EPIQ

Evidence-based Practice for Improving Quality

Hemodynamic Group Update

Co-chairs: Souvik Mitra & Amish Jain

Background: Need for Hemodynamic Group

- Cardiovascular problems are common in preterm neonates
- Associated with very high mortality and short- and long-term morbidities
- Major variability in management across tertiary NICUs in Canada

PDA Pharmacotherapy practices across CNN centers (n=26) [2019 survey]	
Primary pharmacotherapy for symptomatic PDA	**Number of CNN centers**
Standard dose ibuprofen	14
High dose ibuprofen	8
Intravenous indomethacin	1
Acetaminophen	2
No treatment at all	1

Background: National perspective

Teaching

- > 14 tertiary centers with TNE/hemodynamic programs
- Royal College approval for Area of focused competence (Dr. Dany Weisz)
- Harmonizing imaging protocols for TNE (Dr. Audrey Hebert, Dr. Deepak Louis, Dr. Gabriel Altit)

Research

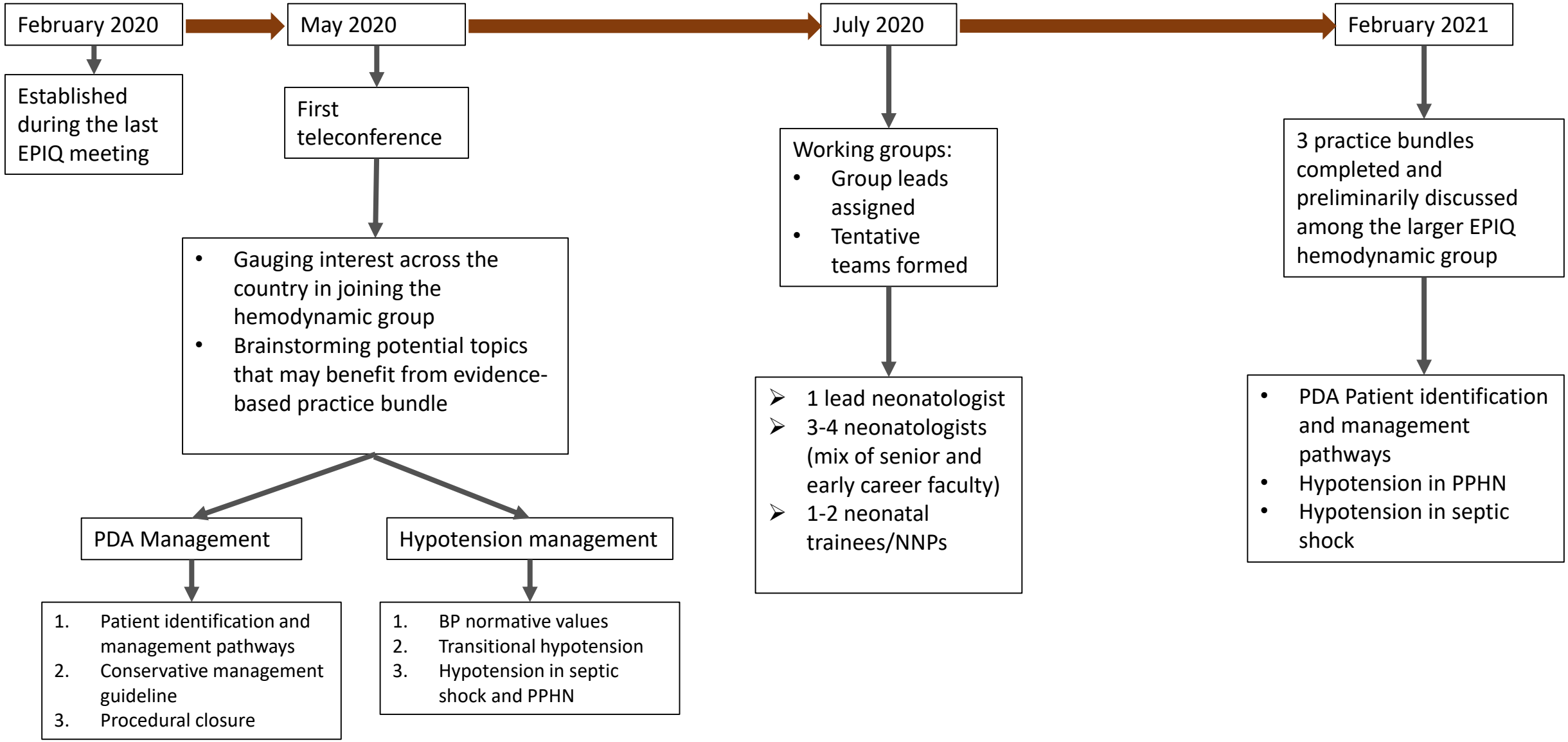
- Use of iNO in preterm neonates [11 sites] (Dr. Amish Jain)
- CER on types of pharmacotherapy for PDA [22 sites] (Dr. Souvik Mitra)

Gap??

- Standardization of hemodynamic management
- Evaluation of clinical outcomes in infants with hemodynamic issues

EPIQ works!

Summary of activities over the past year



Working subgroup teams

PDA Management	
Patient identification and management pathways	• Audrey Hébert • Bonny Jasani • Michael Castaldo • Christine Drolet • Caio Barbosa • Danielle Styranko *Lead* – Souvik Mitra
Conservative management guideline	• Amouchou Soraisham • Kumar Kumaran • Souvik Mitra *Lead* – Gabriel Altit
Procedural closure	• Joseph Ting • Amneet Sidhu • Walid El-Naggar *Lead* – Dany Weisz

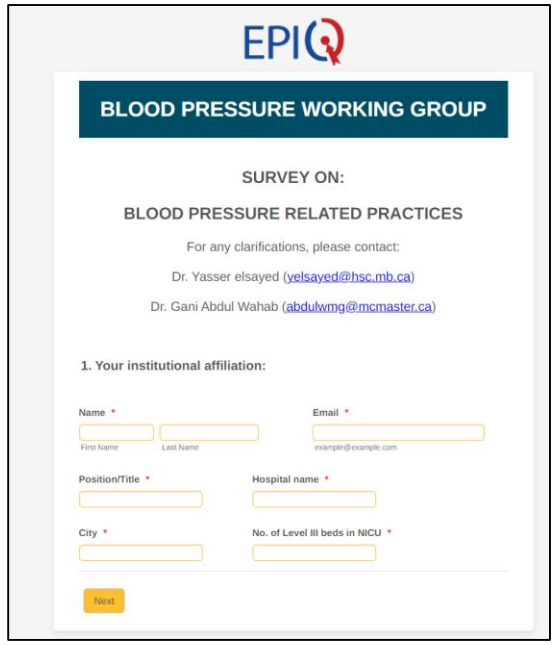
Hypotension Management	
BP normative values	• Muzafar Gani Abdul Wahab • Nadya Ben Fadel • Walid El-Naggar • Debbie Fraser • Maher Shahroor • Nicole Kjartanson *Lead* – Yasser Elsayed
Transitional hypotension	• Abbas Hyderi • Amneet Sidhu • Soume Bhattacharya *Lead* – Amish Jain
Hypotension in septic shock and PPHN	• Soume Bhattacharya • Deepak Louis • Kumar Kumaran *Leads:* Audrey Hébert & Ashraf Kharrat

Development of evidence-based practice bundles: *Process*

- Identify priority questions within each subgroup

[Conduct formal/informal surveys (if required)]

- Each member tasked with summarizing available evidence for each particular question
- Collate and discuss all summarized evidence
- Discuss quality of evidence (and if possible use established methods to assign certainty of evidence, eg, GRADE)
- Finalize the practice bundle within their own subgroup prior to presenting it to the larger group



Completed practice bundle example

PDA Patient identification and management pathways in preterm infants

Priority Questions

- Prophylactic cyclo-oxygenase inhibitor therapy
- ‘Routine echocardiographic screening’ vs ‘echocardiography only when clinically indicated’ to diagnose of hs-PDA
- When should a PDA be treated with pharmacotherapy?
- What is the pharmacotherapy of choice for treatment of hs-PDA?
- Repeat courses of pharmacotherapy
- Feeding during treatment

Domain	Recommendation [with GRADE certainty of evidence]
Prophylactic cyclo-oxygenase inhibitor therapy	• Routine prophylactic treatment of PDA with indomethacin in all preterm infants is not recommended [Strong recommendation, moderate certainty of evidence] • Selective prophylaxis with intravenous indomethacin may be considered in **extremely low birth weight infants at a high risk of severe intraventricular hemorrhage** [conditional recommendation, moderate certainty of evidence] • Routine or selective prophylactic treatment of patent ductus arteriosus with ibuprofen is not recommended [strong recommendation, very low certainty of evidence] • Routine or selective prophylactic treatment of patent ductus arteriosus with acetaminophen is not recommended [strong recommendation, very low certainty of evidence]
'Routine echocardiographic screening' vs 'echocardiography only when clinically indicated' to diagnose of hs-PDA	• Routine echocardiographic screening in the first 72 h of life may be considered in infants born <26 weeks GA, if local resources are available [conditional recommendation, low certainty of evidence] **Additional comments:** For centers considering routine echo screening in <26 wk GA infants within the first 72h, we recommend considering early treatment in the first 72h only if echocardiographic and clinical signs point to a 'large PDA shunt'
When should a PDA be treated with pharmacotherapy?	• Neonatologists may choose to conservatively manage a symptomatic PDA within the first 1-2 weeks after birth (conditional recommendation; moderate-low certainty of evidence). However, clinicians should exercise caution in applying the results of existing RCTs to clinically unstable extremely preterm infants (especially <26 weeks GA) where earlier pharmacotherapy may be considered. • There is insufficient evidence to recommend a PDA severity score based approach to aid clinicians in making the decision whether to initiate pharmacotherapy for PDA • The attached clinical and echocardiographic markers may be used as a guide to determine the degree of hemodynamic significance of the PDA *[please note this guide is based on observational evidence; survey of TNE neonatologists on their most preferred markers to determine hemodynamic significance and consensus of this working group. This has not been validated through rigorous prospective studies](Appendix A)*

Echocardiographic markers of hemodynamically significant PDA

Mild (A and one or more of B)

A. PDA size: <1.5 mm shunting predominantly left-right (>66% of the cardiac cycle)
B. Pulmonary and systemic shunt effects
   i. Left atrium:Aortic root ratio <1.5
   ii. Transductal peak systolic velocity >2.0 m/s
   iii. Left Ventricular Output (ml/kg/min) <200
   iv. Diastolic flow pattern in descending aorta: Normal antegrade flow

Moderate (A and one or more of B)

A. PDA size: 1.5-2.5 mm shunting predominantly left-right (>66% of the cardiac cycle)
B. Pulmonary and systemic shunt effects
   i. Left atrium:Aortic root ratio 1.5-2.0
   ii. Transductal peak systolic velocity 1.5-2.0 m/s
   iii. Left Ventricular Output (ml/kg/min) 200-400
   iv. Diastolic flow pattern in SMA: Absent/retrograde

Severe (A and one or more of B)

A. PDA size: >2.5 mm shunting predominantly left-right (>66% of the cardiac cycle)
B. Pulmonary and systemic shunt effects
   i. Left atrium:Aortic root ratio >2.0
   ii. Transductal peak systolic velocity <1.5 m/s
   iii. Left Ventricular Output (ml/kg/min) >400
   iv. Diastolic flow pattern in SMA: Retrograde

What is the pharmacotherapy of choice for treatment of hs-PDA?	**Extremely preterm infants (<27 wk GA) in the first week of life** • ***Preterm <27 wk GA & not tolerating PO feeds:*** ➢ Intravenous standard dose ibuprofen (10 mg/kg followed by 2 doses of 5 mg/kg) may be considered as the first choice ➢ Intravenous indomethacin may be considered as an alternative to intravenous ibuprofen [Conditional recommendation; low-certainty of evidence] • ***Preterm<27wk GA & tolerating PO feeds:*** ➢ Acetaminophen PO may be considered as a safer treatment option for hs-PDA compared to NSAIDs (ibuprofen or indomethacin) ➢ Standard dose oral ibuprofen may be considered as an alternate choice [Conditional recommendation; low-certainty of evidence] **Extremely preterm infants (<27 wk GA) more than 1 week of age** • ***Preterm <27 wk GA & not tolerating PO feeds:*** ➢ Intravenous high dose ibuprofen (20 mg/kg followed by 2 doses of 10 mg/kg) may be considered as the first choice ➢ Intravenous indomethacin may be considered as an alternative to intravenous ibuprofen [Conditional recommendation; low-certainty of evidence] • ***Preterm<27wk GA & tolerating PO feeds:*** ➢ Acetaminophen PO may be considered as a safer treatment option for hs-PDA compared to NSAIDs (ibuprofen or indomethacin) ➢ High dose oral ibuprofen may be considered as an alternate choice [Conditional recommendation; low-certainty of evidence] **Preterm infants >27wks GA** • Adjustable dose ibuprofen (standard doses in the first 3-5 days; higher doses beyond 5 days) should be considered as the first line treatment [Strong recommendation; moderate-high certainty of evidence] • Acetaminophen (oral) should be considered as an alternative if there is a concern of side effects with high dose ibuprofen. [Strong recommendation; moderate-high certainty of evidence]
Repeat courses of pharmacotherapy	• A second course of pharmacotherapy (ibuprofen or indomethacin) should be considered for persistent hs-PDA, if there is no contraindication [Strong recommendation; low-certainty of evidence] • Prior to considering procedural closure, a 3rd course of oral acetaminophen may be considered [Conditional recommendation; low-certainty of evidence] ***Additional comments:*** A third course of Indomethacin is not recommended, as it appears to increase the risk of PVL. The literature is unclear about 3rd course of ibuprofen.
Feeding during treatment	• We recommend against stopping or cutting back on feeds during PDA medical treatment [conditional recommendation; low-certainty of evidence] **Additional comments:** There is insufficient evidence for or against progression of feeds during PDA medical treatment

Hypotension management bundles

Hypotension in PPHN

- Monitoring of clinical variables
- Choice of fluids
- Ventilation
- Sedation / Muscle relaxants
- Vasopressor / Inotropes
- Pulmonary vasodilator therapy
- Adjunct therapies
- TNE recommendations

Hypotension in Sepsis

- Monitoring of clinical variables
- Choice of fluids
- Vasopressor / Inotropes
- Adjunct therapies
- TNE recommendations

Plan for 2021-22

- Distribute practice bundles once finalized and approved by the EPIQ hemodynamic group
  - May be modified as per local resources/practices
- May be used by local centers to conduct QI projects to improve clinical outcomes of extremely preterm infants with hemodynamic issues
- Seek opportunities for national-level pragmatic clinical studies to test the effectiveness of practice bundles
  - Comparative effectiveness research projects
  - Cluster RCTs

Thank You!

Image courtesy: cardiac-alliance.org

Contact Information

Souvik Mitra (Souvik.Mitra@iwk.nshealth.ca)

Amish Jain (Amish.Jain@sinaihealth.ca)