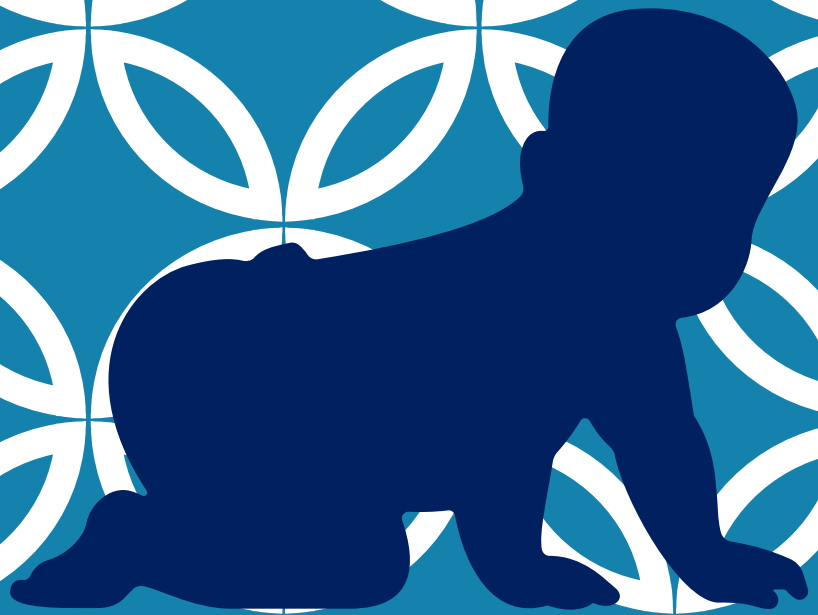


NHS
University Hospitals Plymouth
NHS Trust

UHP MOH ALGORITHM

ROTEM DRIVEN TRANSFUSION MANAGEMENT 2019

Dr Daryl Thorp-Jones
Dr Stuart Cleland
Caroline Lowe

AIMS

(1) MOH. Definition, Incidence and Impact on critical care

(2) Impact of Maternal Physiology on Massive Haemorrhage

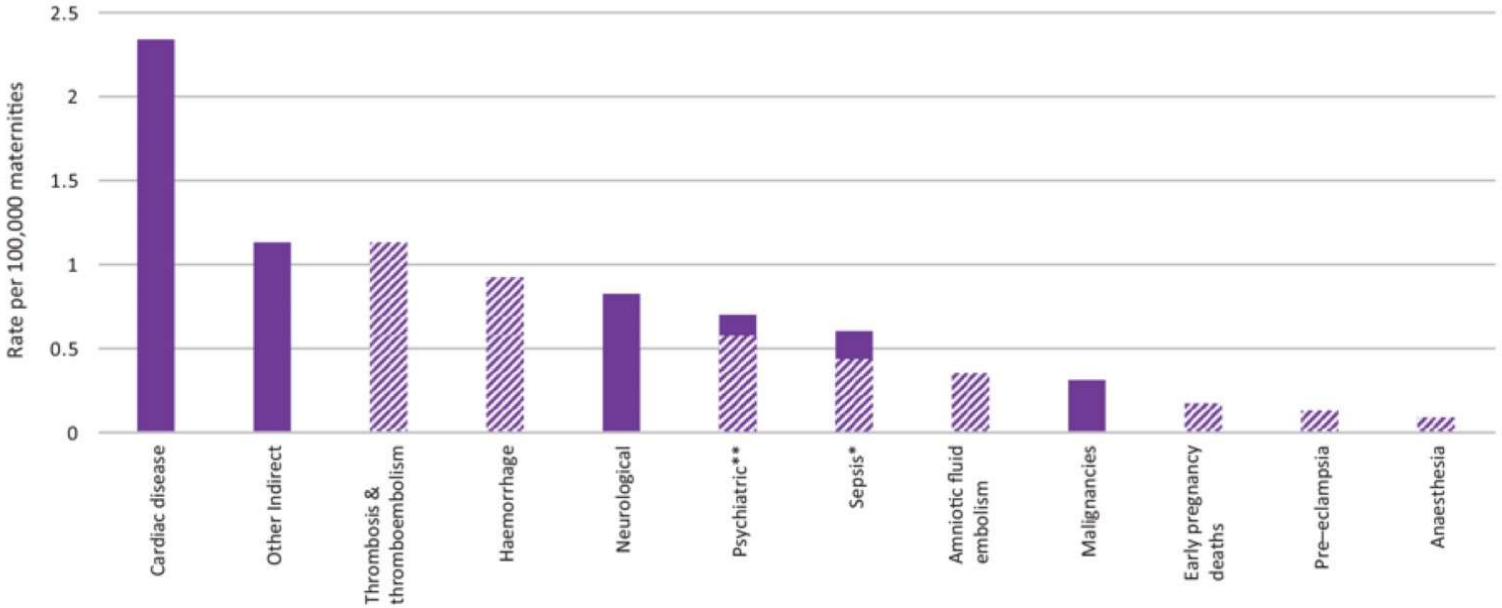
(3) The EBM behind the use of fibrinogen concentrate and ROTEM

(4) HOW UHP does it! Algorithm

(5) Our successes so far

(6) Future change/ Lessons learned

Causes of maternal death 2013-15



MBRRACE-UK

ICNARC OBSTETRIC ADMISSIONS

11% of female admissions to critical care

Antenatally (20%): Predominately Pneumonia

Postnatally (80%): Predominantly PPH

Obstetric admissions to critical care have a low mortality than matched controls (2 vs 11%)

Female admissions (aged 16–50 years) to adult, general critical care units in England Wales and Northern Ireland, reported as 'currently pregnant' or 'recently pregnant'. 1 January 2007 to 31December 2007. ICNARC 2009.

SCOTTISH CONFIDENTIAL AUDIT HAEMORRHAGE

Scottish Confidential Audit of Severe Maternal Morbidity:

MOH (>2500 mls) or 5 Units or Coagulopathy

2005. 3.7 per 1000 births

2012. 5.8 per 1000 births

In 2012. MOH responsible for 80.1% of severe maternal morbidity in Scotland

MASSIVE OBS HAEMORRHAGE (MOH)

DEFINITION

NO actual consensus

Most institutions: 1500 mls OR 4g/dl HB drop after acute blood loss OR a transfusion of 4units +

UHP.. Currently 1000 mls WITH ONGOING LOSSES (new protocol)

RELEVANT PHYSIOLOGY

Protective changes (against Haemorrhage)

Cardiac output increase 40-50%

SV by 25%

Blood volume 70 ml/kg to 100 ml/kg

FIBRINOGEN increases

BUT

Uterine Blood Flow at term 800 ml/min!

Haemostasis can be challenging

Plymouth Hospitals NHS
NHS Trust

BLOOD MANAGEMENT

Estimating blood loss is difficult – MEASURE!

Cell salvage recommended if abnormal bleeding occurs during LSCS, advise leucocyte filter.

Severe early consumptive coagulopathy is associated with:

- abruption
- amniotic fluid embolus
- severe bleeding with pre-eclampsia

PPH due to atony/trauma unlikely to be associated with coagulopathy

Plymouth Hospitals NHS
NHS Trust

BLOOD MANAGEMENT

Protocol-led use of blood products will often lead to **overtransfusion of FFP**:

- If coag unknown, 4 PRC's before FFP
- After 4 PRC's give 4 FFP.
- Maintain 1:1 ratio until results known.
- Point-of-care (POC) testing recommended.

Hypofibrinogenaemia predicts risk of ongoing PPH

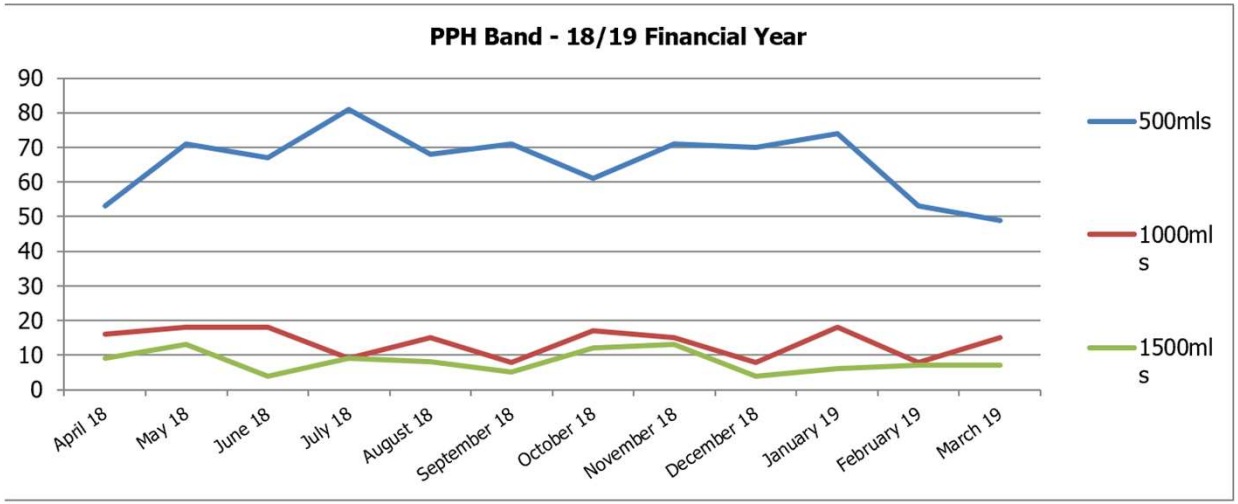
- Normal fibrinogen = 4–6 g/l
- < 3 and especially < 2 with bleeding predicts progression to major bleed

UHP BLOOD PRODUCT USE PRE-ROTEM USING TRADITIONAL SHOCK PACKS

1) Month-by-Month Postpartum Haemorrhage (PPH) Statistics for Last Year

Month	500mls	1000mls	1500mls	Grand Total
April 18	53	16	9	78
May 18	71	18	13	102
June 18	67	18	4	89
July 18	81	9	9	99
August 18	68	15	8	91
September 18	71	8	5	84
October 18	61	17	12	90
November 18	71	15	13	99
December 18	70	8	4	82
January 19	74	18	6	98
February 19	53	8	7	68
March 19	49	15	7	71
Grand Total	**789**	**165**	**97**	**1,051**

18-19 Financial \Year
MH Incidence just below 10/month
1000-1500 mls approx. 20/month
TXA/Fib/ROTEM Protocol starts from Feb 2019
MTP trigger 1500 mls during this period



1500 MLS PPH

1500 mls MTP trigger (note taught in team training)

MTP activation : 24/97 (24.7%)

Blood transfusion 15/97 (15.4%). 2unit use the norm

One use of fib concentrate (during 9 unit transfusion/2FFP/1 Plt)

FFP use 4/97 (4%)

FFP thawed/returned for used 6/97 (

FFP wasted %

DESTINATION OF FFP ISSUED

In 10 month period before new protocol (April 18-Jan 19)

- 24 units given
- 29 returned to blood bank and re-issued
- 10 units wasted

Since new protocol – 2 months data

- 0 units FFP given
- 4 units returned to blood bank and re-issued
- 2 units wasted

OBSTETRIC HAEMORRHAGE + THE ROLE OF FIBRINOGEN

Fibrinogen levels higher in pregnancy (~5g/dL)

- Physiological excess to prepare for peripartum haemorrhage

Clauss Fibrinogen levels <3g/dL, in particular if <2g/dL, are associated with larger and more significant PPH. <1g/dl =Haemostatic failure!!

FFP has a problem…ie a much lower fibrinogen content (1.5g/dl in FFP) than that seen in term parturients.

Fib concentrate is the obvious answer. But needs guided administration re cost.

POCCT IN OBSTETRIC HAEMORRHAGE

Standard laboratory tests are slow and results may be irrelevant by the time of reporting (60mins)

Cardiff and Liverpool ROTEM® work show direct correlation between FIBTEM A5 times and clauss Fibrinogen levels. Show decrease losses/decreased product use

ROTEM® allows rapid real-time identification of coagulopathy and targeted transfusion of blood products

- EXTEM measures effect of extrinsic pathway
- FIBTEM measures effect of fibrinogen by eliminating effect of plt
- FIBTEM A5 closely correlates to max clot firmness (MCF) but have result for A5 more rapidly (5 minutes)

Cardiff (2017): A5 >10mm. Time in HDU 11hrs vs 24 hrs

- R.E.Collis and P.W.Collins. Haemostatic management of obstetric haemorrhage. Anaesthesia 2015;70(supp 1):78-86.
- Collins PW, Cannings-John R, Brynseels D, Mallaiah S, Dick J, Elton C et al. Viscoelastometric-guided early fibrinogen concentrate replacement during post-partum haemorrhage: OBS2; a double-blind, randomised controlled trial. BJA 2017;119(3):411-21.

LIVERPOOL – KEY POINTS

LWH using ROTEM POCCT routinely alongside the MOH protocol since 2011

Fibrinogen concentrate used in Europe more than cryo

- ?safer, pasteurised, no thawing or cross-match necessary

Compared use of 'shock packs' (4 PRC, 4 FFP, 1 Plt), to new algorithm using ROTEM-guided fibrinogen concentrate administration in obstetric patients with PPH >1500ml.

- Sig reduction in FFP, cryo + platelet transfusion
- Sig reduction in TACO
- Non-sig reduction in TRALI, hysterectomy,
- ICU admission (10% admission in shock pack vs 1% in Fibrinogen group)

Note – study not powered for sig diff in all outcomes (e.g. hysterectomy) and therefore **need RCT**

Mallaiah S, Barclay P, Harrod I, Chevannes C, Bhalla A. Introduction of an algorithm for ROTEM-guided fibrinogen concentrate administration in major obstetric haemorrhage. Anaesthesia 2015;70:166-175.

WOMAN TRIAL

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

*WOMANTrial Collaborators**

Published Online
April 26, 2017
http://dx.doi.org/10.1016/S0140-6736(17)30638-4

See Online/Editorial
http://dx.doi.org/10.1016/S0140-6736(17)31111-X

*Collaborators listed at end of the report

Correspondence to:
Clinical Trials Unit, London School of Hygiene & Tropical Medicine, London, UK
thewomantrial@LSHTM.AC.UK

Summary

Background Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces deaths due to bleeding in trauma patients. We aimed to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

Methods In this randomised, double-blind, placebo-controlled trial, we recruited women aged 16 years and older with a clinical diagnosis of post-partum haemorrhage after a vaginal birth or caesarean section from 193 hospitals in 21 countries. We randomly assigned women to receive either 1 g intravenous tranexamic acid or matching placebo in addition to usual care. If bleeding continued after 30 min, or stopped and restarted within 24 h of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given. Patients were assigned by selection of a numbered treatment pack from a box containing eight numbered packs that were identical apart from the pack number. Participants, care givers, and those assessing outcomes were masked to allocation. We originally planned to enrol 15 000 women with a composite primary endpoint of death from all-causes or hysterectomy within 42 days of giving birth. However, during the trial it became apparent that the decision to conduct a hysterectomy was often made at the same time as randomisation. Although tranexamic acid could influence the risk of death in these cases, it could not affect the risk of hysterectomy. We therefore increased the sample size from 15 000 to 20 000 women in order to estimate the effect of tranexamic acid on the risk of death from post-partum haemorrhage. All analyses were done on an intention-to-treat basis. This trial is registered with ISRCTN76912190 (Dec 8, 2008); ClinicalTrials.gov, number NCT00872469; and PACTR201007000192283.

Findings Between March, 2010, and April, 2016, 20 060 women were enrolled and randomly assigned to receive tranexamic acid (n=10 051) or placebo (n=10 009), of whom 10 036 and 9985, respectively, were included in the analysis. Death due to bleeding was significantly reduced in women given tranexamic acid (155 [1·5%] of 10 036 patients *vs* 191 [1·9%] of 9985 in the placebo group, risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045), especially in women given treatment within 3 h of giving birth (89 [1·2%] in the tranexamic acid group *vs* 127 [1·7%] in the placebo group, RR 0·69, 95% CI 0·52–0·91; p=0·008). All other causes of death did not differ significantly by group. Hysterectomy was not reduced with tranexamic acid (358 [3·6%] patients in the tranexamic acid group *vs* 351 [3·5%] in the placebo group, RR 1·02, 95% CI 0·88–1·07; p=0·84). The composite primary endpoint of death from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] deaths or hysterectomies in the tranexamic acid group *vs* 546 [5·5%] in the placebo group, RR 0·97, 95% CI 0·87–1·09; p=0·65). Adverse events (including thromboembolic events) did not differ significantly in the tranexamic acid versus placebo group.

Interpretation Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no adverse effects. When used as a treatment for postpartum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.

- 20,000 women
- 1g TXA vs placebo
- Reduction in death due to bleeding if given within 3 hours
- Other cause death and rates of hysterectomy not affected
- No increase in VTE or other adverse events

- TXA should be given if:
  - > 500 ml after a vaginal delivery
  - > 1000 ml after LSCS

A PERFECT STORM. CURRENT UHP ACTIVITY

Consultant haematologist engaged and active on the project (Wayne Thomas at UHP)

The presence of auditable use data and costings helped considerably (Engaged trainees: Pippa Squires and Chris Leighton)

Existing evidence base for ROTEM in Obstetrics (as presented)

HTC approved and engagement (Stu Cleland). Obs CG engaged

Surgeons engaged

Lab training and engagement. Dependent on Transfusion Practitioners (Caroline Lowe)

2019 UHP MATERNAL HAEMORRHAGE

Severe MH redefined as 1000mls with ONGOING losses (trying to prompt early intervention and MTP activation)

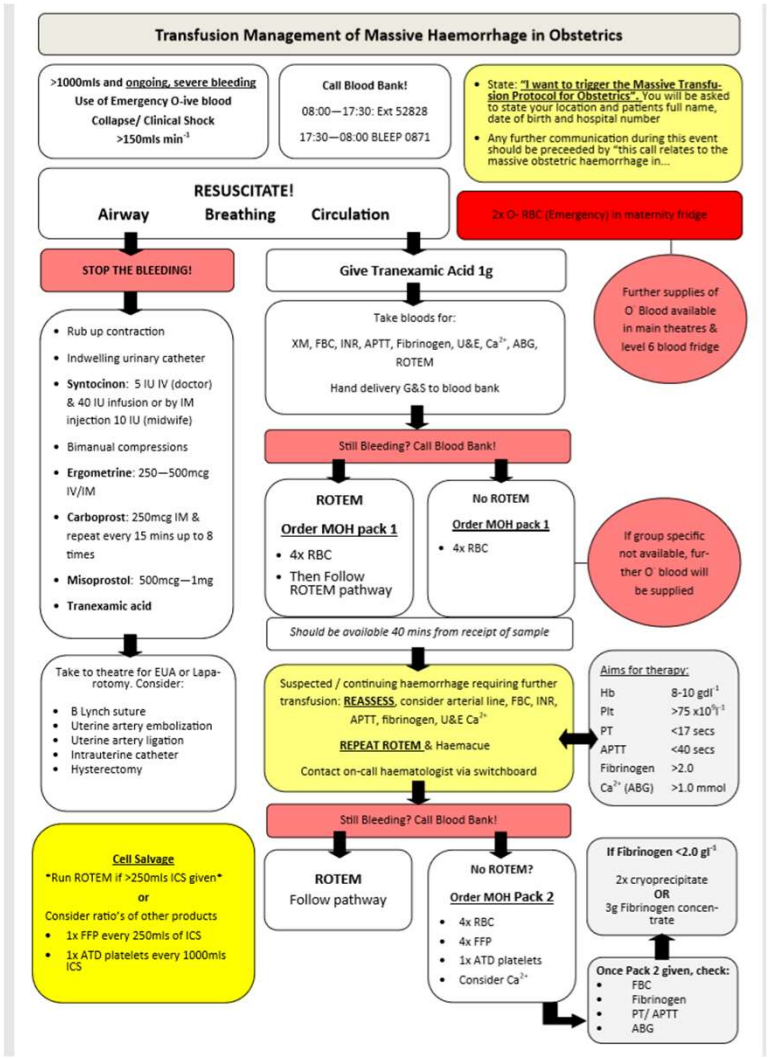
Early TXA 1g promoted (in delivery room)

Early 2nd citrated SAMPLE (for rotem)

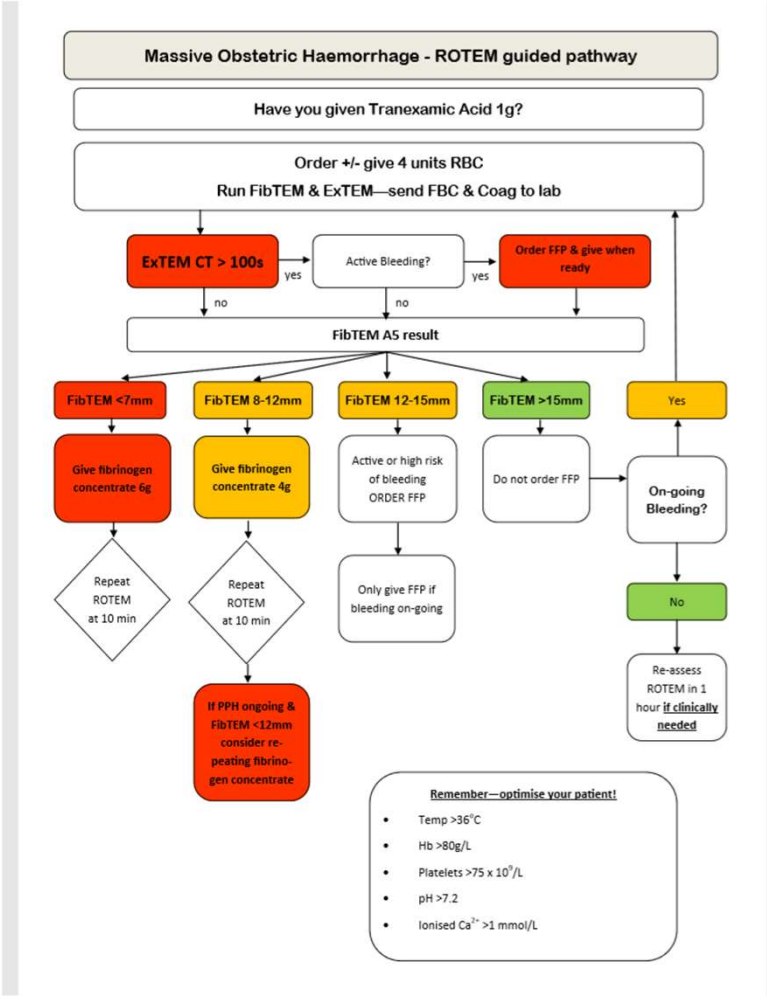
ROTEM driven Pathway. Emphasis of fibrinogen replacement

IPL training/haemorrhage sim (via PROMPT and theme of the week)

MOH ALGORITHM



ROTEM ALGORITHM



FIBRINOGEN CONCENTRATE

Two products:

(1) **Haemocomplettan P (CSL Behring). All the evidence base and our algorithm using this at declared doses. Used in many MOH studies in Europe/known safety. Disadvantage: Slow to prepare however.**

(2) **FibClot** (LFB Biopharmaceuticals). Advantages. Increased viral inactivation procedures, Quicker preparation time, Increased bioavailability of fibrinogen so you give less to achieve comparable rises in fibrinogen levels. Long shelf-life (this stuff is expensive). Same price/cheaper than current preparations. Disadvantages: No Obstetric evidence base/altered doses in our PHNT algorithm

IS IT WORTH IT?

Too early to say but FFP use has dropped off in the trust overall in 2019

We now need to revisit the data

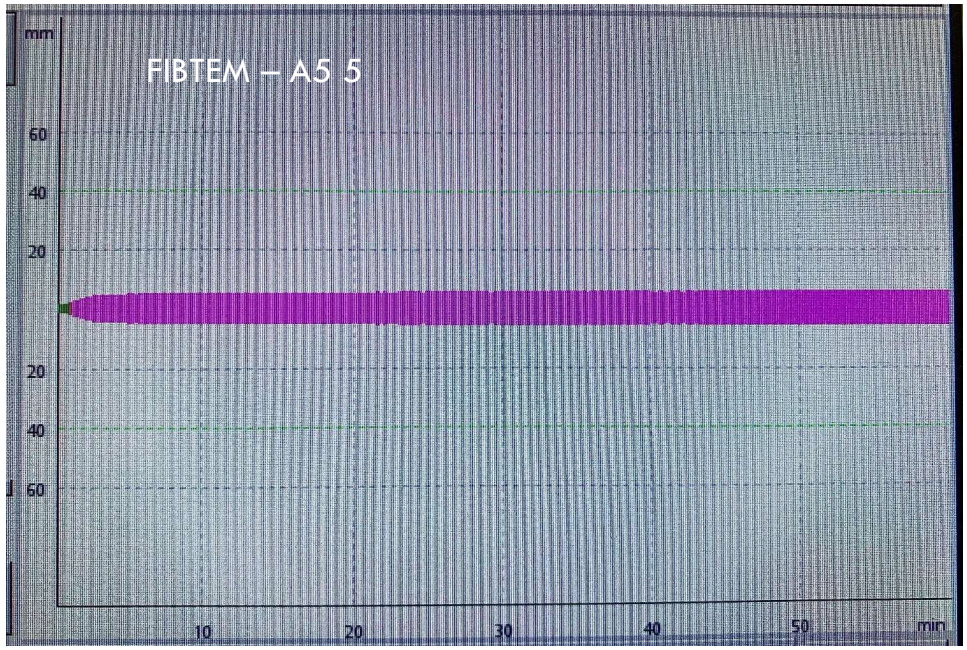
PRESUMPTION: will be an impact on FFP use with a consequential rise in Fib Concentrate use

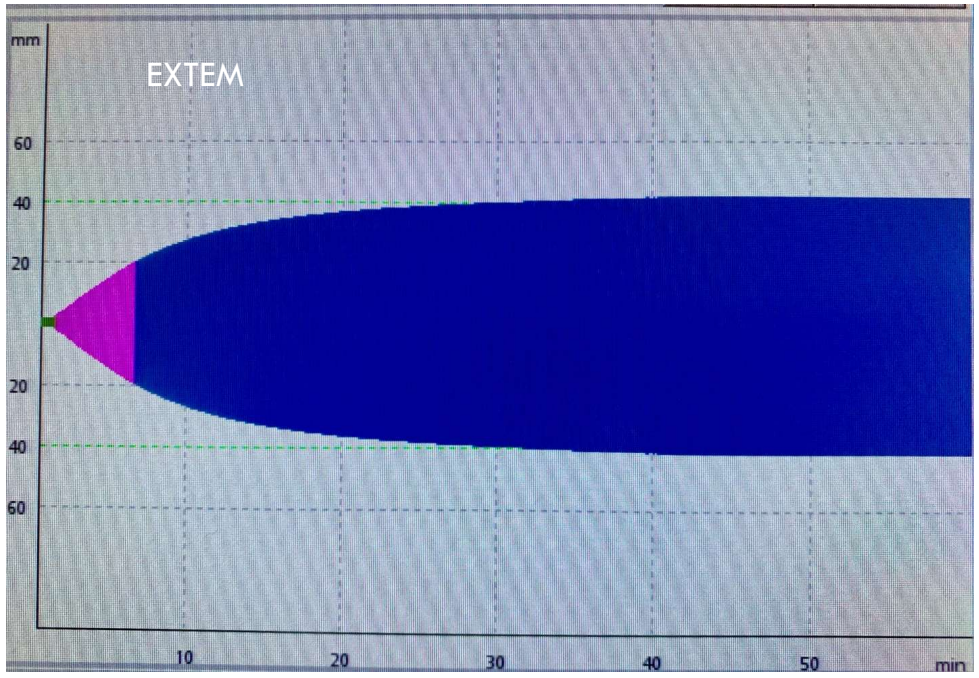
Too early/too small in numbers to extrapolate further although incidence of ICU admissions POST PPH will be interesting to examine between 18-19 and 19-20 financial years

CASE STUDY .

- Primip, presented in labour following SROM ? Element PET.
- 04:16 - Vaginal birth following unremarkable labour.
- 04:34 – Placenta delivered, continuous trickle blood loss, uterus boggy.
- 04:55 - Hypotension/tachycardia - > Dx uterine inversion -> theatre (GA)
  - EBL estimate 1800ml, Hb 69 (133 pre-delivery)
  - 2 units PRBCs transfused intra-op, 1 more due to be given but stopped as spiked temperature.
- 12:45 – Hb 102 -> 71, spreading vulval haematoma – plan return to theatre.

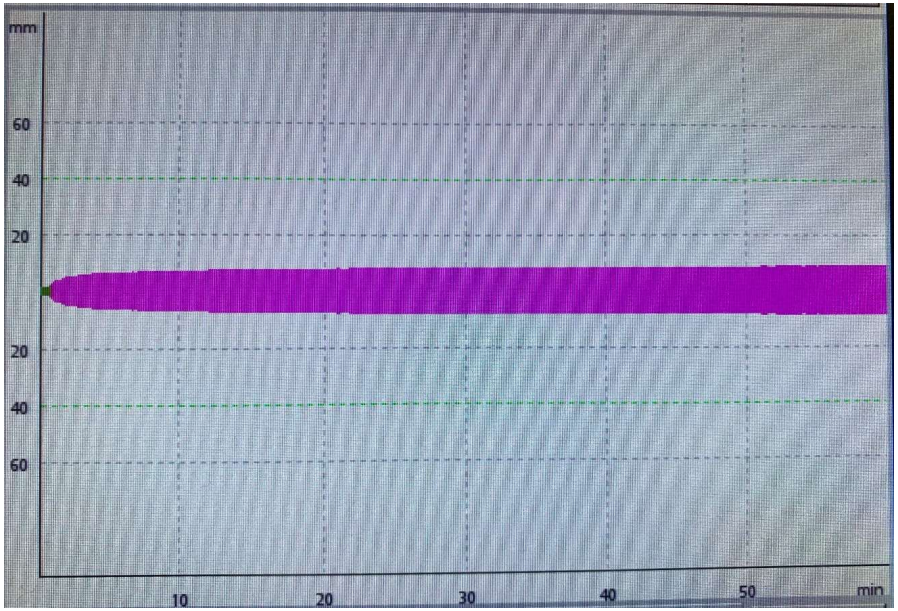
Pre-return to theatre – 2 units RBCs

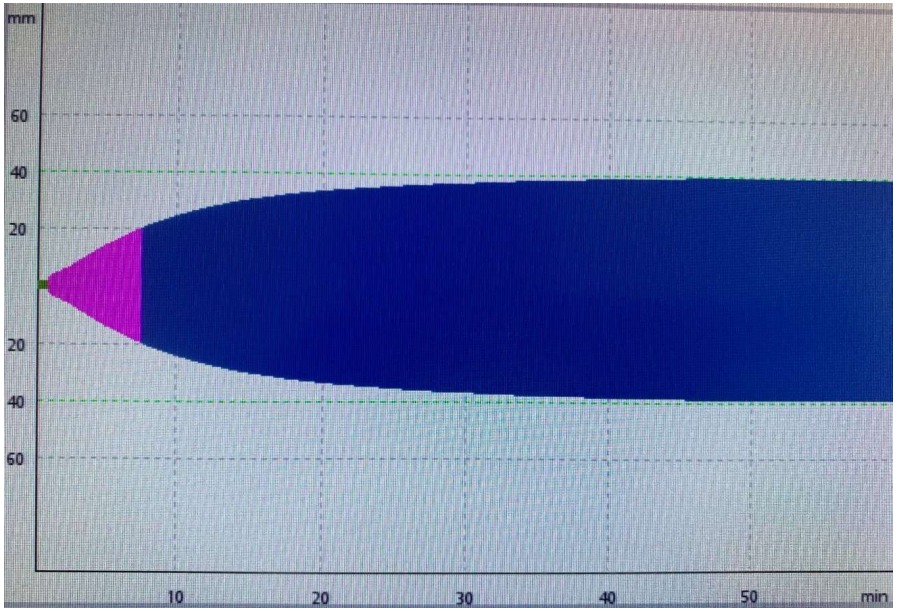




Hb 72
Plt 39
INR 1.2
Fib 1.10

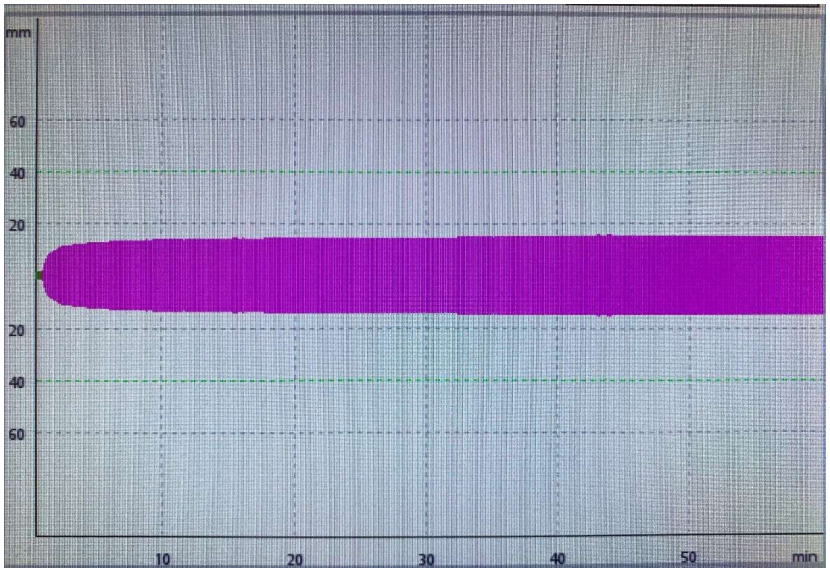
Post-op – 3 further units RBCs + 2 cryo

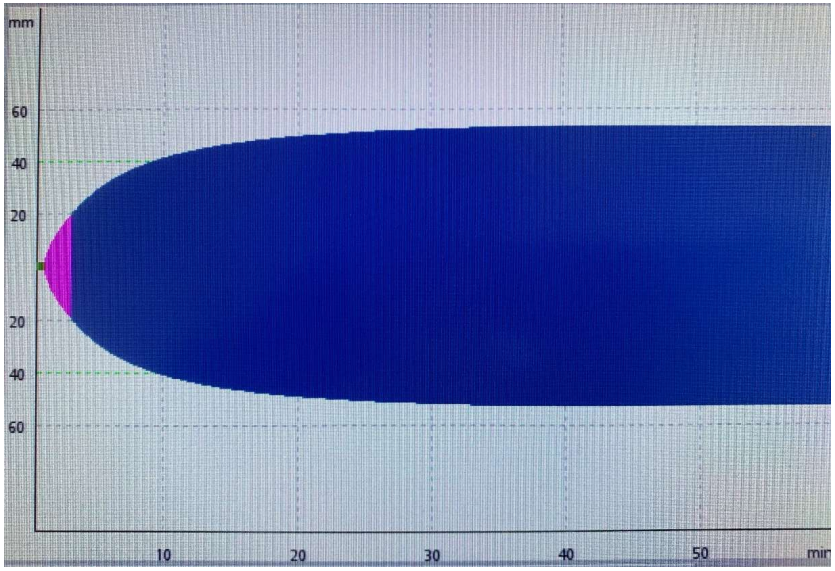




Hb 78
Plt 27
INR 1.2
Fib 1.30
D-dimer 4.30

Further resuscitation – 2 units RBCs, 1 pool platelets, 2 FFP, 2 grams fib concentrate.





Hb 87
Plt 70
INR 1.1
Fib 2.7
D-Dimer 0.8

OUR EXPERIENCE SO FAR

Anecdotal Evidence at Present… but

Rapid correction of coagulopathy and stabilisation with Fib Concentrate when fib tem is low

Fib Clot mixing slow BUT not as slow as thawing Cryo. Moving to new FASTER Fibclot

Occasional resistance to issuing fib concentrate without formal clauss fibrinogen. Now dealt with!

Review of mild reduction FIBTEM group (12-15). Thoughts are FFP NOT NEEDED

FUTURE DEVELOPMENT AT UHP

Fib-Clot 3g (two bottles) rather than 2g. Easier to mix. UHP will switch once current Fib concentrate used

Establishing new antenatal iron pathway (based on Kings Lynn pathway) to attempt to abolish anaemia at term/elective section

The same team engaged in this!

Our blood conservation strategy includes routine suction VIA ICS. Correct anti-D dosing remains an issue and is being targeted by team training/sign out changes

CONTACT AND QUESTIONS

Dr Daryl Thorp-Jones

Consultant Obstetric Anaesthetist

UHP Blood Conservation Lead

dthorp-jones@nhs.net

Dr Stuart Cleland

Consultant Obstetric Anaestheist

UHP HTC Chair