ORBCoN
Ontario Regional Blood Coordinating Network

Inspiring and facilitating best transfusion practices in Ontario.

Ontario's Massive Hemorrhage Protocol

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Conflict of Interest

- No commercial conflicts of interest
- Co-Chair Ontario Contingency Planning Working Group for Blood Shortages
- Member of Ontario Emergency Blood Management Committee (OEBMC)

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Objectives

1. List the 7 important elements of a Massive Hemorrhage Protocol.
2. Discuss the options for fibrinogen replacement and the advantages of each.
3. Describe the indications for use of prothrombin complex concentrates.

Thanks to Drs. Jeannie Callum (Sunnybrook) and Katerina Pavenski (St. Michael's Hospital) for MHP slide content

Massive Transfusion Situations

- Trauma
- Upper GI bleeds
- Obstetrical catastrophe
- Surgical misadventure
- Vascular catastrophe
- Surgery: cardiac, vascular
- Complex situations with high mortality
  - e.g. 50% mortality in trauma

These patients may have:

- mechanical bleeding
- coagulopathy

Massive Hemorrhage Protocol (MHP)

- an algorithm for management of a massive hemorrhage
- may improve patient outcomes, including mortality
  - standardised care
  - improved communication and coordination
  - improved quality and safety of patient care
- reduces wastage of blood components

Where are we now?

- different (and perhaps outdated?) transfusion goals
- different transfusion rules
  - issuing only O Rh negative RBC in emergencies (regardless of recipient's age and sex)
  - 2 O Rh positive and 2 O Rh negative -> unable to interpret Rh
  - never switching to group specific components
- different supportive care: TXA (not given or given too late), temperature (not measured and not corrected), anticoagulant reversal (not done), crystalloid (too much given)
- different (and generally poor) records, challenging transfer of care
- no ability to compare to peers

Chin et al. Injury (epub) https://doi.org/10.1016/j.injury.2018.11.026

Key elements of MHP: “T7”

1. Trigger and Treat bleeding (apply damage control resuscitation principles)
2. Team (including communication) and Training
3. Tranexamic acid
4. Temperature
5. Testing
6. Transfusion
7. Termination and Tracking performance

Triggering process (activation)

- the protocol shall be called the Massive hemorrhage protocol (MHP)
- MHP is a code
- announced overhead as CODE TRANSFUSION
  - announcing overhead instantaneously alerts all of the relevant parties and brings additional resources
- single call to Locating/Switchboard with dissemination to all team members

Triggering Criteria

- ABC score, Shock Index, traumatic bleeding severity score, volume of blood loss, number of RBC transfused, etc.
- may be different for different patient populations
- may vary from hospital to hospital – KNOW YOURS

Patient group	Validated activation criteria	Description
Adult	Shock Index	HR/SBP > 0.9 has 1.6x risk of massive hemorrhage
	ABC Score for trauma	1 point for: penetrating injury, BP≤90mmHg, HR≥120bpm, positive FAST Score ≥2 has higher risk of massive hemorrhage
	Resuscitation intensity	≥4 units of fluid within first 30 minutes 1 unit = 1 unit RBC or 1 unit plasma or 1L crystalloid or 500ml colloid

Treat Bleeding

- Damage Control Resuscitation
  - immediate hemorrhage control
    - pressure, damage control surgery, angiography, etc.
  - restoration of blood volume and physiologic/hematologic stability
    - IV fluids
      - early transfusion
      - avoid too much crystalloid
    - correct hypothermia
    - correct acidosis
    - correct calcium

Team/Communication

Large Hospital

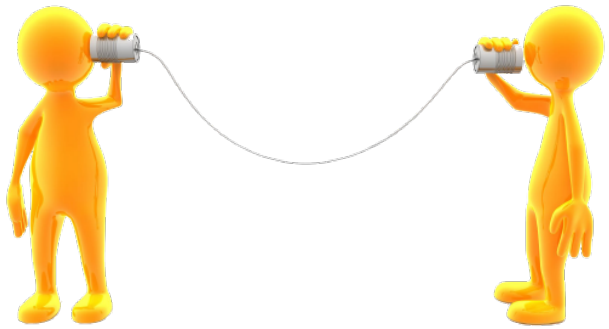
- Physician Lead
- Nursing Lead
- Charting Nurse
- RT
- Anesthesia
- Rapid Response/Code Team
- Porter
- MLT – Transfusion Medicine
- MLT – Core lab (Hematology, Coagulation, Biochem)
- OB: back up anesthesia, second call OB, neonatologist, NICU RN
- Chaplain

Small Hospital

- Physician Lead
- Nursing Lead
- Charting Nurse
- Code Team
- Anesthesia if available
- Porter
- MLT – Transfusion Medicine and Core Lab
- OB: Obstetrician on call

Communication

- How?
  - established, reliable and mobile means to communicate
- Who?
  - MHP clinical team, laboratories, porter, other services
- When?
  - activation/termination, location change, clinical status change, goals of care change, transfer of care



Training

- training, competency assessment, maintenance of competence
  - didactic, case-based, simulation
  - mock codes/drills
    - in situ mock codes significantly improve response times, increase staff confidence levels and are correlated with improved patient survival

Herbers & Heaser Am J Crit Care 2016; Andreatta et al Pediatr Crit Care Med 2011; Oldroyd et al BMC Res Notes 2016

Tranexamic Acid (TXA)

- TXA is an antifibrinolytic and can stabilize a clot, minimizing bleeding
- give TXA ASAP within the first 3 hours of injury (but if possible <1 hour) in trauma patients and as soon as MHP is called for all other patients
- dosages and infusion rates vary

  1g bolus plus 1g infusion over 8 h,

  1g bolus and 1g bolus repeated at 1 h,

  1g bolus and repeated if ongoing bleeding at ≥ 30 min,

  2g bolus at the scene of the injury or before patient transfer

Temperature Management

- studies show that temperature is poorly monitored during pre-hospital and pre-OR phase
- temp <34°C is associated with an increase in mortality
- each 1°C drop will increase blood loss by 16% and risk of transfusion by 22%
- in the pre-hospital phase, trauma patients with minor injury have a fall in temperature with passive warming (blankets) vs. a rise in temperature with resistive warming blankets

Reynolds BR, et al. J Trauma Acute Care Surg. 2012; **73**(2): 486-91.
Dirkmann D, et al. Anesth Analg. 2008; **106**(6): 1627-32.
Kober A, et al. Mayo Clin Proc. 2001; **76**(4): 369-75.
Walpoth BH, et al. N Engl J Med. 1997; **337**(21): 1500-5.
Lundgren P, et al. Scand J Trauma Resusc Emerg Med. 2011; **19**: 59.

Temperature Management

- check temperature within 15 min of MHP activation and then every 30 min or continuously
- promote normothermia by passive and/or active warming
- use warmer to give IV fluids and to transfuse RBC and plasma
- warming a patient increases their comfort

Testing

- should be done at activation/termination and at pre-defined intervals (at least hourly during MHP, prior to each pack, etc.)
- some hospitals create order sets/bundles and have prepared packs with tubes and requisitions
- lab calls critical results and important coagulation parameters (Hb, platelets, INR, fibrinogen)

Large Hospital	Small Hospital
CBC (Hgb, PLT)	CBC (Hgb, PLT)
INR, fibrinogen ROTEM	INR, fibrinogen if available
Lactate or ABG/VBG	Lactate or ABG/VBG
Ionized calcium	Calcium
Lytes, Creatinine, Troponin	Lytes, Creatinine, Troponin

Urgent Reversal of Anticoagulants

Be familiar with antidotes and reversal policies

Drug	Warfarin	Dabigatran	Rivaroxaban Apixaban Edoxaban
Mechanism	causes vitamin K deficiency	inhibits IIa	inhibit Xa
Effect on coagulation testing	increases PT/INR	may increase aPTT	may increase PT/INR
Antidote	Vitamin K and PCC (or plasma)	Praxbind (idarucizumab)	No
If no antidote, what can be tried?	N/A	N/A	PCC

Transfusion: Large Hospital

TM Lab Shipments (q30min):

- Box 1 : 4 RBC
- Box 2: 4 RBC , 4 plasma
- Box 3: 4 RBC, 2 plasma, 4g FC
- Box 4+: 4 RBC, 2 plasma

- transfuse platelets based on platelet count
- give more FC as per fibrinogen level
- switch to lab-based transfusion as soon as active bleeding is controlled

RBC

- O Rh neg to females <45 years old and O Rh pos to all others
- switch to group specific RBC when group determined
- switch to crossmatched RBC when possible

Plasma

- AB plasma
- switch to group specific or compatible plasma when group is known/plasma thawed

Platelets

- any group

Fibrinogen Concentrate

Transfusion: Small Hospital

TM Shipments

- Box 1: 4 RBC
- Box 2: 4 RBC and where plasma not stocked 2,000 IU PCC, 4g FC
- Box 3 and subsequent: transport out
- transfuse platelets based on platelet count

RBC

- O Rh neg to females <45 years old and O Rh positive to all others

Platelets

- if not stocked, order
- if patient is transferred out before platelets are transfused, communicate this to receiving hospital

Switch to lab-guided transfusion ASAP to avoid overtransfusion

- maintain Hb > 80 g/L
- maintain platelets > 50 x 10^9/L
  - > 100 with intracranial hemorrhage
- maintain INR less than 1.8
- maintain fibrinogen greater than 1.5 – 2.0 g/L
- maintain ionized calcium greater than 1.15 mmol/L

Termination

- Termination criteria
  - hemorrhage is controlled or patient succumbed or transferred
- Termination process determined by hospital
- Transfer of care including completion of charting and hand-over
- Return coolers and any unused blood components to transfusion medicine
- Inform patient and/or their substitute decision maker about MHP and risks of massive transfusion
- Women of child-bearing potential should undergo red cell antibody screening at 6 weeks and/or 6 months after transfusion

T^7 Summary

	T
1	Trigger
2	Team
3	Tranexamic acid
4	Temperature
5	Testing
6	Transfusion
7	Termination

Ontario MHP Toolkit: Outline

- under construction on ORBCoN website
- MHP statements, infographic
- presentations, CMAJO publication
- implementation checklist
- educational e-learning modules for nurses (and for porters, lab technologists, physicians, communications personnel)
- will address pediatric patients too

On to Fibrinogen Concentrate and Prothrombin Complex Concentrate

Fibrinogen Replacement

- Fibrinogen is necessary for 1° hemostasis and fibrin clot formation
- Hyperfibrinolysis is feature of the coagulopathy of trauma
- Reduced fibrinogen is associated with increased death after trauma
- Reduced fibrinogen is associated with increased bleeding
- Very low fibrinogen levels are seen in massive post partum hemorrhage

Fibrinogen Levels

- transfuse cryoprecipitate (or FC) if fibrinogen less than 1.0 g/L and bleeding or planned procedure
- transfuse cryoprecipitate or fibrinogen concentrate if fibrinogen less than 1.5 g/L in trauma
- fibrinogen less than 2 g/L predicts severe postpartum hemorrhage

Rossaint. Critical Care 2010, 14:R52 Charbit. J Thromb Haemostasis 2006;5:266

Fibrinogen Replacement

- CBS supplies RiaSTAP (CSL Behring) and fibryga (Octapharma)
- I vial = 1 gram, use 4 vials
- each vial reconstituted in 50 mL sterile water
- takes 5-15 minutes to dissolve
- draw into 50 mL syringe
- fibryga is Health Canada approved for acquired hypofibrinogenemia, CSL Behring has applied for RiaSTAP

Fibrinogen Replacement

Attribute	Cryo	Fibrinogen
Accessibility	Frozen	Lyophilized
Room temp storage	No	Yes (1), No (1)
Shelf life	1 year	3 years
Volume	300 mL	200 mL
Rapid preparation/injection	No	Yes
Pathogen reduction	No	Yes
Increase in fibrinogen level (g/L)	0.55 in trauma	0.80 in off-label studies
Cost per dose (4 g), approx.	$1400	$1400

FC Reconstitution Videos

RiaSTAP

https://www.youtube.com/watch?app=desktop&v=B0JlXpCT6cQ

fibryga

https://vimeo.com/250325106

Prothrombin Complex Concentrate

≠

Plasma – all the clotting factors

PCC – II, VII, IX, X only
(plus Proteins C and S, heparin)
Informed consent required

Indications for PCC

- INR > 1.5 AND:
  - urgent (< 6 hours)* warfarin reversal
    - life or limb-threatening bleeding
    - urgent surgery
  - urgent (< 6 hours)* correction of Vit K deficiency

- PCC is a warfarin ‘antidote’, works in minutes
- effective half life is 6 hours, so need 10 mg IV vitamin K also, to prevent rebound bleeding

*6 hour time frame reflects half life of the product, not the urgency of the surgery

Administration of PCC

	INR < 3.0	INR 3.0 – 5.0	INR > 5.0
Dose PCC	40 mL (1000 IU)	80 mL (2000 IU)	120 mL (3000 IU)

- dose is measured by IU factor IX per vial
  - not to be confused with factor IX concentrate
- each vial (reconstituted) has 20 mL vol. and 500 IU factor IX
- 3 options: standard 2-vial dose, INR-based dosing or INR- and weight-based dosing
- 2 vials is the usual starting dose in the 50-90 kg patient
  - with 10 mg Vit K IV
- if major bleeding and INR unknown use 4 vials
- measure INR immediately following infusion and at 6 h post infusion

PCC is Not Indicated for:

- non-urgent warfarin reversal e.g. before elective procedure
- correcting an elevated INR in a non-bleeding patient
- coagulopathy associated with liver dysfunction
- massive transfusion where plasma is available

Summary

1. MHPs should address: trigger, team, tranexamic acid, temperature, testing, transfusion and termination.
2. Fibrinogen replacement can be achieved with fibrinogen concentrate (FC), cryoprecipitate or plasma
    1. FC has the advantages of pathogen inactivation, predictable fibrinogen content, longer shelf life, low infusion volumes, and ease and rapidity of reconstitution.
    2. Cryoprecipitate has the advantage of familiarity.
    3. Plasma has the advantage of availability when neither of the other products is available.
3. Prothrombin complex concentrate is used to reverse the effect of warfarin anticoagulation or to treat Vitamin K deficiency, if urgent (< 6 hrs) treatment is required.

Thank you. Questions?

Globe and Mail. October 19, 2020.