used for extracorporeal anticoagulation at an anticoagulant to whole blood ratio of 1:13**
- **Plasma used for replacement fluid**

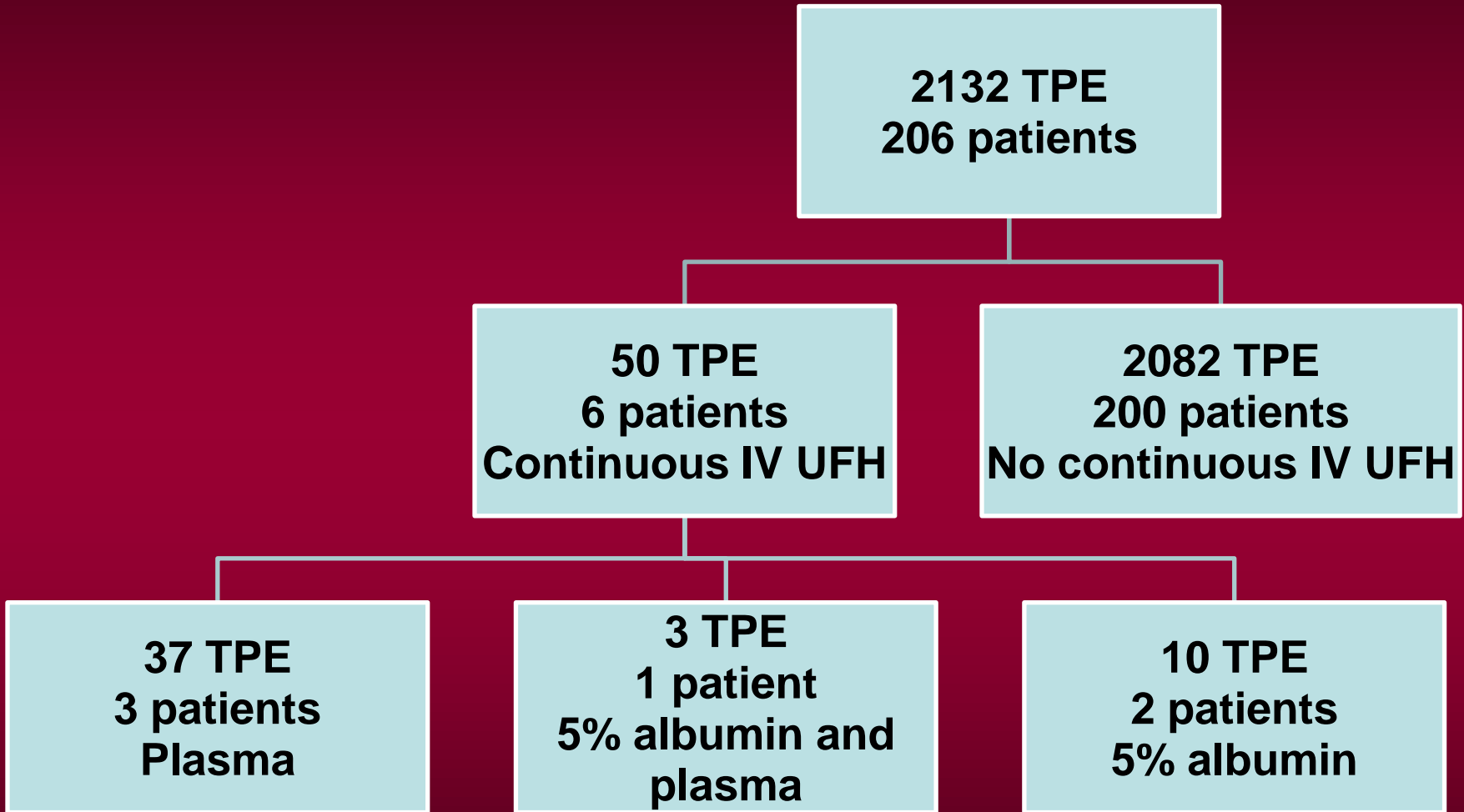


Heparin Monitoring

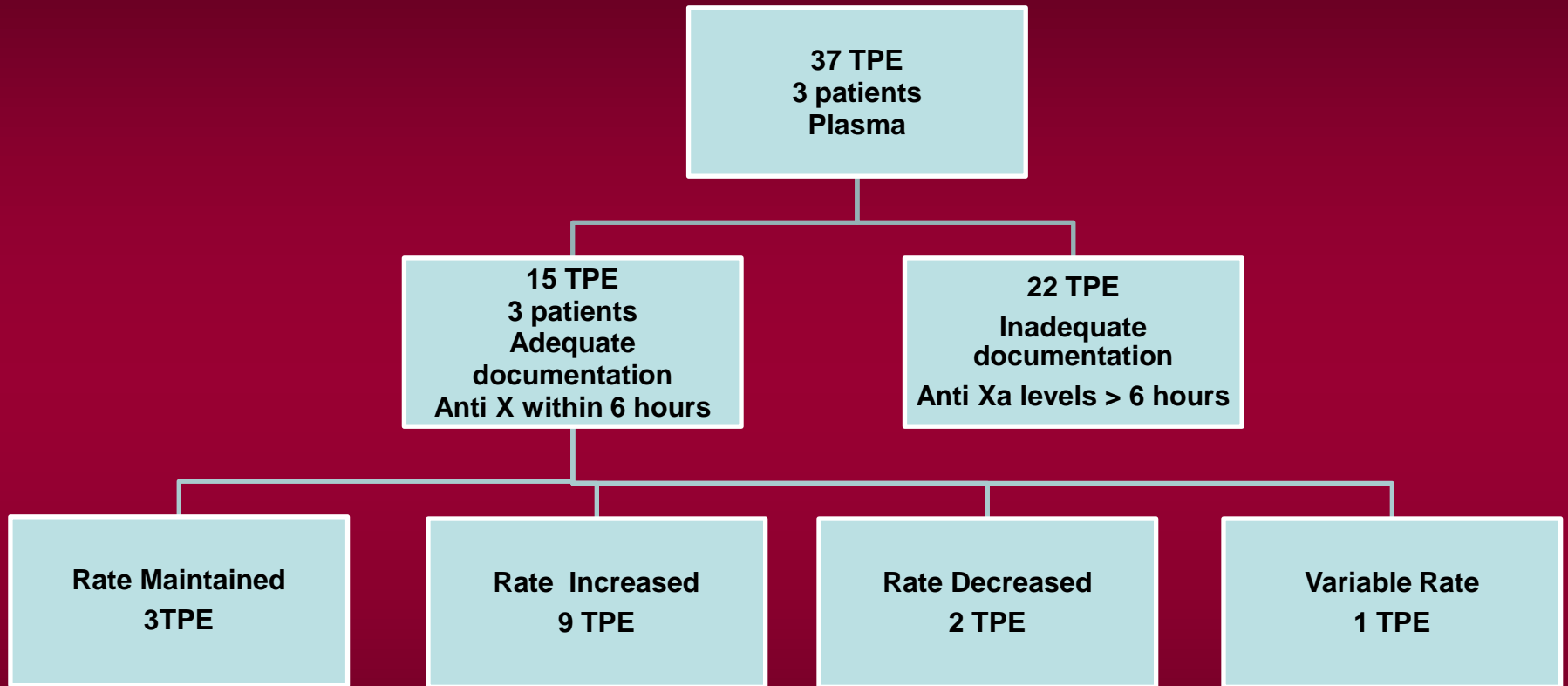
- Systemic heparin levels were monitored by chromogenic anti Xa assay levels = STA®-Rotachrom® Heparin on a STAR-R® analyzer (Stago Diagnostica)
- Low intensity therapy
 - Anti Xa 0.15-0.35 IU/mL or aPTT 45-65 seconds
- High intensity therapy
 - Anti Xa 0.30-0.70 IU/mL or aPTT 60-101 seconds
- Pre and post anti Xa levels within six hours of TPE
- Change of ± 0.05 IU/mL by anti Xa considered significant



TPE Procedures



TPE with UFH and Plasma Replacement



Patient Characteristics

ID	Age/Sex	Indication for TPE	Indication for Heparin	Procedures (n)		
				Total	On UFH	On UFH + met study criteria
1	46/F	Acute heart transplant rejection	Acute coronary syndrome	3	3	0
2	61/M	ABO incompatible living donor kidney transplant	Lupus anticoagulant inhibitor + Factor V Leiden with venous thrombosis	8	5	0
3	21/M	*CAPS	Bilateral DVT*	25	22	6
4	52/F	Desensitization prior to heart transplant	Thrombosis in LVAD*	5	5	0
5	52/F	CAPS	Right upper extremity DVT	3	3	2
6	26/F	CAPS	Left upper extremity DVT	17	12	7

*CAPS = Catastrophic antiphospholipid syndrome

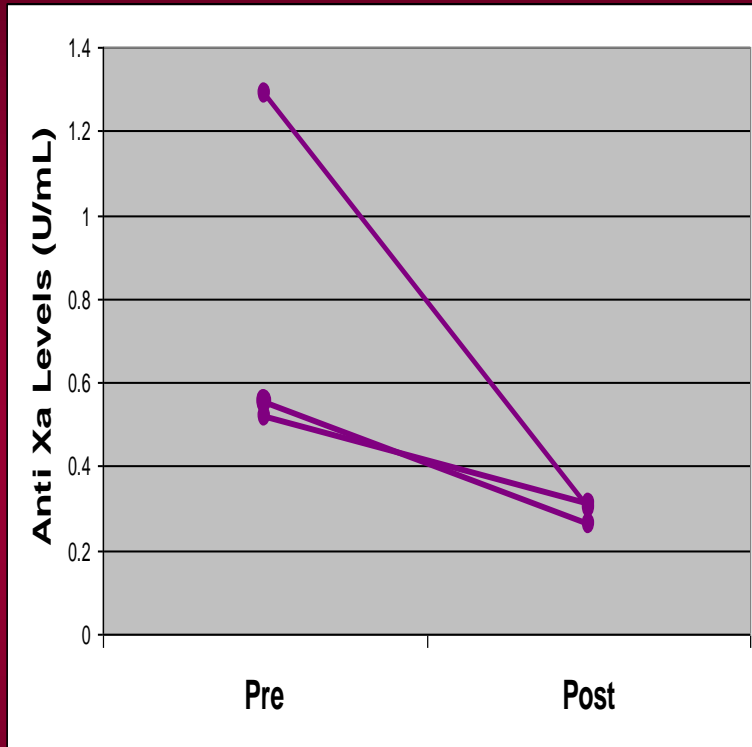
*DVT = Deep vein thrombosis

*LVAD = Left ventricular assist device



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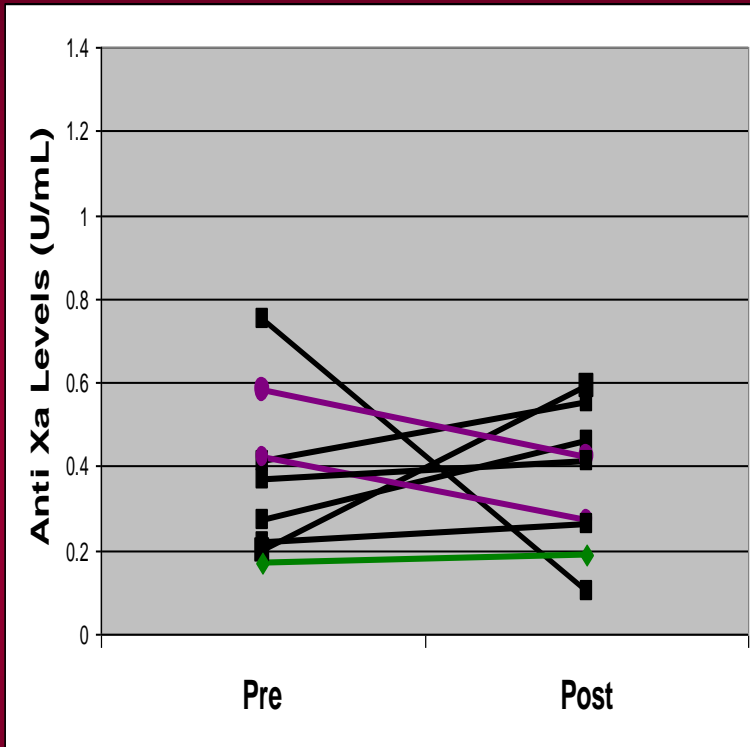
TPE with UFH Rate Maintained



- 3 TPE, 1 patient (#6)
- 26 year old female with CAPS and DVT
- Change in anti Xa
 - Average ↓ 56.7%
 - Range ↓ 40.3 to 76.7%

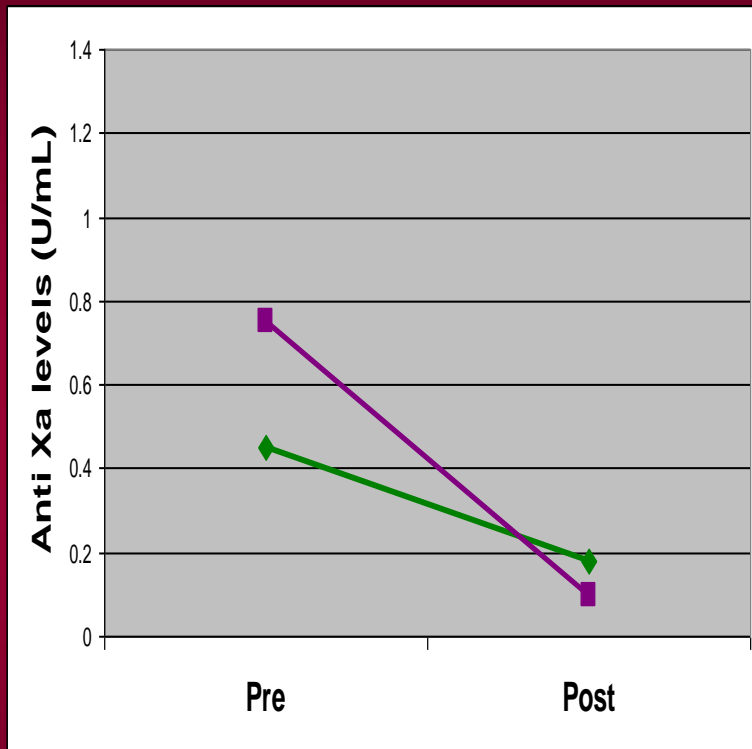


TPE with UFH Rate Increased ~65%



- 9 TPE, 3 patients (# 3, 5, 6)
- CAPS and DVT
- Change in anti Xa
 - Average \uparrow 21.1%
 - Range \downarrow 86.7% to \uparrow 195%
- #3 (decrease 86.7%)
 - UFH drip stopped at end of procedure
 - post procedure sent ~5.5 hours after TPE

TPE with UFH Rate Decreased



- **2 TPE, 2 Patients**
 - #5 UFH stopped for IV catheter placement and restarted at lower rate
 - #6 increasing subdural hematoma with seizures
- **Change in anti Xa**
 - Average ↓ 73.4%
 - Range ↓ 60 to 86.8%



Limitations

- **Small study**
- **Retrospective**
- **Data needed for procedures with other replacement fluids, such as 5% albumin**
- **Prospective studies are needed**



Current Practice at University of Minnesota

- **Anti Xa within therapeutic range**
 - Increase UFH rate by 65%
- **Anti Xa less than or greater than therapeutic range**
 - Determine new target rate based on nomogram
 - Then increase by 65%
- **Anti Xa level markedly suprathereapeutic or subtherapeutic**
 - Handled on an individual basis
- **Anti Xa level should be drawn before procedure, immediately post TPE, and 6 hours post TPE**



Conclusions

- UFH is removed during TPE,
- A single volume TPE with plasma replacement results in an average decrease of ~56.7% in anti Xa level
- Adjustment of the UFH rate may maintain therapeutic levels during TPE
- More studies are needed



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