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
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 31 December 2007. ICNARC 2009.
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 4 units + 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
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
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

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 PIt)

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

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

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

Summary

Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces death due to bleeding 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 195 hospitals in 21 countries. We randomly assigned women to receive either 1g intravenous tranexamic acid or placebo as an additional treatment 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 1g of tranexamic acid or placebo could be given. Patients were assigned to receive treatment in one of two randomisation periods by using eight-numbered packet that were identical to the pack number. Participants, care givers, and those assessing outcomes were masked to allocation. Women randomly assigned to 15000 women with a composite primary endpoint of death from all causes or hysterectomy within 62 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 to 15000 to 20000 women to estimate the effect of tranexamic acid on the risk of death from post-partum haemorrhage. All women were assigned to an intention-to-treat basis. This trial is registered with ISRCTN07231230 (Nov 8, 2000). ClinicalTrials.gov number NCT00973669, and FACTSIS201077688913200.

Findings

Between March, 2010, and April, 2016, 2000 women were enrolled and randomly assigned to receive tranexamic acid (n=1000) or placebo (n=1000), of whom 998 and 999, respectively, were included in the analysis. Death due to bleeding was significantly reduced in women given tranexamic acid (35 [1.7%] of 2000 patients) vs 51 [2.5%] of 2000 patients) (OR 0.66, 95% CI 0.46-0.95; p=0.02). In the placebo group, the rate of death in the haemorrhage group was 51 [2.5%] in the placebo group; 45 [2.3%] in the placebo group (RR 0.80 [95% CI 0.66-0.98], p=0.02). All other causes of death did not differ significantly by group. Hysterectomy was not reduced with tranexamic acid (35% [496/1000] patients in the tranexamic acid group vs 39% [479/1000] in the placebo group; RR 0.88 [95% CI 0.76-1.00], p=0.05). The composite primary endpoint (death from all causes or hysterectomy) was not reduced with tranexamic acid (24% [249/1000] deaths or hysterectomies in the tranexamic acid group vs 30% [300/1000] in the placebo group; RR 0.82 [95% CI 0.70-0.95], p=0.002). Adverse effects (including thromboembolic events) did not differ significantly in the tranexamic acid and placebo group.

Interpretation

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

Leading with excellence, caring with compassion

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

Early TXA 1g promoted (in delivery room)

Early 2\textsuperscript{nd} 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
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 Anaesthetist
UHP HTC Chair