

EPIQ III – Severe Neurological Injury Bundle		
Domain	Interventions	Level of Evidence
Avoid hypocapnia or hypercapnia	Avoid PCO ₂ below 35 or above 55, pH above 7.40 in the first week of life by: <ul style="list-style-type: none"> • monitoring blood gas closely when initiating ventilation (utilize non-invasive tcPCO₂ if available) • using aggressive approach to wean the ventilation • avoiding hand bagging, particularly prolonged hand bagging 	1C: Strong recommendation, low quality evidence There is literature suggesting a link between <ul style="list-style-type: none"> • low PCO₂ (high pH) and PVL • high PCO₂ and IVH
Avoid the use of Bicarbonates	Avoid the use of bicarbonate <ul style="list-style-type: none"> • tolerate pH down to 7.20 • avoid reacting to a single blood gas, particularly if it is the first one after birth and/or a capillary blood gas • optimize ventilation if it is a mixed acidosis (with respiratory component) 	1C: Strong recommendation, low quality evidence Bolus of bicarbonate has been linked with IVH
Minimal handling & Gentle Care	Develop a team strategy in the NICU for Minimal Handling & Gentle Care of the extremely premature infant <ul style="list-style-type: none"> • Implementation of an intervention bundle • Focus on the first days of life where the risk of IVH is high and the events that increase the risk of PVL may occur. The first hours of life are crucial. 	1C: Strong recommendation, low quality evidence Even though it is difficult to demonstrate, we believe that this is the most important intervention that may explain the differences among the CNN sites
	<ul style="list-style-type: none"> • Avoid significant rotation of the head especially for GA < 26 weeks for the first 72 hours. Consider raising the head by 30 degrees for the first 72 hours. 	2B. Weak recommendation, low quality evidence
Saline bolus	Avoid boluses of normal saline	2B. Weak recommendation, low quality evidence
Antenatal Steroids	2 doses of steroids started 48h before delivery	High prevalence of treatment among the sites. Little room for improvement 1A: Strong recommendation, high quality evidence
Delayed Cord Clamping	<ul style="list-style-type: none"> • DCC for < 32 weeks GA DCC for 45 seconds to 1 minute 	Decrease hypotension requiring treatment 2A: Weak recommendation, moderate quality evidence (for its neurological impact)

Special Consideration Interventions

Domain	Interventions	Level of Evidence
Use antenatal MgSO ₄	Administer MgSO ₄ to mother at risk of premature delivery	Three meta-analyses concluded that MgSO ₄ for fetal neuroprotection decreases the risk of childhood CP 1B: Strong recommendation, moderate quality evidence
Prophylactic Indomethacin	Administer indomethacin 0.1 mg/kg/day for 72 hours starting within 6 h of age in baby < 1kg	The TIPP trial showed a significant decrease in IVH grade 3 and 4, but no benefit at 18 month and significant short term side effects 2A: weak recommendation, high quality evidence