Special Article

Thai Healthy Newborns Have a Higher Risk

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Kernicterus is a preventable but devastating neurologic disorder with life long complications. It is caused by severe and inadequately treated hyperbilirubinemia during the newborn period. In the present paper potential causes and risk factors for the occurrence of kernicterus related to the Thai health system that are responsible for the care of newborn infants before and after discharge are discussed. Potential risk reduction strategies for the Thai health system are purposed. Some efforts to improve the quality of Thai newborn care particularly newborns with jaundice that have been made are mentioned. An adherence to the American Academy of Pediatrics clinical guideline for management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation for those strategies that are feasible to follow will help reduce the prevalence of severe hyperbilirubinemia and bilirubin encephalopathy.

Keywords: *Hyperbilirubinemia, Newborn, Kernicterus, Bilirubin encephalopathy, Neonatal jaundice, Thailand*

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Kernicterus (German *kern*, kernel, nucleus, + *ikteros*, jaundice) a condition associated with high levels of bilirubin in the blood. It is characterized by deep yellow staining of the basal nuclei, globus pallidus, putamen, caudate nucleus, cerebellar nuclei, bulbar nuclei, and gray substance of the cereburm, accompanied by widespread destructive changes[1].

Bilirubin encephalopathy describes the clinical central nervous system findings caused by bilrubin toxicity to the basal ganglia and various brainstem nuclei. To avoid confusion and encourage greater consistency in the literature, the Subcommitte on Hyperbilirubinemia of the American Academy of Pediatrics recommends that the term "acute bilirubin encephalopathy" be used to described the acute manifestations of bilirubin toxicity seen in the first weeks after birth and that the term "kernicterus" be reserved for the chronic and permanent clinical sequelae of bilirubin toxicity.[2]

Clinical manifestations

Acute bilirubin encephalopathy

In the early phase of acute bilirubin encephalopathy, severely jaundiced infants become lethargic and hypotonic and suck poorly. The intermediate phase is characterized by moderate stupor, irritability, and hypertonia. The infant may develop a fever and high-pitched cry, which may alternate with drowsiness and hypotonia. The hypertonia is manifested by backward arching of the neck (retrocollis) and trunk (opisthotonos). There is anecdotal evidence that an emergent exchange transfusion at this stage, in some cases, might reverse the central nervous system changes. The advanced phase, in which central nervous system damage is probably irreversible, is characterized by pronounced retrocollis-opisthotonos, shrill cry, no feeding, apnea, fever, deep stupor to coma, sometimes seizure, and death[2].

Kernicterus

In the chronic form of bilirubin encephalopathy, surviving infants may develop a severe form of athetoid cerebral palsy, auditory dysfunction, dental-enamel dysplasia, paralysis of upward gaze, and, less often, intellectual and other handicaps. Most infants who develop kernicterus have manifested some or all of the signs listed above in the acute phase of bilirubin encepalopathy. However, occasionally there are infants who have developed very high bilirubin levels and, subsequently, the signs of kernicterus but have exhibited few, if any, antecedent clinical signs of acute

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bilirubin encephalopathy[2].

Higher risk for kernicterus in Thai healthy newborns

The prevalence of kernicterus among Thai healthy term infants is unknown since it is not a reportable condition in Thailand. However, it has been brought to attention because there are several cases of kernicterus whose parents filed petitions to the pediatricians taking care of the victims.

The Thai health care practice patterns have risked Thai healthy newborns for kernicterus by several contributing factors. Should the prevalence of kernicterus be reduced, these contributing factors have to be ameliorated. Regional perinatal health care systems, developed in the US since 1976, emphasizes professional expertise, consultation, communication, and education for the effective use of resources based on local and individual needs. It was concluded in 1993 that regionalization is the best option for reducing perinatal morbidity[3]. Unfortunately, there is no regionalization for perinatal health care in the Thai health system. Only 35 neonatologists are currently practicing in the government hospitals throughout the kingdom of which 29 are working at university hospitals and 21 in the nation's capital. For a total birth of 600,194 in 2004, 2.82% were delivered at a university setting, 40.67% at provincial general hospitals and 47.56% at district hospitals[4]. Of the 719 district hospitals, obstetricians are available in less than 0.5% while there are less than 5% for pediatricians.

Most health care providers taking care of healthy newborns have limited experience in assessing clinical jaundice visually, assessing its severity, and are unaware of proper plasma bilirubin screening and monitoring. Healthy newborns at most university hospitals are taken care of by pediatric residents and a few by obstetricians or obstetric residents due to overwhelming sick newborns and academic work that neonatologists are responsible for. Healthy newborns at all general hospitals are taken care of by pediatricians who also have limited skill in assessing and managing jaundice. During a three-year course of the residency training program, there is an average of three to six months for a pediatric resident to rotate to neonatology section that is not enough for obtaining adequate experience in basic newborn care, assessing jaundice visually, being cognizant of the variables influencing the efficacy of phototherapy and using the device appropriately. The significant role of an obstetrician in preventing kernicterus is not realized and emphasized. Obstetric-gynecological residents rotate to neonatology section for two to four weeks and, most of the time, are involved in neonatal resuscitation in the delivery room. They do not concern themselves about improving the skill in detecting clinical jaundice and learning appropriate plasma bilirubin screening and monitoring as well as the AAP Practice Guideline for Management of Hyperbilirubinemia in the Healthy Term Newborn.

At district hospitals newborns are taken care of by nurses and newly graduate physicians who are responsible for patients of all age groups and have limited experience in newborn care. During studying in the medical school, the length of practicing newborn care for medical students is about two weeks. There is no training course in assessing visible jaundice and its management for nurses and physicians before and after job placement. Furthermore, the significance of a nurse's role in preventing kernicterus is not recognized.

In the university setting, plasma bilirubin assessments have to be ordered by physicians and by nurses at general hospitals and district hospitals. The bilirubin testing devices are available at less than 10% of district hospitals due to their high cost (150,000 baht) which result in an inability to measure plasma bilirubin level and provide phototherapy. When jaundice is detected, either sending a blood specimen for bilirubin measurement or referring a newborn to the general hospital is routinely done.

As a result of the antecedent, most newborns are discharged home while severity of jaundice or plasma bilirubin levels are not known. Moreover, healthy newborns of an uncomplicated vaginal birth are usually observed at the hospitals for 36 to 48 hours while bilirubin levels have not peak. If there is a miss in detecting jaundice, a healthy newborn is discharged home without medical follow-up nor home visit by a nurse.

The high price of an imported conventional phototherapy device (200,000 baht) is another risk factor for kernicterus. Almost all hospitals have produced their own conventional phototherapy lamps or purchased locally made devices (25,000 baht) without quality control. Daylight lamps are usually used because of the costly imported special blue fluorescent lamp (40 vs.1,500 baht per tube). The proper maintenance system for phototherapy device nor the measures enhancing the efficacy of phototherapy has not been fully adopted at most hospitals. When there is no existing national practice guideline on the management of hyperbilirubinemia in the healthy term newborn appropriate for the Thai health system but

adherence to the AAP Practice Guideline for Management of Hyperbilirubinemia in the Healthy Term Newborn by some pediatricians while using phototherapy devices not capable of working effectively, phototherapy failure is high. Should a blood exchange transfusion be indicated, a major blood bank system is not available at all provincial hospitals, especially when group O, Rh-negative blood is needed. A delay in performing blood exchange transfusion is the result. Some newborns with severe jaundice were referred to university hospitals after kernicterus had developed.

Risk reduction strategies to prevent kernicterus in Thai newborns

Kernicterus is almost always preventable through bilirubin screening and the early and aggressive use of effective phototherapy. Should a reduction in the risk of kernicterus in Thai newborns be expected, resources necessarily used in the care of newborns with jaundice have to be developed, i.e. human and medical devices. All authorities (the Ministry of Public Health, the Thai Royal College of Obstetricians and Gynecologists, the Thai Royal College of Pediatricians, and the Thai Nursing Council) responsible for the resources used in newborn care must be aware of this devastating neurologic disorder with life long complications and its threat to Thai newborns. They must cooperate in training students, residents and related health care providers with the skill in detecting jaundice visually and appropriate plasma bilirubin screening and monitoring. For those taking care of newborns, they must increase awareness and identify strategies and practice to enhance the processes of diagnosis and management of hyperbilirubinemia. At hospitals where there is a lack of devices for bilirubin testing, physicians and nurses should be trained to assess infants and determine the need for serum bilirubin testing on the basis visual inspection of skin color. Visual inspection is the most commonly used means of screening newborns for jaundice. Digital pressure that blanches the skin diminishes local cutaneous perfusion and allows for the detection of jaundice. Although visual estimation of bilirubin levels from the degree of jaundice can lead to error[5-7], in the Thai health system it is still considered helpful for experienced health personnel to use as a means to screen for hyperbilirubinemia because Thai newborns' skins are not darkly pigmented and there is limitation to precise measurement of bilirubin levels. Moreover, newborns should be discharged 48 hours after birth with careful scrutiny for risk of hyperbilirubinemia.

Pediatricians should be informed that adherence to AAP Guideline is legitimate only if the phototherapy devices is capable of producing high irradiance in the 430- to 490-nm band and at 30 microW/cm^2/nm or higher[2]. Some harmful advice and beliefs have to be changed. All health personnel should not advise parents to supplement water or dextrose water to newborns or expose newborns to sunlight[2]. The lack of hemolysis in jaundiced breast-fed newborns has led some to believe that when severe hyperbilirubinemia occurs in these infants, it cannot result in kernicterus. This belief is erroneous and dangerous. Kernicterus can develop in otherwise healthy full-term breast-fed newborns or breast-fed infants with sepsis and, if the hyperbilirubinemia is sufficiently severe, or phototherapy does not promptly lower the bilirubin level, exchange transfusion is indicated[8,9].

Parents should be educated and provided with adequate educational materials at discharge regarding jaundice, feeding adequacy and symptoms to watch for, the risks of untreated hyperbilirubinemia, and the need for close follow-up of their infants after discharge[2].

All phototherapy devices should be checked and approved for uses. Measures to maximize the effectiveness of phototherapy should be emphasized and strictly followed. Regarding the expensive related and essential devices, should the risk for kernicterus be reduced, Thailand has to be able to depend on her own low-cost but high effecacy equipment. Under the effort of the author, measures to increase the irradiance (energy output) that influences the efficacy of phototherapy have been studied and a low cost (15,500 baht) conventional phototherapy lamp that emits an irradiance of more than 30 microW/cm^2/nm has been produced and distributed throughout the nation since 1997[10]. The device has reduced the rate of exchange transfusion from 15.4% to 4.3%[11]. The measures proved to enhance the irradiance are positioning phototherapy lamps less than 30 cm above the infant with a newborn below the center of the phototherapy unit, increasing surface area of the neonate exposed to light, using special blue light lamps (higher irradiance with more special blue light lamps), replacing new lamps 2000 hours after use, keeping the plastic beneath the lamps clear and without scratching or cracks, and lining with white cloth around the housing of lamps to reflect light on the infant's skin[10]. A low-cost (2,500 baht) bilirubin color scale for visual assessment of plasma bilirubin level has also been invented to compensate for the standard bilirubin tester. The accuracy

of readings when compared to the standard device is ≤1.0 mg/dL in 59.94%, ≤1.5 mg/dL in 81.37% and ≤ 2.0 in 94.26% of comparisons[12]. The Thai Toshiba Electric Company has manufactured special-blue-light fluorescent lamps (Deep Blue) that costs 260 baht per tube upon the author's request.

Besides necessary resources used in taking care of the newborn, a national guideline for preventing kernicterus appropriate for Thai health system needs to be developed. The strategies intended to prevent kernicterus in healthy newborn recommended by the American Academy of Pediatrics (AAP) should be thoroughly considered for cost-effectiveness and implemented if feasible.

AAP Practice Guidelines for Management of Hyperbilirubinemia

A revised American Academy of Pediatrics Clinical Practice Guideline (2004), Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation, emphasizes the importance of universal in-hospital screening for the risk of severe hyperbilirubinemia, medical follow-up within the first few days of hospital discharge, and prompt treatment with intensive phototherapy (at least 30 microW/cm^2/nm) when indicated. The new guidelines recommend the establishment of nursery protocol for the evaluation of hyperbilirubinemia which include circumstances in which nursing staff can obtain a bilirubin level without a doctor's order. Prior to discharge, every newborn should be asessed for the risk of developing severe hyperbilirubinemia. This should include assessing clinical risk factors and/or measuring the total serum bilirubin or transcutaneous bilirubin level. The guidelines also recommend that all bilirubin levels be interpreted according to the infant's age in hours by plotting the predischarge serum bilirubin values on a percentile-based nomogram to identify and follow up infants who are identified to be at risk for severe hyperbilirubinemia. All parents should be provided with written and oral information on newborn jaundice, the need to monitor infants for jaundice, and advice on how monitoring should be done. The guideline also urges pediatricians and hospital medical staff to promote and support breastfeeding efforts, as low caloric intake and dehydration associated with poor breastfeeding can contribute to severe jaundice[2].

Conclusion

In Thailand, healthy newborns have a higher risk for kernicterus due to the health care pattern. Should it be prevented? Both governmental and health care system interventions will be required to resolve the problem. Authorities responsible for all resources necessary to the care of newborns have to cooperate and make every attempt to reduce risk factors for kernicterus. A national practice guideline on prevention of kernicterus and management of hyperbilirubinema appropriate for the Thai health system should be developed and implemented. Awareness of kernicterus, its contributing factors, and strategies to prevent it should be disseminated to all health care personnel responsible for newborns. Obstetricians and nurses must be proactive in the assessment and management of hyperbilirubinemia in the newborn. Furthermore, a reporting system should be set up for public health surveillance and institution of appropriate interventions to prevent or limit occurrence.

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ภาวะเสี่ยงสูงในเด็กไทยแรกเกิดที่มีสุขภาพดี

เกรียงศักดิ์ จีระแพทย์

Kernicterus เป็นพยาธิสภาพของสมองที่เกิดจากการทำลายของบิลิรูบินจากภาวะบิลิรูบินในเลือดสูง และไม่ได้รับการรักษาที่เหมาะสมในวัยทารกแรกเกิด มีผลให้เกิดความพิการทางสมอง ภาวะนี้สามารถป้องกันได้ หากมีการเฝ้าติดตามระดับบิลิรูบินในเลือด ระหว่างที่ทารกอยู่ในโรงพยาบาลและภายหลังออกจากโรงพยาบาล และได้รับการรักษาที่เหมาะสมและทันเวลา ด้วยการส่องไฟ และการถ่ายเปลี่ยนเลือดหากการส่องไฟไม่ได้ผล อุบัติการณ์ของภาวะนี้ในประเทศไทยยังไม่ทราบ เพราะเป็นโรคที่ไม่ต้องรายงาน แต่ได้รับความสนใจ เนื่องจากมีการฟ้องร้องแพทย์ที่ให้การรักษาทารกที่เป็นภาวะนี้ จากการประเมินมาตรฐานการดูแลทารกแรกเกิดของประเทศในโครงการ "ลูกเกิดรอด แม่ปลอดภัย" ของกระทรวงสาธารณสุข พบว่า ทารกไทยแรกเกิดมีความเสี่ยงสูงต่อการเกิดภาวะนี้ เพราะร้อยละ 47 ของการคลอดในปี พ.ศ. 2547 คลอดในโรงพยาบาลชุมชน ที่มีกุมารแพทย์ประจำเพียงร้อยละ 5 และมีเครื่องมือวัดบิลิรูบินในเลือดประมาณร้อยละ 10 ของโรงพยาบาล อีกทั้งได้รับการดูแลโดยแพทย์ใช้ทุนที่ขาดประสบการณ์ในการประเมินตัวเหลือง และความรู้เกี่ยวกับการป้องกันภาวะนี้ การลดความเสี่ยงของการเกิดภาวะนี้ ต้องอาศัยความร่วมมือของกระทรวงสาธารณสุขและสถาบันที่เกี่ยวข้องกับการผลิตบุคลากรทางสุขภาพที่ต้องดูแลทารกแรกเกิด ได้แก่ แพทย์ใช้ทุน พยาบาล กุมารแพทย์และสูติแพทย์ จัดอบรมบุคลากรให้มีความสามารถในการประเมินภาวะเหลืองโดยการตรวจร่างกาย ทราบวิธีและความถี่ของการติดตามระดับบิลิรูบินในเลือด และวิธีรักษาด้วยการส่องไฟที่ให้ประสิทธิภาพสูงสุด ปัจจัยเสี่ยงที่เกิดจากการขาดแคลนอุปกรณ์ที่วัดระดับบิลิรูบินในเลือด เครื่องส่องไฟและหลอดไฟที่ให้แสงสีฟ้าพิเศษที่นำเข้าจากต่างประเทศมีราคาแพง ได้รับการแก้ไขแล้ว แต่ยังขาด practice guideline ที่เหมาะสมกับสภาพทางสาธารณสุขของประเทศสำหรับ ป้องกันภาวะนี้ และการให้บุคลากรทางสุขภาพที่เกี่ยวข้องตระหนักถึงความสำคัญและทราบวิธีป้องกันภาวะนี้ร่วมกัน