CABG in the Post-Aprotinin Era: Are We Doing Better?

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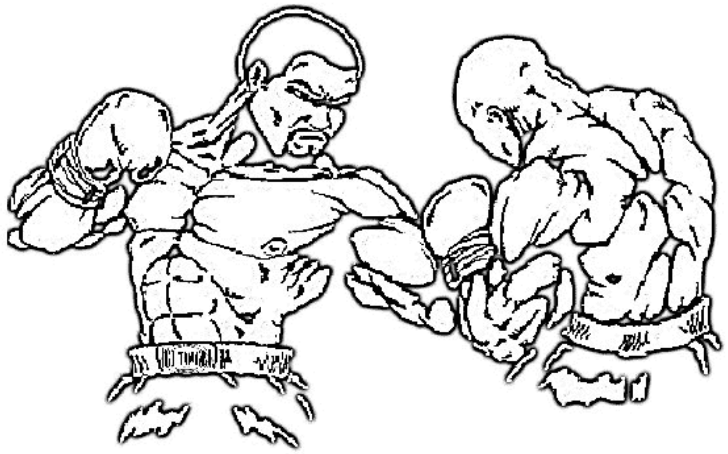


DISCLOSURES

None

Objective(s):

- Our department routinely used Aprotinin as an antifibrinolytic agent until Jan 2008.
- **May 2007**: FDA recommended *suspending its distribution*:
  - Acute renal failure
  - CVAs
  - Mortality
- Blood Conservation Using Antifibrinolytics in a Randomized Trial (BART) - study showed higher mortality in a high-risk patient group

* *Ferguson et al*. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. N Engl J Med. 2008;358(22):2319-31.

Objective:

- The routine use of prophylactic Aprotinin was stopped at our institute in January 2008.

- This study was aimed at comparing the efficacy and associated morbidity and mortality in a high-risk cardiac surgery population between 2 eras:
  - Aprotinin (Trasylol) Era before 2008
  - Tranexamic acid (Hexakapron) Era after 2008

Methods (i)

The study question focused on a cohort of patients who underwent high-risk surgical procedures, defined as:

- (1) Double or triple valve replacements
- (2) Aorta surgery
- (3) Combined procedures (coronary artery bypass combined with valve replacement and/or repair and/or aorta surgery)

Inclusion criteria

- Patients undergoing elective or emergent open heart surgery
- Patients demonstrating normal preoperative coagulation profiles, including normal platelet count (PLT), partial thromboplastin time (APTT), prothrombin time (PT) and international normalized ratio (INR)
- (iii) patients with preoperative creatinine <2 mg/dl
- (iv) patients not on preoperative clopidogrel or anticoagulation treatment

Outcome measures:

- Primary outcome measure was 30 day mortality.
- Secondary outcome measures were: postoperative cerebrovascular accidents, postoperative thrombocytopenia, and postoperative kidney function.
- Efficacy was evaluated in terms of postoperative bleeding and requirement for infusions of blood and blood products.
- Massive bleeding was defined as more than 1300 ml/day.

Methods (i):

- We compared two patient groups:

Group A (n=101; 44.3%)	Group B (n=127; 55.7%)
Operated before 2008 (Jan 2006 to Dec 2007)	Operated after 2008 (Jan 2009 to Dec 2010)
Received **Aprotinin** routinely	Received **Tranexamic** acid

Antifibrinolytic treatment protocol:

- Aprotinin was routinely administered to all patients in group A according to the half-Hammersmith regime.

Low dose (half Hammersmith): $<5 \times 10^6$ KIU total	140 mg IV (1×10^6 KIU) bolus prior to sternotomy, then 35 mg/h (2.5×10^5 KIU/h) IV infusion, plus 140 mg (1×10^6 KIU) added to CPB

- The Tranexamic acid treatment regime in group B was based on the patient's body weight.
- A loading dose was given immediately before skin cut (calculated as 12.5 × BW in mg), and a maintenance dose was started and continued for 4 hours post-surgery (calculated as 6.5 × BW in mg/hr).

Results (i): Demographics & Pre-Operative

Parameter	Group A (Aprotinin) (n=100)	Group B (Tranexamic Acid) (n=128)	P value
Demographics			
Age	66.9±12.9	68.2±11.7	NS
BMI	29.01	28.21	NS
Past Diagnosis			
Hyperlipidemia	**46 (46%)**	**79 (55%)**	**0.016**
Hypertension	70 (69%)	97 (76%)	NS
Diabetes Mellitus	32 (32%)	51 (40)	NS
Renal Failure	18 (18%)	29 (23%)	NS
Congestive Heart Failure	31 (31%)	43 (34%)	NS
Cerebrovascular accident	4 (4%)	7 (6%)	NS
COPD	11 (11%)	8 (6%)	NS
Chronic Atrial Fibrillation	17 (17%)	19 (15%)	NS
Paroxysmal Atrial Fibrillation	12 (12%)	20 (16%)	NS

Results (ii):

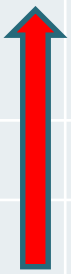
	Group A (Aprotinin)	Group B (Tranexamic acid)	Total	P value
Double Valve	25 (25%)	22 (17%)	47	NS
Triple Valve	2 (2%)	3 (2%)	5	NS
Aorta	2 (2%)	4 (3%)	6	NS
Combined	72 (72%)	98 (78%)	170	NS
Total	101	127	228	

Results (iii): Operative

Parameter	Group A (Aprotinin)	Group B (Tranexamic acid)	P value
Cross clamp time (min)	142.0±-41.4 ↑	120.6±40.3	<0.001
Bypass time (min)	187.3±49.5 ↑	120.6±40.3	<0.001
Activated clotting time (min)	137.0±100.6	153.6±113.7 ↑	0.001
Packed cells (cc)	187.1 [0-1000]	261.8 [0-1500]	NS
Packed cells (patients)	49 (49%)	68 (53%)	NS

Results (iv): Post-Operative

Parameter	Group A (Aprotinin)	Group B (Tranexamic acid)	P value
Bleeding ml (First 3 days after surgery)			
Mean	660 [220-2650]	870 [260-5320]	0.001
Average	799±470	1171±960	0.001
Pts with bleeding >1300ml	16 (16%)	37 (29%)	0.019
Blood products			
Packed cells (transfused patients)	85 (85%)	97 (76%)	NS
Packed cells (mean transfused volume)	444±330	455±459	NS
Platelets (patients)	3 (3%)	9 (7%)	NS
Fresh frozen plasma (patients)	11 (11%)	20 (16%)	NS
Total blood products given	85 (85%)	98 (77%)	NS



Results (v): *Morbidity and mortality*

	Group A (Aprotinin)	Group B (Tranexamic acid)	P value
Cerebrovascular accident (patients)	5 (5%)	2 (2%)	NS
Postoperative atrial fibrillation	13 (13%)	12 (9%)	NS
Postoperative creatinine >1.8	35 (35%)	45 (35%)	NS
Platelet count (minimum)	109.9±41.8	100.6±50.7	0.036
Troponin (max post-operative)	7.8±6.2	10.3±8.8	0.004
30-day mortality (patients)	11 (11%)	7 (6%)	NS

Limitations

- Retrospective
- Time interval bias
- Preoperative parameters: hyperlipidemia
  - Hexacapron group

Conclusions

- The abrupt change and usage of Tranexamic acid in our institute was shown to result in a significantly **greater bleeding** tendency.
- In our cohort, the routine use of Aprotinin was **not associated** with a higher incidence of stroke, ARF, post-operative MI or mortality.

IS IT JUSTIFIED TO STOP USING APROTININ ?

Thank you