Hyperbilirubinaemia in the newborn

Preventing kernicterus: a wake-up call

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Perspective on the paper by Manning *et al* (***see page 342***)

Despite advances in neonatal care there has been a recent resurgence of bilirubin encephalopathy and clinical kernicterus in several parts of the world. In this issue Manning and colleagues provide worrying evidence to suggest that the UK and Republic of Ireland may be participants in this trend.[1] While the aim of their study was to determine the incidence of severe hyperbilirubinaemia, and to identify clinical and demographic variables and short-term outcomes, the authors have extended discussion to some important risk management lessons. The results of this important surveillance study should be made known to all paediatricians and related health professionals responsible for the newborn.

The British Paediatric Surveillance Unit (BPSU) reporting system has been used for this prospective survey. The BPSU has a good reputation of providing a high response rate. The investigators sought to capture all cases of ''severe'' neonatal hyperbilirubinaemia, defined by them as an unconjugated serum bilirubin of ⩾510 μmol/l in the first month of life, between May 2003 and May 2005. It could be argued that the level chosen was more than ''severe''. The nomenclature of different degrees and forms of jaundice has been critiqued recently by Maisels.[2] He suggests the term ''extreme hyperbilirubinaemia'' should be used to categorise this level of jaundice. As with the label ''extreme sport'' this signifies an element of risk, but it does not go as far as the proposal of Bhutani *et al*[3] that levels >510 μmol/l should be referred to as ''hazardous''. Whatever we choose to call it the incidence of this level of jaundice was quantified through this BPSU survey as 7.1/100 000 live births.

Of the 108 patients with an unconjugated serum bilirubin of ⩾510 μmol/l, 14 (13%) had features consistent with acute bilirubin encephalopathy. Of this group three appear to have long-term morbidity with cerebral palsy consistent with kernicterus, one has hearing loss, three died (two underwent postmortem examination that revealed kernicteric staining of the brain) and two were lost to follow-up. The clinical features of bilirubin encephalopathy were opisthotonus, seizures or both in 11/14 cases. In three cases the outcome at 12 months was documented as normal, and in the remaining two there were unrelated pathologies.

The understandable medicolegal sensitivity of a diagnosis of kernicterus may have inhibited some reporting, and the six cases that were excluded following initial reporting because ''no information was obtained'' remain an enigma. Similarly, the high figure of 38 reporting errors may reflect confusion about whether unconjugated or total serum bilirubin was being considered. Presumably there were a number of cases in which the total minus the conjugated was <510 μmol/l. This is an important group to consider as it is no longer considered acceptable practice to subtract the conjugated element when managing hyperbilirubinaemia. The authors cite the paper by Bertini *et al*,[4] which highlights the risk of kernicterus in these circumstances. They also make reference to the 2004 American Academy of Pediatrics (AAP) clinical practice guideline[5] which recommends that total bilirubin levels are used for treatment thresholds with no substitution of the conjugated element.

As this is a novel survey we cannot say whether there has truly been a resurgence of kernicterus in this population. The move to a ''kinder, gentler approach'' to jaundice in the healthy term infant[6] has coincided with an era when most newborns are at home by 24–48 h of age. The safety margin for treatment has been reduced and there may be a delay in the diagnosis of more sinister causes of jaundice. There is evidence that the 1994 AAP practice parameter on treatment of hyperbilirubinaemia[7] was being ''stretched'' to apply to treatment in near-term infants with gestational ages of 35 weeks and above[8] and that among term infants the recommended phototherapy thresholds were not being adhered to.[9] Cases of kernicterus were occurring as a result of failure to heed the practice parameter exclusion criteria, such as clinical jaundice within 24 h of life, prematurity, evidence of haemolysis or a sick infant.

Despite publication in 2004 of the more rigorous AAP clinical practice guideline on the management of hyperbilirubinaemia in the newborn infant 35 or more weeks of gestation,[5] the more lenient approach of the preceding decade would appear to persist among those responsible for the care of a number of babies in this survey. The failure to give exchange transfusion to 60/108 (55%) babies with levels of unconjugated bilirubin ⩾510 μmol/l bears this out. Similarly, haemolysis and infection do not seem to have influenced treatment decisions, and even more surprisingly acute symptoms of bilirubin encephalopathy did not necessarily trigger an exchange transfusion.

This interesting cohort of babies prompts many questions beyond the planned scope of the survey. For instance, was information available on the duration of severe hyperbilirubinaemia as well as the peak value? The duration of exposure may be more relevant than the absolute peak value in terms of risk of bilirubin encephalopathy.[10] What was the mode of delivery of phototherapy in this group? Babies with this severity of jaundice merit multiple phototherapy delivered by the most efficient equipment. What percentage of the babies had a formal hearing assessment?

The study does, however, confirm that dehydration, and what some authors refer to as ''lack of breast milk jaundice'', are risk factors for kernicterus, along with being born near term. There were three 36 weeks' gestation and three 37 weeks' gestation infants in the group with signs of bilirubin encephalopathy. The heightened risks of shortened gestation[11] and the failure to establish adequate breast feeding[12] have been shown before. There are also similarities of the affected patient profile in this survey to that of the US-based Kernicterus Registry[13] in terms of breast feeding, male predominance, racial pigmentation that may mask jaundice, and glucose 6-phosphate dehydrogenase deficiency.

Kernicterus is a preventable condition and this study highlights the failure of clinical observation and awareness to identify severe jaundice in a timely manner to prevent injury. Equally worrying is the apparent failure to adequately treat severe jaundice once identified. The occurrence of kernicterus in the hospital or community setting should prompt critical incident reporting, and is likely to be subjected to medicolegal scrutiny. Heightened awareness of aspects of the clinical history and examination that suggest the likelihood of severe jaundice need to be emphasised to health professionals. Parents should be made aware of the importance of severe jaundice, particularly in the context of failure to establish adequate breast feeding.

In the UK and Republic of Ireland the responsibility for detecting significant postdischarge jaundice rests with the primary healthcare team of midwives, health visitors, general practitioners and informed parents. This survey throws up concerns that this early warning system is insufficiently robust. It may be necessary to consider the type of predictive testing being adopted in the USA. Bhutani *et al*[3] recommend a universal predischarge total serum bilirubin measurement plotted on an hour-specific bilirubin nomogram to help customise the appropriate timing of follow-up appointments. It would be interesting to know how many of the 108 babies in this cohort would have been in the high risk >95th percentile zone on the nomogram, had such testing been done.

It is a woeful situation in the UK that there are no nationally agreed guidelines for the assessment and management of hyperbilirubinaemia in the newborn. A recent survey of more than 160 respondent UK neonatal units revealed a ''massive variation in the choice of the threshold levels at which treatment was recommended'' (J M Rennie personal communication, 2006). Equally, there is no agreement about whether treatment thresholds should take into account sickness (however defined), prematurity or the conjugated fraction of bilirubin. Because bilirubin encephalopathy is comparatively rare, a degree of complacency towards treatment has evolved. Manning and colleagues have woken us up to a likely resurgence of kernicterus in our present day practice, and it is to be hoped that lessons will be learned from this important study. One lesson should be to call for a consensus agreement on UK treatment guidelines and to monitor the incidence of kernicterus through surveys such as this and a national registry of cases. Definitive randomised trials of jaundice management are unlikely to be conducted, and future refinement of treatment guidelines may evolve more readily from a well-observed experience base.

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Competing interests: NKI receives medicolegal instructions in cases of litigation related to kernicterus.

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Sleeping positions of preterm infants

Placing preterm infants for sleep: first prone, then supine

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Perspective on the paper by Kassim *et al* (***see page 347***)

Supine sleeping is recommended to prevent the sudden infant death syndrome (SIDS). In preterm and/or low birthweight infants in particular, prone or side sleeping is associated with an increased risk of SIDS with an odds ratio of between 37 (side position) and 140 (prone position) compared with term infants sleeping on their back. This risk is multiplicative to the individual risks associated with either prematurity or the prone/side position.[1 2]

These epidemiological data contrast with the fact that infants who are born prematurely exhibit less apnoea and intermittent hypoxia, have better thoracoabdominal synchrony, higher lung volumes and better oxygenation when nursed in the prone position, which is particularly true for those with chronic lung disease.[3–11] Once the infants are nearing discharge, however, these physiological advantages of the prone position become less clear.[12] Nonetheless, these advantages, plus an unsubstantiated fear of a higher risk of aspiration in the supine position, may be responsible for many maternity hospitals in both the USA and Europe continuing to advocate a non-supine sleeping position for infants at the time of discharge.[13 14]

The study by Kassim *et al* in this issue of the *Archives* adds to the wealth of pathophysiological studies on this issue. They measured lung volume and pulse oximeter saturation repeatedly until discharge in a group of infants born at 24–31 weeks' gestation and found higher functional residual capacity (FRC) as well as significantly higher baseline oxygenation in those still requiring additional inspired oxygen, while placed prone.[15]

What conclusions can be drawn from these data? Using sophisticated equipment for pulmonary function testing and a pulse oximeter, Kassim *et al*[15] confirm previous work suggesting that the prone position is associated with a higher lung volume and a better ventilation/perfusion matching.[3 5] This is why these infants are nursed predominantly in the prone position in neonatal intensive care units (NICUs) throughout the world, and there is no reason to change this practice, particularly as SIDS is not an issue in these infants during their first few weeks of life in the NICU. However, soon after discharge SIDS becomes the leading cause of death, and then the benefits associated with a 1% increase in baseline oxygenation or a 10–15% increase in FRC have to be weighed against the dramatically increased risk of dying suddenly and unexpectedly. Because of this situation, and because the seeing-is-believing paradigm is also valid for parental behaviour