Severe coagulopathy in serotoninergic syndrome secondary to MDMA overdose

March 2019

Thanks to Angie Monk and the team in ICU at Joondalup Health Campus for sharing this case.

Disclaimer / Pre-amble

- These cases have been de-identified to protect the identity of the patient and the treating teams.
- These are all real cases and real ROTEMs. The individuals involved in these difficult cases have agreed to anonymously share these with us thank you for your generosity.
- Successful management of the bleeding patient involves much more than just administration of blood products.
- The primary aim of these cases is to teach the use ROTEM guided blood product therapy. We have deliberately not included a lot of detail about some of the other aspects of management which might detract from this focus.



ROTEM ANALYSIS AND TREATMENT PLAN

Nurse or JMO to circle algorithm used then insert results from ROTEM Next circle range (action red range) and use algorithm to create a plan.

Date: / / Time:

ALGORITHM USED (circle one): CARDIAC/VASCULAR or GENERAL/OBSTETRIC

For CARDIAC/VASCULAR start here and do all:
 INTEM CT = Below 205 / 205 & Above
 HEPTEM CT = Below 205 / 205 & Above

• For GENERAL/OBSTETRIC start here(this section only): EXTEM A5 = Below 35 / 35-40 / Above 40 FIBTEM A5 = Below 10 / 10-15 / Above 15

EXTEM	СТ =В	elow 80 / 80-90	/ Above 90
EXTEM	ML =	Below 5	5 & Above

Management Plan:

Please stick this label in the patients progress notes

KEMH ROTEM Algorithm for Critical Bleeding

Key Points: This algorithm should be used in conjunction with the KEMH Blood Product Guidelines for Major Obstetric Haemorrhage. Only treat abnormal values if active bleeding or at high risk of bleeding. Repeat ROTEM analysis 10 mins after intervention to assess response.

	ABNO	RMAL ROTEM	I	CRITERI	A	DIAGNOSIS	INTE	RVENTION	CORRECTED ROTEM
FIBRINOGEN		17 (2004) 17 (2004) 17 (2004) 17 (2004) 17 (2004) 17 (2004) 18 (20		FIBTEM A5≤1	0mm	Low fibrinogen	Cryopi Fibrinoge (see d AND Trane	recipitate OR en concentrate osing guide) examic acid 1 g	1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
LETS		617863 57.221464 67.472461 67. 1971 107. 107.		EXTEM A5 ≤ and FIBTEM A5 ≥1	8 5mm Omm	Low platelets	Platelets (correlate v	s: 1 adult dose with platelet count)	
PLATE				EXTEM A5 ≤2 and FIBTEM A5 ≤1	5mm Omm	Low platelets and Low fibrinogen	Platelets (correlate v	and fibrinogen with platelet count)	4 12 12 12 12 12 12 12 12 12 12 12 12 12
ORS		41 1 41 1		EXTEM CT 80-1 FIBTEM A5 ≤1	40s and ^{0mm}	Low fibrinogen	Correct 1	librinogen and reassess	1 1125 1125 1125 1125 1125 1125 1125 11
FACT			EXTEM CT >14 FIBTEM A5 ≤1	0s and ^{0mm}	Low fibrinogen and Low coagulation factors	FF Fibrinoge (Consider Pro	P 1-2U + en as indicated thrombinex-see below)	8 5 6 ann 8 4 125 8 5 7 125 8 5 7 125 8 5 7 125 12 7 125	
OLYSIS		17704) (7.17248 (7.17248) (7.1945) (7.1945) (7.1945) (7.1945)		Early Diagno EXTEM A5≤35 or FIBTEM CT >	osis imm •600s	High likelihood of excess fibrinolysis	Tranex	amic acid 1g	ения и лакия и лак
FIBRING		Late Diagnosis EXTEM or FIBTEM ML ≥5%		osis IML ≥5%	Excess fibrinolysis	Consider repea blood volur	it dose if has lost over 1 ne since initial dose	4 474 41 4 128 41 4 11 41 41 41 41 41 41 41 41 41 41 41	
		Fibrinogen [Dosing Gu	lde		Fibrinogen Concentrate		Cry	oprecipitate
*	FIBTEM A5 Target: ≥12mm		m	Guidelines F Oonsulta	Guidelines For Use • Consultant anaesthetist or haematologist approval regulted.		 1 dose is equivalent to 10 whole blood units or 5 apheresis units. May be supplied as whole blood units or as apheresis units (or a combination of the supplied as whole blood units or as apheresis units). 		
	FIBTEM A5	Increase required	Cryoprecipitat	e Fibrinogen Concentrate	Patients r Fibrinoge	nust be experiencing life threatening haemorrhagen concentrate may be indicated instead of, or in	ge. addition to,	1 apheresis unit = 2 whole 1 3. Availability time: generally a	blood units. available within 10 minutes of request being made
	9-10mm	2-3 mm	1-2 doses	2g*	cryoprec suspicior	ipitate if the FIBTEM A5 is 6mm or below, OR the of coagulopathy in a life threatening haemorrha	re is a high ge.	P	rothrombinex
	7-8mm 4-5 mm 1-2 doses 3g* • Use at h cryopre		higher FIBTEM values may be appropriate in patients refusing ecloitate.		1. Haematologist approval required				
	4-8mm	6-8 mm	2 doses	4g	Administratio	<u>n</u>		2. Consider as an alternative to FFP for patients with coagulation factor defi prolonged EXTEM CT see above) in the following circumstances:	
	<4mm	29mm	2 doses	6g	Reconstit Swiri gen	ute 1g in 50ml warm sterile water (use prepared ki tiy and do not shake (to avoid foaming).	t in fiuld warmer).		
	*Outside of curre	ently approved guideline	es, must be discus	 Administer each 1g via syringe driver over 2-4 mins if life-threatening haemorrhage or over 10 mins if not. 			reatening		

Endorsed by the Department of Anaesthesia and Pain Medicine and the Hospital Transfusion Committee on 31/05/2017

SCGH ROTEM Algorithm for Critical Bleeding

Key Points: This algorithm should be used in conjunction with the SCGH Critical Bleeding Protocol. Only treat abnormal values if active bleeding or at high risk of bleeding. Repeat ROTEM analysis 10 mins after intervention to assess response.

	ABNORMAL ROTEM	CRITERIA	DIAGNOSIS	INTERVENTION	CORRECTED ROTEM
OLYSIS	00005 311 112245 81 110224 (81) 51 11224 (81) 51 1125 (81)	Early Diagnosis EXTEM A5≤35mm or FIBTEM CT >600s	High likelihood of excess fibrinolysis	Tranexamic acid 1g	01001 71 50 500 71 61 20 30 72 50 50 72 1041 72 1041 72 1041
FIBRIN		Late Diagnosis EXTEM or FIBTEM ML ≥5%	Excess fibrinolysis	Consider repeat dose if has lost over 1 blood volume since initial dose	407 67 m 14 15 1
FIBRINOGEN		FIBTEM A5≤10mm	Low fibrinogen	Cryoprecipitate (see dosing guide)	6 1973 1974 177 1975 1975 177 1975 1975 177 1975 1975 177
LETS		EXTEM A5 ≤35mm and FIBTEM A5 >10mm	Low platelets	Platelets: 1 adult dose (correlate with platelet count)	71 (14) (7, 12) (7, 12) (7, 14) (7, 14) (7, 14)
PLATE	4. · · · · · · · · · · · · · · · · · · ·	EXTEM A5 ≤25mm and FIBTEM A5 ≤10mm	Low platelets and Low fibrinogen	Platelets and fibrinogen (correlate with platelet count)	425 Clime 6, * K 9 S2* 435 Clime
Я	1 (1) 575 (1) (1) (1) (1) (1) (1) (1) (1) (1) (1)	EXTEM CT 80-140s and FIBTEM A5 ≤10mm	Low fibrinogen	Correct fibrinogen and reassess	б ^{тоно} 57 (1924) 02 17 (1923) 17 (1923) 17 (1923) 17 (1923)
CT0	13 Minn 13 Minn 16 3 Minn	EXTEM CT >80s but FIBTEM A5 > 10mm	Low coagulation factors	FFP 1-4U or	671: 1841 753: 60mm 460: 67mm
Α.	Ka Bina	EXTEM CT >140s and FIBTEM A5 ≤10mm	Low fibrinogen and Low coagulation factors	(+ fibrinogen if indicated)	a 20° Ada 41 mm
	Fibringgen Dosing (Suide			

Fibrinogen Dosing Guid

FIBTEM A5 Target: ≥12mm					
FIBTEM A5	Increase required	Cryoprecipitate*			
9-10mm	2-3 mm	10 Units			
7-8mm	4-5 mm	15 Units			
4-6mm	6-8 mm	20 Units			
<4mm	≥9mm	20-25 Units			
*Cryoprecipitate dosing is for standard adult units (Cryo 5 units = Fibtem A5 increase of approx 2mm)					





Consider lower dose 10U/kg (round to nearest 500U).

Endorsed by the Department of Anaesthesia and Pain Medicine and the Haematology department January 2017 Adapted from KEMH hospital algorithm with permission

FSH ROTEM Algorithm for Critical Bleeding

This algorithm should be used in conjunction with the FSH Major Haemorrhage Protocol Treat abnormal values only if there is active bleeding or the patients is at high risk of bleeding. Repeat ROTEM analysis 10 mins after any intervention to assess response.

	ABNORMAL ROTEM	CRITERIA	DIAGNOSIS	INTERVENTION	CORRECTED ROTEM
OLYSIS	eres Prinat Freds- co CF Mi	Trauma (within 3hrs) OR Post partum haemorrhage	\longrightarrow	Tranovamia agid 1g	1000 11000 11000 11000 1100 1100 1100
FIBRIN		Flat trace OR Maximal lysis >5%	Hyperfibrinolysis	franckanic acid ry	47 Dram No X 3 Dram No Stram No Stram
FIBRINOGEN		FIBTEM A5 ≤10mm	Hypofibrinogenaemia	Cryoprecipitate	алана аланана алана алана алана алана алана алана алана алана
PLATELETS	45 - 21 - 21 - 21 - 21 - 21 - 21 - 21 - 2	EXTEM A5 ≤35mm with normal fibrinogen*	Thrombocytopaenia	Platelets	envision posterior en posterior en poster
FACTORS	11 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	EXTEM CT 90-140sec with normal fibrinogen** OR EXTEM CT >140sec	Low coagulation factors	Fresh Frozen Plasma 2-4u OR Prothrombinex 25IU/kg	67962 07454 m 07454 m 07454 m 07454 m 07454 m 0745 m 07
	Cryoprecipitate D	osing Guide			Key components

· · · · · ·	• •	-		
FIBTEM A5	Non-obstetric	Obstetric		
7-10	1 dose	2 doses		
<6	2 doses	3 doses		
One dose = five apheresis units = Fibtem A5 increase of approximately 4mm				

*If EXTEM ≤25 and FIBTEM A5 ≤10 consider replacing both factors

**Fibrinogen replacement in the context of hypofibrinogenaemia may overcome a minor prolongation of olotting time



Key components			
EXTEM CT Clotting Time	Thrombin generation		
EXTEM A5	Fibrinogen and platelet		
Amplitude at 5 minutes	concentration and function		
FIBTEM A5	Fibrinogen concentration and		
Amplitude at 5 minutes	function		
ML %	Degree of fibrinolysis over		
Maximal lysis	temogram		

Version 1.2. Endorsed by the Department of Anaesthesia and Pain Medicine and the FSH Transfusion Services Committee on 10/11/16. Adapted from the King Edward Memorial Hospital ROTEM algorithm

History

- Young male, usually fit and healthy
- Ecstasy OD, MDMA toxicity (serotonin syndrome) multiple organ failure
- Seizure
- T42.2 BP 80/50 HR 183 GCS 3
- Noradrenaline, renal impairment, hypoglycaemia, lactic acidosis
- Noted to be bleeding from his lines and mouth

• Initial bloods were FBC and COAG profile

COAG Profile

- INR > 10
- APTT > 180
- Fibrinogen < 0.1g
- Platelets 64

So an urgent ROTEM was done – guess what you think it might look like!

MCF: - mm	ML: - %	CFT: - s
CT: *3593s	A5: – mm	A10: - mm
FIBTEM	2017-05-06 07:05	2: 84784678

1	1	3
	ļ	ļ
INTEM	2017-05-06 07:07	2: 84784678
CT: *3595s	A5: – mm	A10: - mm
MCF: - mm	ML: - %	CFT: - s

MCF: - mm	ML: - %	CFT: - s
CT: *3594s	A5: - mm	A10: - mm
EXTEM	2017-05-06 07:06	2: 84784678

ROTEM 1

0700

Key Findings

- Fibtem A5 = unrecordable
- Extem CT = unrecordable
- Extem A5 = unrecordable
- Intem CT = unrecordable

Have a go and try and interprete this one yourself! Easy to see what's wrong but what are you going to give???



- Fibtem A5 = unrecordable
- Extem CT = unrecordable
- Extem A5 = unrecordable
- Intem CT = unrecordable

Interpretation

This patient has a massive consumptive coagulopathy probably DIC.

1) Give TXA 1-2g!!

2)Fibrinogen – Why is there no Fibtem A5 displayed even after
60minutes run time. Because by definition CT doesn't finish until the amplitude reaches 2mm which it never does b/c the fibrinogen is so low! This patient needs <u>a huge dose of</u>
<u>fibrinogen</u> - 3 adult doses of cryoprecipitate or 5-6g of fibrinogen concentrate would be a sensible start.
3) Platelets – Extem A5 unrecordable – give platelets 1-2 doses
4) Thrombin - Extem CT = unrecordable – this could just be because of no fibrinogen but it's so severe you should consider FFP 1-2 units or possibly better prothrombinex 10u/kg.

History

- Patient was given 20 units of cryoprecipitate (2 adult doses)
 - Not sure if TXA was given
 - A repeat ROTEM was done





- Fibtem A5 = 6mm
- Extem CT = 347s
- Extem A5 = 6mm

Have a go and try and interprete this one yourself! What do you think about the COAGs?

		·····
FIBTEM	2017-05-06 09:32	2: 84784705
CT: 69s	A5: 6mm	A10: 7mm
MCF: 7mm	ML: * 2%	CFT: - s

Coags: PT=28 INR=2.5 APTT=50 Fib=1.1 PLTS: 67



- Fibtem A5 = 6mm
- Extem CT = 347s
- Extem A5 = 6mm

Interpretation

			20032
-			
FIBT	EM	2017 - 05 - 06	09:3
ст:	69s	A5:	6mm
MCF :	7mm	ML: *	2%

Coags: PT=28 INR=2.5 APTT=50 Fib=1.1 PLTS: 67 1) Give TXA 1-2g if not already given.

2)Fibrinogen – Fibtem A5 = 6mm still severe fibrinogen deficiency

give 2 adult doses of cryoprecipitate or 4g of fibrinogen concentrate.

3) Platelets – Extem A5 = 6mm – *don't worry about the platelet count* this patient needs platelets give 1-2 doses!

4) Thrombin - Extem CT = 347s – this could just be because of low fibrinogen /platelets but it's severe so you should consider FFP 1-2 units or possibly prothrombinex 10u/kg.

The COAGs are not normal but nevertheless a plt count of 67 and a fib of 1.1g are low but don't appear as concerning. The ROTEM howvere as a viscoelastic test is actually assessing clot *strength and thus function* and treatment decisions should be based on the more disturbing ROTEM results.

History

- Patient was given 10 units of cryoprecipitate
 - 1 adult dose platelets
 - A repeat ROTEM was done



Coags: PT=28.5 INR=2.5 APTT=42 Fib=1.8 Plts: 67



Key Findings

- Fibtem A5 = 14mm
- Extem CT = 73s
- Extem A5 = 17mm

Have a go and try and interprete this one yourself! What do you think about the COAGs?

- Fibtem A5 = 14mm
- Extem CT = 73s
- Extem A5 = 17mm



Coags: PT=28.5 INR=2.5 APTT=42 Fib=1.8 Plts: 67

ROTEM 3

- 1) Give TXA 1-2g if not already given.
- 2)Fibrinogen Fibtem A5 = 14mm fibrinogen is actually ok now.
- 3) Platelets Extem A5 = 17mm <u>don't worry about the platelet count</u> this patient needs platelets give 1-2 doses!
- 4) Thrombin Extem CT = 73s normal and note that this has normalised with only cryo and platelets. The patient is making adequate thrombin but the clot they are forming is weak (so FFP won't necessarily help – but platelets will)

The COAGs are not normal with a INR 2.5 you could falsely interprete this as the patient needs FFP – but INR is a very blunt tool and many aspects of haemostatic function can affect this result. Viscoelastic tests which are actually measuring function tell a different story and are much better at delineating the actual cause of the problem. The EXTEM tells us he is generating thrombin (CT normal) but needs platelets! (Tip: if you don't have platelets give more fibrinogen this will also improve clot strength).

Take Home Points

- <u>Large</u> doses of fibrinogen are required when it is really low.
- COAG / INR / Platelet count don't measure function and can be quite misleading in some patients.
- Functional viscoelastic tests are better at delineating what the true problem with haemostasis is.

Thanks again to Dr Peter Garnett from the Dept of Anaesthesia Royal Perth Hospital WA for sharing this case.

A great case! Thanks again to Angie Monk and the team in ICU at Joondalup Health Campus for sharing this case.