Should we rethink administering anaesthesia to young children?

The fact that anaesthetic agents may affect the development of young children has received increased media attention in the last 5 years. Suspicion was raised when animal studies showed that giving various cocktails of anaesthetic agents to baby animals caused apoptosis in some brain areas during certain vulnerable ages (Jevtovic-Todorovic et al, 2003). This apoptosis was then linked to behavioural and learning abnormalities in animal models.

Subsequently, a number of retrospective human studies concluded that children who were exposed to anaesthesia before the age of 4 years were more likely to develop learning or behavioural disorders (Kalkman, 2009; Wilder et al, 2009; DiMaggio et al, 2011).

Dilemmas that anaesthetists face include the ethics of administering anaesthesia to a young child for an elective procedure, what to tell parents who question the need for their child to be exposed to anaesthesia, and whether anaesthetic practice should be modified based on current scientific knowledge.

We should rethink use of anaesthetic in young children

Anaesthetic agents cause excessive apoptosis in baby animal models during periods of neuronal development (synaptogenesis) (Jevtovic-Todorovic et al, 2003). Triggers include most anaesthetic agents in common use (Loepke et al, 2008). Thus far in humans, only retrospective studies have been used to postulate the effects. DiMaggio et al (2011) looked at data from 1999–2005 and reported that children exposed to anaesthesia before the age of 3 years were 60% more likely to be diagnosed with developmental or behavioural disorders than those unexposed.

In 2009 Wilder et al concluded that one exposure to general anaesthesia before the age of 4 years did not increase the risk of learning disabilities while more than one exposure increased the risk significantly.

In 2009 Kalkman concluded that children who received anaesthesia at <24 months of age had equal or greater incidence of behavioural disturbances than >24 months, but this was not statistically significant.

We should not change our use of anaesthetic in young children

The animal studies have been criticized for their methodological flaws and because of the difficulty in extrapolating animal findings to a paediatric surgical population.

The human studies have been criticized as it is not yet known if learning disability is a relevant outcome measure for any potential neurotoxic effects of anaesthesia in humans, given that learning disability may be linked to genetic, family and socioeconomic factors as well (Kalkman, 2009).

Other criticisms included a lack of documentation of anaesthetic technique, complications and comorbidity (DiMaggio et al, 2011), problems related to cohort composition, issues related to intraoperative patient monitoring (Wilder et al, 2009), and issues related to quantifying learning disability (Kalkman, 2009).

A Dutch twin study evaluated 1143 monozygotic twin pairs and found equivalent levels of learning-related outcome in monozygotic twins discordant for having received anaesthesia (Bartels et al, 2009). This showed that the risk of anaesthesia 'causing' later learning disabilities is not related to the toxic effects of the anaesthesia but to the underlying genetic vulnerability of the individual to learning disability.

Current advice

While awaiting definitive answers from the many studies currently underway, two worldwide trials to be aware of are the Pediatric Anesthesia NeuroDevelopment Assessment (PANDA) study (a multicentre study that will study neurodevelopmental outcome in 500 sibling pairs, between their 6th and 12th birthdays, who are discordant for exposure to anaesthesia for inguinal hernia surgery before 36 months of age) and the GAS study (an international multisite randomized control trial that will determine if neurodevelopmental outcome is equivalent between children who have general or regional anaesthesia for hernia repairs) (Sun et al, 2008).

Owing to the lack of human evidence, one cannot provide specific recommendations at present.

Timing of surgery may be important as synaptogenesis is thought to occur from the third trimester to the age of 3 years in humans, so less urgent surgery could be postponed until after this time.

Keep anaesthetics simple, safe and rational: using the least amount of drug and duration required while minimizing multiple exposures. As most anaesthetic agents have been implicated, changing agents may not offer any benefit.

Always consider the risk/benefit ratio. A child who does not receive anaesthesia for a procedure he/she needs is always worse off. BJHM

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