

The Golden Hour: Providing Very Premature Infants a Favorable Beginning

Abstract

The first hour of life in a very premature neonate is a critical period of transition requiring extra-uterine adaptation of multiple organ systems for which the vulnerable neonate is ill prepared. Medical interventions provided to the neonate during this golden first hour of life can have significant implications on immediate survival and long term morbidities. Delayed cord clamping, delivery room temperature stabilization, strategies to establish functional residual capacity and gentle ventilation, early administration of dextrose and amino acid infusions, antibiotics when indicated and timely successful placement of peripheral or umbilical venous catheters are areas of focus during golden hour care. Premature infants born and resuscitated at tertiary and quaternary care centers have improved survival chances and outcomes when compared to similar "out-born" infants which highlight the role of experienced and skilled resuscitation teams in the golden hour. Strategies to standardize the various elements used in the resuscitation and stabilization of the very premature neonate that utilize quality improvement measures such as a golden hour protocol may help improve timeliness and efficacy of care provided in the first hour of life.

Keywords: Very premature; Golden hour; Hypothermia; Hypoglycemia; Sepsis; Surfactant; Delayed cord clamping; Parenteral nutrition

Mini Review

Volume 5 Issue 3 - 2016

Aparna Patra, Prasad Bhandary and Peter Giannone*

Department of Pediatrics, Division of Neonatology, University of Kentucky College of Medicine, USA

***Corresponding author:** Peter J Giannone, Professor of Pediatrics, Kentucky Children's Hospital, University of Kentucky College of Medicine, 138 Leader Ave, Lexington, KY 40508, USA, Office: 859-323-1496; Fax: 859-257-6066; Email: petergiannone@uky.edu

Received: May 01, 2015 | **Published:** September 21, 2016

Abbreviations: IVH: Intraventricular Hemorrhage; BPD: Bronchopulmonary Dysplasia; ELBW: Extremely Low Birth Weight; VLBW: Very Low Birth Weight; CPAP: Continuous Positive Airway Pressure; SI: Sustained Inflation; FRC: Functional Residual Capacity; TPN: Total Parenteral Nutrition

Introduction

Preterm birth is the greatest contributor of infant death and is also a leading cause of long term disabilities in children throughout the world. Infants born very preterm (<32 weeks) are at high risk of prematurity related mortality and morbidity [1,2]. The first hour of life is a critical period of transition requiring multiple adaptations to extra uterine life, for which the fragile preterm neonate is not prepared. Therefore, the vulnerable premature infant faces profound challenges in this transitional process that may adversely affect numerous short and long term outcomes and contribute to an increased risk of mortality and morbidities such as intraventricular hemorrhage (IVH), developmental delays, cerebral palsy and bronchopulmonary dysplasia (BPD) [3]. The concept of care during the first hour of life in a premature infant parallels the concept of golden hour in trauma and emergency medicine where the first 60 minutes of definitive and critical care has a direct impact on patient outcome [3,4]. The golden hour strategy in neonatal medicine is an approach that reinforces effective communication and collaboration between multiple care providers using evidence based protocols and measures with a goal to deliver initial resuscitation and stabilization of a very premature infant in relatively short period of time.

There are numerous factors related to prematurity and the resultant underdeveloped organ systems that increase the

complexity of stabilization following the birth of a very premature infant. The immature lung with underdeveloped alveoli, surfactant deficiency, immature nervous system with poor respiratory drive and weak compliant chest muscles which predisposes to alveolar collapse contribute to poor lung expansion and difficulty with gas exchange in these infants. Their extremely immature skin and lack of epidermal barrier promotes evaporative heat loss and higher body surface area-to-weight ratio and ineffective thermogenesis makes heat preservation in this population challenging, especially in the first precious hour of life. The detrimental effects of hypothermia may result in increased oxygen and metabolic demands, acid-base derangements, respiratory and circulatory compromise, hypoglycemia and even death [1,5,6]. Additionally, they have poor energy stores and are prone to develop metabolic derangements such as hypoglycemia due to failure in glycogen accretion. The preterm infants lack the cerebral defenses against hypoglycemia seen in term infants making them more prone to brain injury from these derangements [7]. On the flip side, early protein administration in this population helps prevent catabolism and buffer against hyperglycemia by initiating endogenous insulin production [8]. These neonates are also at an increased risk of serious blood stream infections due to their underdeveloped immune function. In addition, the presence of fragile germinal matrix blood vessels in the immature brain predisposes these infants to intracranial hemorrhage, the risk of which increases if there are lapses in the initial resuscitation and stabilization period. Many recent studies have reported improved outcomes for very preterm and very low birth weight (VLBW) babies born in tertiary neonatal intensive care units versus infants first born elsewhere and subsequently transferred to the tertiary NICU [9-11]. This suggests that presence of experienced neonatal

resuscitation team and enhanced multidisciplinary approach during initial stabilization may significantly impact survival and outcomes in this population. The golden hour approach in neonatology thus relies not only on evidence based treatment and resuscitation protocols but also in team structure, communication and proficient work flow for prompt and skilled stabilization of this very vulnerable population within a critical time frame.

Discussion

The key areas of focus that require timely completion during the first golden hour of life of a very premature baby incorporates the following:

Delayed cord clamping

Delayed cord clamping in premature neonates is a simple procedure that the current evidence in medical literature seems to support for improving neonatal morbidity [12]. Systematic review of trials conclude that in uncomplicated premature deliveries delaying cord clamping for 30 secs to 3 minutes following delivery improves blood pressure, decreases IVH, lowers risk of necrotizing enterocolitis and need for blood transfusions or vasopressors [13]. However, long term benefits of this intervention and its impact on death or neuro-development are so far inconclusive. Also there is limited data on optimal timing of delayed cord clamping and potential benefits in non-vigorous or extremely premature periviable neonates. Cord milking has been suggested as an alternate and quick method of placental transfusion in deliveries which warrant immediate resuscitation in non-vigorous neonate [14]. Animal studies in preterm lambs demonstrate that onset of ventilation prior to umbilical cord clamping improves cardiac function by increasing pulmonary blood flow and also enhances cerebral and systemic oxygenation leading to a smoother extra-uterine cardiovascular adaptation [15,16]. Replicating such a setup to provide effective resuscitation and ventilation while still being attached to the placenta may be of immense benefit to a compromised premature neonate and is an area of further research.

Prevention of hypothermia

Heat loss usually exceeds heat production after birth. This is especially true in very premature neonates with minimal thermogenesis, a poorly developed skin barrier, exposure to multiple routes of heat loss (evaporative, conductive and convective) in the delivery room and increases in oxygen consumption putting them at increased risk of developing hypothermia if heat loss prevention measures are not initiated immediately after birth. For low birth weight infants, every 1 °C below 36 °C on admission temperature is associated with 28% increase in mortality risk [17]. Maintaining ambient temperature of the delivery room at 25-26 °C was shown to decrease cold stress in premature infants born at less than 32 weeks gestation [18]. Currently the standard practice during delivery and resuscitation of very premature neonates is not to dry the infant, but rather to place them in polyethylene bags or wraps and perform resuscitative measure within the plastic bag or occlusive skin wrapping. Additional heat loss is prevented by covering the head of the infant not covered by a plastic barrier with a hat. This minimizes evaporative heat loss and allows warming of

infant from the radiant warmer [19-21]. The use of transwarmer or exothermic mattress have been studied in combination with plastic bags and hats and has successfully led to a reduction in incidence of hypothermia in premature infants less than 35 weeks gestational age [22]. There has been concern for inducing hyperthermia with such approach in some smaller studies and these infants need to be monitored closely [23,24].

Respiratory stabilization

Very preterm neonates often have decreased alveolar compliance, a highly compliant chest walls, surfactant deficiencies, floppy airways and weak respiratory muscles. Hence, they are at increased risk for respiratory distress syndrome, pneumothorax and pulmonary interstitial emphysema in the short term and chronic lung disease and increased incidence of reactive airway disease in the long term. The goal of respiratory management is to provide adequate minute ventilation by improving lung compliance, avoiding apnea and decreasing work of breathing. During the initial resuscitation and first several minutes of life, oxygen supplementation is provided as required to keep oxygen saturations in the target range for age (1 min -60-65%, 2 mins - 65-70%, 3 mins - 70-75%, 4 mins - 80-85%, 5 mins -80-85% and 10 mins- 85-95%) [25]. Neonatal resuscitation program suggests starting FiO₂ to be 21-30% and recommends against using high oxygen (FiO₂ 65% or greater) as it is a preference to avoid exposing preterm neonates to additional oxygen without data demonstrating a proven benefit for important outcomes [25]. The choice of an ideal initial respiratory modality in the delivery room remains elusive. Earlier studies focused on prophylactic administration of surfactant for very preterm neonates showed a decreased risk of air leak and neonatal mortality. However, in the era of greater utilization of maternal steroids and routine post-delivery stabilization on continuous positive airway pressure (CPAP) this view has been challenged [26,27].

Appropriate application of post-delivery CPAP increases functional residual capacity, prevents alveolar collapse, improves compliance, increases airway diameter and splints the airway and diaphragm. The choice of CPAP vs prophylactic surfactant should be based on institutional experience, local practices and comfort with delivery room CPAP. While many techniques have been utilized to provide appropriate respiratory support to promote gentle ventilation and avoid iatrogenic injury due to volutrauma. Again, ventilation strategies selected should be based on institutional experience, local practices and comfort levels with certain modes of ventilation,

Sustained inflation (SI)

Adequate lung inflation is important for successful transition at birth. Most preterm neonates require assistance to aerate the lungs and establish functional residual capacity (FRC). CPAP and intermittent positive pressure ventilation are used as standard methods. In animal models, prolonged sustained inflations for 10-20s have been used alternatively to achieve FRC and lung aeration [28]. Clinical trials using SI at birth in neonates at birth showed decreased requirement for mechanical ventilation however decrease in BPD is not consistent [29]. Further studies to optimize the SI technique and address concerns of risk with pneumothorax are needed before this technique can be used routinely in practice.

CPAP

Immediate application of CPAP after preterm birth reduces the need for intubation, exogenous surfactant administration, and ventilator days, but does not change rates of BPD and/or death in this population. Appropriate application of post-delivery CPAP increases functional residual capacity, prevents alveolar collapse, improves compliance, increases airway diameter and splints the airway and diaphragm. Higher levels of CPAP (CPAP of 8 compared to CPAP of 5) resulted in increased risk of pneumothorax, so pressure needs to be delivered judiciously [30,31]. One may consider intubation and surfactant therapy (see below) to attenuate this risk. Both flow inflating bags and T-piece resuscitators can deliver CPAP in the delivery room, however self-inflating bags cannot deliver CPAP.

Intubation

Preterm neonates have highly compliant chest walls, surfactant deficiencies, floppy airways and weak respiratory muscles. Although many preterm neonates require positive pressure ventilation for stabilization, with appropriate post-delivery application of CPAP about half of the extremely low birth weight (ELBW) infants who are born can be managed without intubation or mechanical ventilation [30]. The subset of infants still showing signs of significant distress despite administration of non-invasive positive pressure may benefit from intubation and subsequent positive pressure ventilation. When requiring intubation, very preterm neonates may likely benefit for early administration of surfactant since severe distress is often tied to surfactant deficiency. At our institution, we deliver early surfactant in two aliquots, gently turning the infant on one side for one minute for the first aliquot then on their other side for minute for the subsequent aliquot. This is done while the infant remains in his/her plastic covering to allow for appropriate thermoregulation.

Early Initiation of Total Parenteral Nutrition (TPN)

Early administration of parenteral nutrition immediately after birth aims at minimizing postnatal deprivation of amino acids, glucose and nutrients as the prematurely born neonate is adapting to extrauterine life. The early initiation of parenteral amino acids is vital for prevention of protein catabolism and metabolic shock in the very low birth weight infants where the decline in essential amino acids in blood after disconnection from placenta triggers a starvation response leading to endogenous irrepressible glucose production and glucose intolerance. Early initiation of parenteral amino acids is also known to stimulate insulin secretion in the premature neonate in the absence of which insulin dependent pathways of transporter mediated glucose transfer may be affected leading to disruption of Na⁺ K⁺ ATP-ase activity and resultant intracellular energy failure and hyperkalemia [32]. Hence providing parenteral nutrition in the first hour of life is an important goal of aggressive nutrition in prematurity and may promote better growth at 36 weeks postmenstrual age in extremely low birth weight infant population [33,34]. Successful early placement of peripheral vascular access or umbilical venous catheter and the delay in its radiologic placement confirmation may be barriers towards achieving early administration of parenteral nutrition. Many quality improvement studies have reported successful delivery of parenteral nutrition in first hour of life, prompt placement of umbilical venous and arterial catheters,

timely completion of placement radiograph and faster acquisition of stock standard parenteral nutrition solution from pharmacy after implementation of a golden hour protocol [6,35,36].

In our institution we administer 5% amino acid stock solution with 3 gram/kg/d protein infusion rate for all very an extremely premature infants in the first hour of life to deliver protein accretion similar to that of a reference fetus. The use of such standardized stock TPN with predetermined amounts of glucose and amino acid has increasingly become prevalent in neonatal care due to ease of availability, storage and focus on early initiation of TPN in this population [37]. Parenteral amino acid intake of 3-3.5 gram/kg/d in the first day of life has been shown to be both safe and effective in improving protein accretion in the very premature neonate [38,39] without any adverse clinical sequelae such as metabolic acidosis or hyperammonemia [40]. Recently, there have been some concerns about electrolyte derangements such as hypokalemia, hypophosphatemia and hypercalcemia in growth restricted extremely low birth weight premature infants who were exposed to such standardized high amino acid parenteral nutrition in first days of life [41,42]. Whether an individualized parenteral nutrition approach is more appropriate in such population starting on the first day of life needs further examination.

Prevention of hypoglycemia

Early transient hypoglycemia is a frequent occurrence in premature neonates shortly after birth. VLBW infants are at higher risk of neonatal hypoglycemia secondary to restricted reserve of glycogen and fat which are typically accreted in the third trimester of pregnancy [43]. Although there is no consensus on what level and duration of hypoglycemia is detrimental, recurrent periods of hypoglycemia have been shown to result in lower head circumferences and neuro developmental deficits in small-for age- premature infants [44]. Early initiation of dextrose infusion is critical during the first hour of life to prevent hypoglycemia induced cerebral energy failure and prevent possible damage as well as ensure a smooth extrauterine adaptation for very premature infants. In a study of VLBW infants, initiation of glucose intravenous infusion within thirty minutes of birth was recommended as best practice [36]. In our institution, we initiate parenteral nutrition in very premature neonates with 10% dextrose in combination with 5% amino acid stock solution in the first hour of life aiming for glucose delivery of 5-6 mg/kg/min.

Early initiation of antibiotics

Serious blood stream infections and early onset sepsis are important causes of morbidity and mortality in premature infants. Several studies on early onset sepsis in neonates have emphasized initiation of antibiotics in the first hour of life when sepsis is clinically suspected to prevent serious sequelae [45-47]. Challenges in establishing intravenous access or central venous catheter in a very premature neonate may impact adversely the time to initiation of antibiotics. Application of golden hour quality improvement initiatives, having dedicated personnel for placement of vascular access and better communication and collaboration with pharmacy can lead to improvement in antibiotic initiation time in the first sixty minutes of life [48].

The success of any golden hour protocol for premature neonate begins with a highly skilled and effective team in the delivery room and includes a standard road map guiding workflow during the resuscitation and the stabilization process that starts in the delivery room and continues in the NICU. The road map and workflow should focus on the key areas of safe and timely interventions aimed at improving outcomes and subsequent completion of the admission process to the neonatal intensive care unit in the first sixty minutes of life. In Table 1, we briefly outline five quality improvement projects that were

reported and presented at national meetings in recent years to improve the timeliness and quality of interventions on premature infant during the golden hour of life and the outcomes that were achieved.

These projects demonstrate that adoption of a standardized interdisciplinary team approach in the delivery room and NICU to care for the very premature infant in the first golden hour of life can be advantageous in delivering more efficient and timely care to the vulnerable neonate.

Table 1: Quality improvement projects centered on improving golden hour care in premature neonates.

Study and Year	Study Design	Study Population	Significant Outcomes
Ashmeade et al. [35]	Quality Improvement: Golden hour Pathway (GHP)	ELBW (N=295, 173 infants pre GHP and 173 in Post GHP Cohort)	<ol style="list-style-type: none"> 1. Improved Birth to Surfactant Administration Time 2. Improved Admission Body Temperature 3. Sooner Administration of TPN
Lambeth et al. [48]	Quality Improvement: Golden Hour	(N=205, 50 Infants Pre-Protocol and 105 Infants Post-Protocol) VLBW	<ol style="list-style-type: none"> 1. Sooner Administration of TPN 2. Sooner Administration of Antibiotics
Bhandary et al. [49]	Quality Improvement: Golden Hour	ELBW	<ol style="list-style-type: none"> 1. Sooner Successful Placement and Verification of Umbilical Catheter 2. Decrease in Severe Grade IVH
Reuter et al. [50]	Quality Improvement: Golden Hour	ELBW	<ol style="list-style-type: none"> 1. Faster Placement of Umbilical Catheter 2. Decrease in IVH (All Grades)
Castrodale et al. [6]	Quality Improvement: Golden Hour	Extremely Premature Infants Born ≤ 28 Weeks Gestation (N=225, 106 Infants in Pre-Protocol and 119 Infants in Post Protocol Group)	<ol style="list-style-type: none"> 1. Higher admission body temperature and avoidance of hypothermia 2. Higher admission blood glucose level in euglycemic range 3. Faster initiation of TPN via peripheral intravenous catheter or umbilical catheter

Abbreviations: ELBW: Extremely Low Birth Weight; VLBWL: Very Low Birth Weight; GHP: Golden Hour Pathway; IVH: Intraventricular Hemorrhage; TPN: Total Parenteral Nutrition

Conclusion

An increasing body of evidence substantiates that medical interventions done during resuscitation and stabilization of a very premature infant may have a direct impact on immediate survival and long term morbidities. A multitude of complex decisions and tasks need to be completed in a brief time period following birth of a very premature infant to provide the best chances for a smooth transition to postnatal life and ensure positive outcomes. A standardized evidence based approach of team development, effective communication and enhanced performance by utilization of a ‘golden hour for neonate’ protocol by interdisciplinary teams caring for high risk newborns may improve timeliness of interventions and advance outcomes.

Acknowledgements

We gratefully acknowledge the enthusiastic participation and dedication of all members of our tiny baby work group in our institution who has been instrumental in providing timely and effective medical care in the golden hour of very premature babies. Our members are fellow physicians - Enrique Gomez Pomar, MD, Lochan Subedi, M.D; participating physicians - Elie G.

Abu Jawdeh, M.D, Mina Hanna, M.D; advanced practice providers - Gina Barber, NNP, Genine Jordan, NNP; Neonatal clinical nurses - Alice Carpenter, BSN; Leanne Kreutz, BSN, Jennifer L Donselman, BSN, Suzy D Ringstaff, BSN, Heather N Green, BSN, Veronica L Stewart, BSN, Amy N Gadd, BSN, Katherine E Caddle, BSN, Lauren R Sargent, BSN; clinical nurse manager - Shannon Haynes, MSN; clinical nurse specialist - Lisa McGee, MSN; Respiratory therapist - Timothy H Roark, RRT-NPS, MHA; Pharmacist - Karen L Garlitz.

References

1. Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, et al. (2015) Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993-2012. *JAMA* 314(10): 1039-1051.
2. Horbar JD, Badger GJ, Carpenter JH, Fanaroff AA, Kilpatrick S, et al. (2002) Trends in mortality and morbidity for very low birth weight infants, 1991-1999. *Pediatrics* 110(1 Pt 1): 143-151.
3. Annibale DJ, Bissinger RL (2010) The golden hour. *Adv Neonatal Care* 10(5): 221-223.
4. Doyle KJ, Bradshaw WT (2012) Sixty golden minutes. *Neonatal Netw* 31(5): 289-294.

5. Besch NJ, Perlstein PH, Edwards NK, Keenan WJ, Sutherland JM (1971) The transparent baby bag. A shield against heat loss. *N Engl J Med* 284(3): 121-124.
6. Castrodale V, Rinehart S (2014) The golden hour: improving the stabilization of the very low birth-weight infant. *Adv Neonatal Care* 14(1): 9-14.
7. Rozance PJ, Hay WW (2010) Describing hypoglycemia--definition or operational threshold? *Early Hum Dev* 86(5): 275-280.
8. Adamkin DH (2006) Nutrition Management of the Very Low-birth weight Infant. II. Optimizing Enteral Nutrition and Postdischarge Nutrition. *Neoreview* 7(12): e608-e614.
9. Bartels DB, Wypij D, Wenzlaff P, Dammann O, Poets CF (2006) Hospital volume and neonatal mortality among very low birth weight infants. *Pediatrics* 117(6): 2206-2214.
10. Binder S, Hill K, Meinen-Derr J, Greenberg JM, Narendran V (2011) Increasing VLBW deliveries at subspecialty perinatal centers via perinatal outreach. *Pediatrics* 127(3): 487-493.
11. Phibbs CS, Baker LC, Caughey AB, Danielsen B, Schmitt SK, et al. (2007) Level and volume of neonatal intensive care and mortality in very-low-birth-weight infants. *N Engl J Med* 356(21): 2165-2175.
12. Rabe H, Diaz-Rossello JL, Duley L, Dowswell T (2012) Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database Syst Rev* 8: Cd003248.
13. Raju TN (2013) Timing of umbilical cord clamping after birth for optimizing placental transfusion. *Curr Opin Pediatr* 25(2): 180-187.
14. Rabe H, Jewison A, Alvarez RF, Crook D, Stilton D, et al. (2011) Milking compared with delayed cord clamping to increase placental transfusion in preterm neonates: a randomized controlled trial. *Obstet Gynecol* 117(2 Pt 1): 205-211.
15. Bhatt S, Alison BJ, Wallace EM, Crossley KJ, Gill AW, et al. (2013) Delaying cord clamping until ventilation onset improves cardiovascular function at birth in preterm lambs. *J Physiol* 591(8): 2113-2126.
16. Polglase GR, Dawson JA, Kluckow M, Gill AW, Davis PG, et al. (2015) Ventilation onset prior to umbilical cord clamping (physiological-based cord clamping) improves systemic and cerebral oxygenation in preterm lambs. *PLoS One* 10(2): e0117504.
17. Lupton AR, Salhab W, Bhaskar B (2007) Admission temperature of low birth weight infants: predictors and associated morbidities. *Pediatrics* 119(3): e643-e649.
18. Jia YS, Lin ZL, Lv H, Li YM, Green R, et al. (2013) Effect of delivery room temperature on the admission temperature of premature infants: a randomized controlled trial. *J Prenatal* 33(4): 264-267.
19. Vohra S, Roberts RS, Zhang B, Janes M, Schmidt B (2004) Heat Loss Prevention (HeLP) in the delivery room: A randomized controlled trial of polyethylene occlusive skin wrapping in very preterm infants. *J Pediatr* 145(6): 750-753.
20. Leadford AE, Warren JB, Manasyan A, Chomba E, Salas AA, et al. (2013) Plastic bags for prevention of hypothermia in preterm and low birth weight infants. *Pediatrics* 132(1): e128-e134.
21. McCall EM, Alderdice F, Halliday HL, Jenkins JG, Vohra S (2008) Interventions to prevent hypothermia at birth in preterm and/or low birthweight infants. *Cochrane Database Syst Rev* 3: CD004210.
22. Russo A, McCready M, Torres L, Theuriere C, Venturini S, et al. (2014) Reducing hypothermia in preterm infants following delivery. *Pediatrics* 133(4): e1055-e1062.
23. McCarthy LK, O'Donnell CP (2011) Warming preterm infants in the delivery room: polyethylene bags, exothermic mattresses or both? *Acta Paediatr* 100(12): 1534-1537.
24. Singh A, Duckett J, Newton T, Watkinson M (2010) Improving neonatal unit admission temperatures in preterm babies: exothermic mattresses, polythene bags or a traditional approach? *J Perinatol* 30(1): 45-49.
25. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, et al. (2015) Part 13: Neonatal Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 132(18 Suppl 2): S543-S560.
26. Engle WA (2008) Surfactant-replacement therapy for respiratory distress in the preterm and term neonate. *Pediatrics* 121(2): 419-432.
27. Rojas-Reyes MX, Morley CJ, Soll R (2012) Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. *Cochrane Database Syst Rev* 3: Cd000510.
28. Sobotka KS, Hooper SB, Allison BJ, Te Pas AB, Davis PG, et al. (2011) An Initial Sustained Inflation Improves the Respiratory and Cardiovascular Transition at Birth in Preterm Lambs. *Pediatr Res* 70(1): 56-60.
29. Schmölzer GM, Kumar M, Aziz K, Pichler G, O'Reilly M, et al. (2015) Sustained inflation versus positive pressure ventilation at birth: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 100(4): F361-F368.
30. Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, et al. (2008) Nasal CPAP or Intubation at Birth for Very Preterm Infants. *N Engl J Med* 358(7): 700-708.
31. Finer NN, Carlo WA, Walsh MC, Rich W, Gantz MG, et al. (2010) Early CPAP versus Surfactant in Extremely Preterm Infants. *N Engl J Med* 362(21): 1970-1979.
32. Adamkin DH (2006) Nutrition Management of the Very Low-birthweight Infant. *Clin Perinatol* 7(12): e602-e607.
33. Ziegler EE, Thureen PJ, Carlson SJ (2002) Aggressive nutrition of the very low birthweight infant. *Clin Perinatol* 29(2): 225-244.
34. Poindexter BB1, Langer JC, Dusick AM, Ehrenkranz RA (2006) Early provision of parenteral amino acids in extremely low birth weight infants: relation to growth and neurodevelopmental outcome. *J Pediatr* 148(3): 300-305.
35. Ashmeade TL, Haubner L, Collins S, Miladinovic B, Fugate K (2016) Outcomes of a Neonatal Golden Hour Implementation Project. *Am J Med Qual* 31(1): 73-80.
36. Taylor SN, Kiger J, Finch C, Bizal D (2010) Fluid, electrolytes, and nutrition: minutes matter. *Adv Neonatal Care* 10(5): 248-255.
37. Adamkin DH, Radmacher PG (2014) Current trends and future challenges in neonatal parenteral nutrition. *J Neonatal Perinatal Med* 7(3): 157-164.
38. Thureen PJ (2003) Effect of low versus high intravenous amino acid intake on very low birth weight infants in the early neonatal period. *Pediatr Res* 53(1): 24-32.
39. Ibrahim HM, Jeroudi MA, Baier RJ, Dhanireddy R, Krouskop RW Aggressive early total parental nutrition in low-birth-weight infants. *J Perinatol* 24(8): 482-486.
40. Clark RH, Chace DH, Spitzer AR (2007) Effects of two different doses of amino acid supplementation on growth and blood amino acid levels in premature neonates admitted to the neonatal intensive care unit: a randomized, controlled trial. *Pediatrics* 120(6): 1286-1296.

41. Ichikawa G, Watabe Y, Suzumura H, Sairenchi T, Muto T, et al. (2012) Hypophosphatemia in small for gestational age extremely low birth weight infants receiving parenteral nutrition in the first week after birth. *J Pediatr Endocrinol Metab* 25(3-4): 317-321.
42. Boubred F, Herlenius E, Bartocci M, Jonsson B, Vanpée M (2015) Extremely preterm infants who are small for gestational age have a high risk of early hypophosphatemia and hypokalemia. *Acta Paediatr* 104(11): 1077-1083.
43. Cornblath M, Schwartz R (1993) Hypoglycemia in the neonate. *J Pediatr Endocrinol* 6(2): 113-129.
44. Duvanel CB, Fawer CL, Cotting J, Hohlfeld P, Matthieu JM (199) Long-term effects of neonatal hypoglycemia on brain growth and psychomotor development in small-for-gestational-age preterm infants. *J Pediatr* 134(4): 492-498.
45. Kissoon N, Orr RA, Carcillo JA (2010) Updated American College of Critical Care Medicine--pediatric advanced life support guidelines for management of pediatric and neonatal septic shock: relevance to the emergency care clinician. *Pediatr Emerg Care* 26(11): 867-869.
46. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, et al. (2013) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 39(2): 165-228.
47. El-Wiher N, Cornell TT, Kissoon N, Shanley TP (2011) Management and Treatment Guidelines for Sepsis in Pediatric Patients. *Open Inflamm J* 4(Suppl 1-M11): 101-109.
48. Lambeth TM, Rojas MA, Holmes AP, Dail RB (2016) First Golden Hour of Life: A Quality Improvement Initiative. *Adv Neonatal Care* 16(4): 264-72.
49. Bhandary P, Hanna M, Subedi L, Gomez Pomar E, Barber G, et al. (2015) Development of a Golden Hour Protocol for ELBW Infants to Improve Outcomes, in Presented at the Vermont Oxford Network Annual Quality Congress, Vermont Oxford Network: Chicago, USA.
50. Reuter S, Messier S, Steven D (2014) The neonatal Golden Hour-intervention to improve quality of care of the extremely low birth weight infant. *S D Med* 67(10): 397-403.