INTRAVENTRICULAR HEMORRHAGE AND BRAIN INJURY PREVENTION PACKAGE

Preterm Brain Injury Prevention Working Group

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Points of emphasis:

The interventions proposed in this bundle can be divided into two categories:

- Interventions have potential direct impact on brain injury (like hemodynamic and respiratory management)
- Interventions have indirect impact on brain injury (like light, noise, thermoregulation, minimal handling, and vascular access)
- Minimal handling shouldn't compromise clinical care especially when required to make a care plan

This package is meant to target the neonatal population of less than or equal to $31^{6/7}$ weeks gestation in the first 72 hours of life

1. Background and Resources:

- Background

  Intraventricular hemorrhage (IVH) is the most common form of brain injury and a significant cause of moderate-severe brain injury in preterm infants. The majority of IVH occurs within first 72 hours of life. It has been a clinical challenge to avoid causing injury to the immature brain while balancing management of the very sick premature neonate. There is national and international interest in decreasing the prevalence of IVH. The EPIQ III goal is to drive IVH incidence to zero.

- Resources

  This bundle was put together by IVH working group based on:

  (i) Literature review

  (ii) Two site visits to BC Women & Children NICU and McMaster NICU

  (iii) Clinical Practice Guidelines (CPG) including- central vascular access, natural cord clamping, age appropriate care, endotracheal suctioning, hypoglycemia, hyperglycemia, intubation, pain, resuscitation and immediate care, thermoregulation, ventilation, very preterm admission.

  (iv) Systematic review of the head scans images

  (v) Local practice audits:

  - 42 cases of severe IVH reviewed systematically by a group of neonatologists
  - Case control audit for 2012
  - IVH risk factors prospective audit 2013-2014
  - Intubation audit 2014
  - Incidence of temperature fluctuation 2014
  - Incidence of hypoglycemia or hyperglycemia 2014

  (vi) Expert opinions:

  - National Neonatal Brain Health working group
  - Calgary Neonatal clinical committees (CNS, CVS, Open lung, START, and QI)

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2. Lighting

- Rationale

  Light has both positive and negative potential effects on health and development. Our goal is to provide optimal lighting for preterm and ill neonates based on evidence.

  Our NICU has a well-defined protocol for environmental lighting. Lighting at all bed sides has been measured and there are ongoing audits to ensure compliance with the lighting policy

- Recommendation

  (i) Use continuous dim and indirect lighting; use a penlight when direct visualization is necessary.

  (ii) Following the 72 hours, practice should comply with the AHS provincial policy Environmental Lighting Control HCS-203-02

3. Noise

- Rationale

  The current nationally recognized safe sound levels for the infant patient care areas in the NICU should not exceed 45 to 50 dB., Transient sound not exceed 65 to 70 dB. To promote an optimal environment for rest and growth of the neonate, a combination of appropriate continuous background and operational sound should be considered.[1]

- Recommendation

  Follow the provincial guideline AHS Environmental Noise Control HCS-203-03 for recommended noise levels

  (i) Post signs to identify quiet zone

  (ii) Continue to work with Neonatal Age Appropriate Care Committee to reduce noise in the NICU.

4. Thermoregulation

- Rationale

  Both hypothermia and hyperthermia are detrimental to the baby. Hypothermia, particularly in preterm babies, is associated with increased morbidity and mortality. Hyperthermic babies have a worse short-term outcome and this can be particularly detrimental in association with intrapartum asphyxia and infection.

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- Recommendation

  Refer to the NICU Golden Hour Checklist and Thermoregulation Policy 2-T-3

  Maintain the infant's temperature at 36.5-37.5°C by servo control

5. Skin Care

- Rationale

  Newborns undergo adaptation from the aquatic in utero environment to the aerobic environment after delivery. During this process, their skin assists in the process of thermoregulation, functions as a barrier against toxins and infections, facilitates water and electrolyte balance and serves as a reservoir for fat storage and insulation. Skin also mediates tactile sensation.

- Recommendation

  Follow the AHS Provincial Policy Skin Assessment and Injury Prevention Neonatal PS-99-01

6. Minimal Handling

Minimal manipulation refers to a grouping of care in which the infant is seen as the center of care and requires caregivers to act together, prioritizing the needs of the infant

- Recommendation

  Where possible, develop/identify a core group of RN's and RRT's with specialized knowledge and skills to admit and care for infants ≤31 6/7 weeks for the first week of life.

  In the first 72 hours, the intention is to complete most of the invasive therapeutic interventions and monitoring interventions within the first hour. After birth and thereafter, interventions should only be on an 'as needed' basis.

  (i) Newborn Examination: Examinations should be restricted to one brief targeted examination (exclude hips, red reflex pupillary response, primitive reflexes) at the time of admission. If examinations are required thereafter, targeted examinations should be performed only if there is a clinical need.

  (ii) Daily examinations in infants should always be coordinated with scheduled
  (iii) nursing interventions

  (iv) No length measurement for at least the first 72 hours. Complete a length measurement on all infants after 72 hours.

  (v) Measure one limb blood pressure on admission (left arm). Continue with BP measurement as per NICU monitoring policy

(vi) Head circumference must be measured on admission for all infants

(vii) Any one-care cluster must not exceed 10-15 minutes and be based on infant's\ tolerance of handling.

(viii) Whenever possible, provide facilitated tucking by second caregiver/parent during handling and/or immediately after any care cluster [2]

(ix) When changing diapers and performing abdominal girth measurements: lift infant gently by the hips, not the ankles

(x) For intubated infants avoid parent skin to skin holding in first 72 hours. Encourage parent/infant skin to skin contact through touching/facilitated tucking.

- Minimize routine care

ET suctioning is commonly associated with a serious fall in transcutaneous oxygen tension. The resultant hypoxemia may be associated with a rise in blood pressure and increased cerebral blood flow velocity. Consider the schedule of suctioning for each infant individually and continuously review this schedule. Avoid routine PO and ETT suction.

(i) Intravascular Vitamin K (local Calgary Zone NICU data shows the incidence of IVH/intracranial bleeds has diminished significantly in this population since the initiation of this bundle and administering Vitamin K IV)

(ii) Obtain standard admission blood tests; other blood tests in the first should be ordered in consultation with the neonatologist.

(iii) Cluster care: doing as much as tolerated by the infant (diaper changes, feeding, suctioning, repositioning, holding, etc.) at one time to allow the infant an extended time of rest/sleep.

- Initial Care

Refer to Calgary Zone NICU Golden Hour Checklist.

(i) Initial X-Ray

- X-ray should be done as soon as possible after ETT, central lines and OG tube placement. The aim is for X-ray to be taken PRIOR TO the administration of surfactant unless the FiO2 on admission is ≥60%; then CXR should be done first. Once ETT position is confirmed, surfactant administration and line insertion starts.

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(ii) Lumbar Puncture

- The majority of low birth weight infants do not require a lumbar puncture as part of their initial evaluation for early onset sepsis.
- The aim is to avoid unnecessary lumbar punctures in infants who do not need them but also to perform LPs in those infants at highest risk for sepsis/meningitis. It is optimal to have the LP complete prior to the initiation of antibiotics.
- In neonates who are critically ill and likely to have significant cardiovascular or respiratory compromise from the procedure or those with severe thrombocytopenia, the lumbar puncture can be deferred until the infant is more stable.
- The decision not to perform an LP should be regarded as an "active" one and should be documented in the chart. If there is a change in the indications (as above) the LP can still be done 1-2 days after the onset of infection and treatment

Consider doing an LP only in the following clinical situations:

- Infants with a high probability of sepsis on the basis of **clinical signs** and/or abnormal lab values
- Infants with **positive blood cultures**
- Infants who do not respond to appropriate antimicrobial therapy

7. Vascular Access

Refer to the Golden Hour Admission Checklist and PIV algorithm

- Recommendation

(i) Where possible, umbilical lines should be placed by the most senior practitioner who is proficient at inserting umbilical catheters.

(ii) Establish secure vascular access as early as possible with the least amount of handling /pain for infant.

(iii) Our aim is to establish vascular access within 30 minutes; prior to the administration of Surfactant unless the FiO2 on admission is ≥60% then CXR should be done first. Once ETT position confirmed, line insertion starts and surfactant administered.

(iv) Commence IV fluids soon after establishment of access (before CXR) to prevent hypoglycemia.

(v) Second caregiver should provide facilitated tucking during procedures. Do not use infant restraints.

8. Positioning

- Rationale

  Changes in cerebral blood flow and cerebral blood volume can be measured with head in midline and head rotated to the side. It has been observed that the mean cerebral blood volume was significantly higher when the head was rotated 90 degrees to the side. Rotation of the head to one side obliterates the internal jugular vein on the same side.[3] It has also been noted that intracranial pressure is lower when the head is elevated by 30 degrees.[4] Positioning of the infant's head is especially important for critically ill neonates, and all neonates <26 weeks[5]

- Recommendation

  (i) Maintain neutral head position (head/neck in alignment with body) when turning and positioning the infant. Head of bed should be elevated 20- 30 degrees.

  (ii) Avoid prone positioning for at least 72 hours if infant is intubated. Infants on CPAP may require prone positioning. Discuss with clinician if appropriate.

  (iii) Avoid extreme 90 degree head turning

9. Respiratory Management

9.1 Case room resuscitation:

- Rationale

  Intensive resuscitation in the case room may be a risk factor for IVH and brain injury [6]. Effort should be made to ensure resuscitation is as smooth and systematic as possible.

- Recommendation
  The most experienced staff person should manage the infant airway

  Refer to Golden Hour Resuscitation Checklist and Optimal Lung Algorithm for respiratory support in the delivery room

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9.2 NICU Respiratory Support:

- Rationale

  Intubation is a traumatic procedure and evidence shows that brain perfusion and function may be compromised during the intubation.[7] Our audit showed that babies with severe IVH were more frequently reintubated in the first 72 hours of age and CO2 fluctuation was significantly more frequent in the IVH group. There is growing evidence that extreme levels of PCO2 (whether high or low) or fluctuation can increase the risk of brain injury especially if associated with acidosis [8, 9] [10-14].

- Recommendation
  Follow the Optimal Lung Algorithms for respiratory support in the NICU

  Aim for a PCO2 target 45-55 mmHg (15)

  Infants on CPAP should have interface change at least q2h-q6h and hat change q24h for the first 72 hours. Resume care as per unit policy following the 72 hours

- Action
  (i) Infants born at 23 0/6 to 23 6/7 weeks
    - Infants are intubated empirically in the DR after appropriate lung recruitment.
    - Should stay intubated for the first 72 hours.
    - Follow the extubation criteria outlined below after 72 hours of age.
    - Echo/TNE is highly recommended prior to extubation.

  (ii) Infants born at 24 0/7-25 6/7 weeks
    - Infants are managed on primary CPAP in DR.
    - Intubation is selective and based on clinical indications and include, but not limited to:
      1. CPAP 6 with FiO_2 > 0.30
      2. Moderate to severe respiratory distress
      3. Apneas that require PPV or frequent stimulation
    - Surfactant: will be administered based on the clinical picture and CXR findings.
    - Duration of intubation: as those infants are so fragile and have high rate of extubation failure, we recommend they stay intubated after surfactant administration for a minimum period of 24 hours. This will allow for assessment of the need for a second dose of surfactant, and spontaneous respiratory effort.

  (iii) Infants born at >25 6/7
    - Those infants are managed on primary CPAP in DR
    - Intubation is selective and based on clinical indications and include, but not limited to:
      1. CPAP 6 with FiO_2 > 0.30
      2. Moderate to severe respiratory distress
      3. Apneas that require PPV or frequent stimulation

- Minimize extubation failure in the first 72 hours of life by ensuring that the baby meets extubation criteria outlined by the unit guidelines
- Use Ventilation strategies as per optimal lung group recommendations
- PCO2 target of (45-55 mm Hg)[15]
- Have documented criteria for reintubation
- Infants on CPAP should have interface change at least q2h-q6h and hat change q24h for the first 72 hours. Resume care as per unit policy following the 72 hours

9.3 Extubation Criteria

- Minimal ventilator support:
  (i) Conventional ventilation: PEEP 5 cmH2O, VG 4 ml/Kg, $FiO_2 < 0.30$, R 20, measured PIP (or MAP)
  (ii) HFOV: MAP 8, $FiO_2 \leq 0.25$, Frequency ≥ 10,
  (iii) Although extubation from HFOV is well described in the literature, we suggest a short period of conventional ventilation prior to the first extubation to assess spontaneous respiratory effort; especially for infants who were intubated in the DR or due to apnea.

- Acceptable blood gas on minimal vent settings: pH ≥ 7.25; $PCO_2 \leq 55$ mmHg; normal lactate.

- Hemodynamic stability:
  (i) No inotropes
  (ii) TNE: routine TNE is not recommended.
  (iii) If there are clinical signs suggestive of PDA, perform TNE and assess for hemodynamic significance.
  (iv) It is suggested to treat hsPDA prior to extubation.

- Prediction of extubation success:
  (i) Careful assessment of spontaneous respiratory effort.
  (ii) In case of difficult intubation, ensure that there is a degree of leak around the ETT which indicate absence of significant laryngeal edema.

- Preparation for extubation:
  (i) Ensure caffeine is optimized.
  (ii) Discontinue opioids; or wean to a minimal dose if they have been administered for 5 days or more.
  (iii) Follow the unit extubation pathway.

- Nasal interface assessment:
  (i) Assess mask and prongs fitness to the nose.
  (ii) Assess skin maturation

Post Extubation Support:

(iii) Refer to post extubation guideline
(iv) Currently: Biphasic Positive Airway Pressure (BiPAP).
(v) It is crucial to observe those infants carefully after extubation to assess the respiratory effort, breathing pattern, airway patency, and changes in vital signs.

- Positioning:
  (i) Babies should be kept in supine position with the head in midline position (± 30°) while intubated.
  (ii) Post-extubation: prone position is allowed provided the head is not turned more than 45°. Avoid 90° turns (the assumption that 90° turn may block the cerebral venous return)

- Re-Intubation Criteria:
  (i) Before extubation, the attending physician/designate **must** specify and document re-intubation criteria.
  (ii) Respiratory effort: moderate or severe respiratory distress may indicate airway obstruction, loss of nasal interface seal, or loss of FRC and lung derecruitment. Careful assessment of airway patency and seal is crucial. If respiratory distress persists despite measures to ensure seal and airway patency, consider CXR.
  (iii) Apnea:
    - Any non-obstructive apnea that requires PPV.
    - Apnea requiring stimulation (6 in 6 hours)
  (iv) Worsening respiratory acidosis with $PCO_2 > 60$ mmHg
  (v) Increasing oxygen requirement with $FiO_2 > 0.4$
  (vi) Extubation failure is defined as the need for re-intubation within 72 hours after extubation.

- Trial of re-extubation:
  (i) Allow for 72 hours after re-intubation prior a trial of re-extubation, given the fragility of those infants.
  (ii) This will allow recovery and to address the cause of extubation failure.
  (iii) Different extubation criteria should be discussed for babies who are 7 days of age or older.

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10. Hemodynamic Management

10.1 PDA

- Rationale

  Hemodynamically significant PDA is a risk factor for IVH [16] [17]. Our audit showed babies with severe IVH had significantly more PDA ligations later in life. We also found no baby in IVH group was treated for PDA in the first 72 hours of age. This may be an indication for recognizing and treating hemodynamically significant PDA at an earlier stage. There is evidence that early treatment increases the PDA closure rate [18-21].

- Recommendation

  For intubated babies:

  (i) TNE at 24- 48 hours of age (unless clinically indicated earlier) to identify hemodynamically significant* PDA

  (ii) TNE time should be as short as possible

  (iii) It is not recommended to treat bidirectional PDA as it might have protective effect by preventing cerebral ischemia that occurs due to steeling phenomenon in left to right shunting PDA. Treating the PDA may put extra strain on the right ventricle as the PDA may help as a pop off valve in the presence of pulmonary hypertension

  Consider treatment with indomethacin:

  (i) ≤ 25 6/7 weeks GA: if the PDA is hemodynamically significant*

  (ii) ≤26 6/7- ≤28 6/7weeks GA: if intubated, PDA is hemodynamically significant*, and impacting ventilation

  *Hemodynamically significant PDA [22]:

  (i) Size ≥ 1.5 mm

  (ii) Flow pattern: pulsatile or low velocity

  (iii) Flow direction: left to right

  (iv) LA/AO ratio ≥1.5

  (v) Pseudo normalization of mitral inflow velocity (E/A >1)

  (vi) Decreased or absent diastolic flow in middle cerebral artery, celiac/superior mesenteric artery

10.2 Hypotension

- Rationale

Our audit and other studies have shown that use of inotropes is a significant risk for severe IVH [11, 23-25] and white matter injury [26]. However, we do not have a standard definition for hypotension or a standardized approach to the management of hypotension [27]. We know that infusing inotropes (especially dopamine) in an infant brain with compromised auto-regulation, will change the curve to pressure passive and exaggerate reperfusion injury like IVH. [23]

- Recommendation

(i) Natural cord clamping when feasible

(ii) Avoid the use of inotropes if possible**. Allow for permissive hypotension**. Consider inotrope use only if there are at least 2 or more of the following criteria associated with low BP:

- Lactate > 3.5 mmol/l and rising
- CRT > 3 seconds
- Urine output < 1 ml/kg/hour (beyond 24 hours of age)
- Echocardiography shows low cardiac output and/or low SVC flow
- Before commencing Inotropes consider:

1. Rule out hyperinflation and iatrogenic hypotension/raised SVC pressure
2. Fluid status / potential dehydration
3. A fluid bolus administered slowly over at least 30 minutes
4. Consider other markers for hemodynamic instability:

a. Urine Output (beyond 24 hours of age)

b. Capillary refill time

c. Heart rate trends

d. Oxygen saturation

e. Metabolic acidosis

f. Lactic Acidosis

(iii) After initiation of inotropes, allow 30-60 minutes for infant to respond to the medication before increasing dose.

(iv) Accept arterial pH $\geq$ 7.20, provided PCO2 within target range

10.3 Other

- Thrombocytopenia

  Platelet transfusions may be used to lower the risk of serious hemorrhage in a sick, preterm neonate with thrombocytopenia. Generally, the preterm and sick infant should have a platelet count greater than 50 X 109/L) [22].

- Hypo/Hyperglycemia

  Euglycemia is desired. The target glucose range is greater than 2.6 mmol/L and less than 12 mmol/L.

- Electrolytes

  Both sodium and potassium values should be monitored with a goal to maintain the electrolytes in normal range.

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Appendix A

Indications for hands on care of the ≤31 6/7 week infant

*Accompanied by facilitated tucking for infant throughout:

Admission:

- Airway established and effective ventilation
- Weight (if not done in delivery room)
- Place on blue burn sheet
- Attach bedside SpO2 monitor to probe attached to infant in delivery room
- Skin temperature probe attached to infant on right/left lower back inside the diaper (probe works best with infant lying on it. May need 2 probes attached; one on each side and use probe from appropriate side of infant to monitor temp)
- Axilla temperature
- Place chest leads on and attach to monitor
- BP per one upper limb (left)
- Obtain POCT glucose if central lines not inserted by 30 minutes of age
- One admission exam by physician/NP coordinated with bedside RN

Ongoing care:

- limit 10-15 minutes of handling accompanied by facilitated tucking throughout
- Obtain as much information as possible from observation
- "Top down" and 90% humidity once central lines inserted
- Aquaphor sparingly and avoid areas where temperature skin probe and ECG leads applied
- Monitor dryness of blue burn sheeting with each handling of infant and change prn
- Change diaper and monitor output q4-6h
- Reposition infant supine or side-lying q4-6H (as a 2-person task)
- Assess central line placement q1h through observation; leave diaper open for 12-24 hours to assess for bleeding from umbilical cord
- Assess BP continuously through UAC or obtain peripheral BP as needed.
- Assess axilla temperature q1-3h as per policy. Continuously monitor isolette air temperature and how well skin probe attached and reading.
- POCT glucose as per unit policy
- Assess PIPP score with each handling
- Respiratory assessments as needed in conjunction with physician/NP/RRT
- Assess fontanels, activity, tone, heart sounds, air entry, apex, perfusion, peripheral pulses, abdomen, skin as needed while maintaining a 10-15 minute handling maximum and use of a second caregiver for facilitated tucking of infant

  *Care should be infant cue based.

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