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Editorial

EDITORIAL

Continuous cerebral blood flow monitoring: What should we do with these extra numbers?

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Summary

NeoDoppler is a noninvasive monitoring device that can be attached to a patient's head to provide real-time continuous cerebral Doppler evaluation. A feasibility study shows that it can be used in operating theatres during anaesthesia to potentially guide haemodynamic management. We discuss the impact of this new device and which further research would be necessary to find its role in clinical practice.

Keywords: anaesthesia; cerebral blood flow; doppler; haemodynamic management; monitoring; neonates

In the June 2023 issue of *BJA Open*, Vik and colleagues[1] report the first clinical use in operating theatres of the NeoDoppler (Cimon Medial AS, Trondheim, Norway). The NeoDoppler is a noninvasive ultrasound device, initially used in neonatal critical care.[2] It provides continuous monitoring of cerebral blood flow, traditionally obtained by indirect measures such as continuous near infrared spectroscopy (NIRS) monitoring or direct snapshots of cerebral perfusion using ultrasound Doppler by a trained and skilled operator at the bedside.

In this feasibility study, 30 infants referred for noncardiac procedures under general anaesthesia were recruited. They weighed 930–9530 g and were aged 0.10–140 days (gestational age: 24.6–41.4 weeks) on the day of surgery. The authors report a decrease in cerebral blood flow velocities, with the decrease in end-diastolic value particularly marked (59% compared with baseline) during induction and maintenance of anaesthesia. Peak systolic and time-averaged velocities were reduced by 26% and 45%, respectively. All these values returned rapidly to their baseline by the end of the recovery period. Contrary to previous studies, the cerebral blood flow was monitored continuously. NIRS remained stable at the baseline value throughout anaesthesia and the mean arterial pressure did not drop significantly.

This study is of particular interest because it brings to our attention an additional monitoring device to optimise the anaesthetic management of some of our most vulnerable patients. It also promotes discussion on whether, when, and how to treat these patients if a decrease in cerebral flow velocity is observed.

Effects of anaesthesia on the developing brain

'What are the effects of anaesthesia on the developing brain?' is one of the 10 priority questions in anaesthesia and perioperative care listed by the James Lind Alliance and the National Institute for Academic Anaesthesia. A large part of current research in this area focuses on the direct toxicity of anaesthetic drugs on the immature neurological system, especially the induced widespread neuro-apoptosis and alterations in dendritic arborisation. Tremendous efforts have been made to link the clinical observation of neurocognitive deleterious effects in children with previous exposure to general

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anaesthesia.[3] Recent results from the GAS trial show that a single and short exposure (less than an hour) to sevoflurane is not associated with these complications 2 and 5 yr after anaesthesia.[4,5]

However, deleterious cognitive effects can arise through multiple ways. An underlying condition such as sepsis or inflammation induced by the surgery itself can trigger neurobiochemical mediators that can cross the blood brain barrier and affect central nervous system cells. Perioperative anaesthetic management can also be responsible for cerebral injury; intraoperative complications such as hypoxia, hypotension, or cardiac arrest during anaesthesia require prompt responses to avoid brain injury or limit its extent.[6] Even so, it is important to note that no association has been made between hypotension and adverse neurological outcomes in young children undergoing general anaesthesia.[7]

Neonates, especially of very low birthweights or gestational age, are at higher risk of anaesthesia-induced complications[8] from their global immaturity (cardiovascular, respiratory, neurological), specific anatomy, and size. If these risks are important during the induction and emergence phases of anaesthesia, the complexity of the surgery (positioning, duration, pressure on lungs or large vessels, haemorrhage, etc) is also a source of potential anaesthetic instability during the maintenance phase. Providing adequate monitoring is thus necessary to identify potential anaesthetic or surgical complications as early as possible and correct them. Interestingly, in the study of Vik and colleagues,[1] 80% of the cases, where the NeoDoppler was used, were classified as major surgical procedures, showing that the NeoDoppler can be used during complex procedures.

Haemodynamic monitoring

Maintaining good organ perfusion during anaesthesia is critical, especially for the brain and heart. This is usually achieved in neonates by targeting a mean arterial pressure in mm Hg equivalent to the gestational age in weeks of the patient. However, the normal ranges are not well established. Adequate size and positioning of the blood pressure cuff should be carefully considered. It can also be challenging to obtain a reliable preoperative baseline blood pressure measurement with a child that can be crying or agitated.

There are no clear guidelines for the anaesthetic monitoring required specifically for neonatal surgery apart from minimum standards of monitoring set out by the Association of Anaesthetists of Great Britain and Ireland.[9] Recommendations include the prevention of intraoperative hypothermia, use of a perioperative fluid management strategy, and optimisation of the haemoglobin concentration.[10] Regarding blood pressure monitoring, the choice between invasive or noninvasive monitoring is not straightforward: factors that govern that choice include the anaesthetist and their skills and experience, time pressures of inserting the arterial line, risk of vascular damage, and nature of the surgery. The continuous haemodynamic monitoring and arterial blood sampling providing by the arterial line are real benefits during complex neonatal procedures.

The gold standard for cardiac output monitoring is based on thermodilution, using invasive catheterisation of the pulmonary artery and an arterial line. However, there are patient weight restrictions for using the equipment. The cardiac output can be evaluated less invasively using echocardiography. Transthoracic echocardiography is difficult in the operating theatre because the thorax is not easily accessible. Transoesophageal echocardiography can be done in infants as small as 1.7 kg.[11] Both approaches are user-dependent and require highly trained operators.

Many devices have been developed to overcome these difficulties. Uncalibrated pulse contour systems are one option, but they still require an arterial line.[12,13] Their applications in neonates and infants are limited to children above 3 kg. Oesophageal Doppler has been used in children of >3 kg but the probe needs to be carefully introduced and positioned.[14]

Noninvasive monitoring

In addition to devices that directly measure the pressures in the heart or main vessels, other less invasive and indirect approaches are available. More localised systems try to predict good perfusion in specific vascular territories. NIRS[15] can typically be applied on the forehead or the back near the brain or kidneys, to measure oxygenation in these tissues. The plethysmographic variability index may be of additional value to predict fluid responsiveness in anaesthetised children and neonates.[16,17] Thoracic bioimpedance is another noninvasive approach, but the necessity to access the chest precludes its use in many surgical settings.

Noninvasive cerebral haemodynamic monitoring

The gold standard of noninvasive cerebral haemodynamic monitoring in neonates is the transfontanellar cerebral Doppler.[18,19] The NeoDoppler highlighted by Vik and colleagues[1] builds on this and has many advantages. This small noninvasive device allows continuous measurement of cerebral perfusion in infants with an open fontanelle. A trained user is required to position the probe, attach a specifically designed hat, and troubleshoot repositioning the probe in case of signal quality loss or to maintain the same angle of insonation to ensure reproducibility of the data. It is also of note that the NeoDoppler does not focus on a specific vessel (usually the middle or anterior cerebral artery in standard transfontanellar cerebral Doppler), but covers the vessels hit by the beam through the fontanelle window.

Vik and colleagues[1] do not report any difficulties with the NeoDoppler in neonates with small fontanelles. With more traditional Doppler, it is sometimes difficult to find a good insonation window, because of anatomical constraints, and measure cerebral blood flow in the vessels of interest. The broader approach of the NeoDoppler, not targeting specific cerebral arteries, but taking velocity measurements from vessels at different depths of the brain simultaneously, probably explains this difference. Additionally, there does not seem to be any weight restrictions with patients as small as 930g benefitting from it. This report demonstrates that cerebral Doppler can be utilised for an extended length of time, in extremely young patients in an operating theatre. Interestingly, the authors do not report any issues with the blinded attending anaesthetist during surgery, suggesting that the device does not interfere with regular anaesthetic equipment, monitoring, and positioning.

Cerebral blood flow: physiology, management, and outcomes

With Vik and colleagues' feasibility study demonstrating that continuous cerebral blood flow monitoring is achievable, it is necessary to understand how these new variables can be integrated into a clinical decision-making process. The physiological rationale behind the NeoDoppler device is the direct measurement of cerebral perfusion in the context of anaesthesia-induced hypotension and the loss of cerebral autoregulation during hypotension.

Cerebral blood flow physiology and pathophysiology have been extensively studied in neonatal and paediatric intensive care patients. Cerebral blood flow volume has been shown to develop rapidly over the first 2 weeks of life.[20] Below a threshold, arterial vessels lose their ability to constrict or dilate in response to a change in blood pressure to maintain a steady blood flow. In neonates, the autoregulatory blood pressure threshold is around 28–30 mm Hg. Further reductions in blood pressure can lead to the functional blood pressure threshold (the pressure at which cerebral function is compromised) and the ischaemic blood pressure threshold (the pressure at which structural integrity is compromised) being reached. This latter threshold is usually assumed to be at 50% of the baseline cerebral blood flow.[21] The difficulties thus arise when considering that the association between these thresholds and deleterious neurodevelopmental outcomes is not well known. No clear association could be established between cerebral Doppler variables and brain injury or long-term neurodevelopmental outcome in preterm neonates.[22]

From a physiological standpoint, the treatment of clinical hypotension is appealing in order to make sure that organ perfusion is maintained: NIRS or NeoDoppler could highlight that a certain degree of hypotension is leading to inadequate cerebral perfusion. But is there a need to actively manage a decrease in cerebral blood flow on the NeoDoppler with a normal NIRS or even with a drop of the NIRS as well during anaesthesia? These specific questions will need to be explored in future trials including long term (5 yr) neurocognitive outcomes as study endpoints.

Furthermore, how should such hypotension be treated? This is obviously at the discretion of the attending anaesthetist, who will select treatments based on the clinical state of the patient. The difficulties identifying an optimal dose of ephedrine in small children have been recently reported.[23,24] In these populations, blood pressure corrections should be carefully handled as fluid overload or inotrope-induced hypertension can also have catastrophic consequences such as pulmonary oedema or cerebral haemorrhages.[23,25]

A final issue is the blood pressure target. Is it, as in adults, a decrease to 20% below the baseline value,[23,24] or maybe a combination of multiple elements, including those provided by NIRS or the NeoDoppler?[26] Once again, further research will be necessary to establish goal-directed fluid and inotropic therapy in these young and vulnerable patients undergoing noncardiac procedures.

Conclusion

Vik and colleagues[1] report the implementation of the NeoDoppler, a noninvasive device initially developed for neonatal intensive care, to monitor the cerebral blood flow reliably, efficiently, and continuously throughout general anaesthesia. Their study poses many new questions, regarding the interpretation of cerebral flow data and their integration in goal-directed therapy for haemodynamic management. It is still unclear which variables should trigger an intervention, using which modalities, and towards which targets. Lastly, it is uncertain if such therapies would lead to better neurocognitive outcomes, whilst not exposing patients to the additional risks and burden of fluid and inotrope therapy.

Author's contributions

Editorial conception: **BJB**.
Selection/analysis of included articles: **RT**, **BJB**.
Drafting of paper: **BJB**.
Critical review of paper: **RT**, **BJB**.
Writing of final version of paper: **RT**, **BJB**.
Approval of final version of paper: **RT**, **BJB**.

Declarations of interest

The authors declare that they have no conflicts of interest.

References

1. Vik SD, Torp H, Jarmund AH, et al. Continuous monitoring of cerebral blood flow during general anaesthesia in infants. *BJA Open* 2023; **6**, 100144
2. Vik SD, Torp H, Follestad T, Støen R, Nyrnes SA. NeoDoppler: new ultrasound technology for continuous cerebral circulation monitoring in neonates. *Pediatr Res* 2020; **87**: 95–103
3. Robinson EJ, Lyne TC, Blaise BJ. Safety of general anaesthetics on the developing brain: are we there yet? *BJA Open* 2022; **2**, 100012
4. Davidson AJ, Disma N, de Graaff JC, et al. Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial. *Lancet* 2016; **387**: 239–50
5. McCann ME, de Graaff JC, Dorris L, et al. Neurodevelopmental outcome at 5 years of age after general anaesthesia or awake-regional anaesthesia in infancy (GAS): an international, multicentre, randomised, controlled equivalence trial. *Lancet* 2019; **393**: 664–77
6. Merry AF, Mitchell SJ. Complications of anaesthesia. *Anaesthesia* 2018; **73**: 7–11
7. Gleich SJ, Flick R, Hu D, et al. Neurodevelopment of children exposed to anesthesia: design of the Mayo Anesthesia Safety in Kids (MASK) study. *Contemp Clin Trial.* 2015; **41**: 45–54
8. Tiret L, Nivoche Y, Hatton F, Desmonts JM, Vourc'h G. Complications related to anaesthesia in infants and children. A prospective survey of 40240 anaesthetics. *Br J Anaesth* 1988; **61**: 263–9
9. Klein AA, Meek T, Allcock E, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2021. *Anaesthesia* 2021; **76**: 1212–23
10. Brindle ME, McDiarmid C, Short K, et al. Consensus guidelines for perioperative care in neonatal intestinal surgery: enhanced Recovery After Surgery (ERAS®) society Recommendations. *World J Surg* 2020; **44**: 2482
11. Zyblewski SC, Shirali GS, Forbus GA, et al. Initial experience with a miniaturized multiplane transesophageal

probe in small infants undergoing cardiac operations. *Ann Thorac Surg* 2010; **89**: 1990–4
12. Grensemann J. Cardiac output monitoring by pulse contour analysis, the technical basics of less-invasive techniques. *Front Med (Lausanne)* 2018; **5**: 64
13. Mehta Y, Arora D. Newer methods of cardiac output monitoring. *World J Cardiol* 2014; **6**: 1022–9
14. Raux O, Spencer A, Fesseau R, et al. Intraoperative use of transoesophageal Doppler to predict response to volume expansion in infants and neonates. *Br J Anaesth* 2012; **108**: 100–7
15. Yu Y, Zhang K, Zhang L, Zong H, Meng L, Han R. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults. *Cochrane Database Syst Rev* 2018; **2018**: CD010947
16. Desgranges FP, Evain JN, Pereira de Souza Neto E, Raphael D, Desebbe O, Chassard D. Does the plethysmographic variability index predict fluid responsiveness in mechanically ventilated children? A meta-analysis. *Br J Anaesth* 2016; **117**: 409–10
17. Bagci S, Müller N, Müller A, Heydweiller A, Bartmann P, Franz AR. A pilot study of the pleth variability index as an indicator of volume-responsive hypotension in newborn infants during surgery. *J Anesth* 2013; **27**: 192–8
18. Brackley K, Kilby M, Evans D. Doppler assessment of the fetal and neonatal brain. In: Levene MI, Chervenak FA, Whittle MJ, editors. *Fetal and neonatal neurology and neurosurgery*. £rd edition. London: Churchill Livingstone; 2001. p. 121–9
19. Jarmund AH, Pedersen SA, Torp H, Dudink J, Nyrnes SA. A scoping review of cerebral Doppler arterial waveforms in infants. *Ultrasound Med Biol* 2023; **49**: 919–36
20. Kehrer M, Blumenstock G, Ehehalt S, Goelz R, Poets C, Schoning M. Development of cerebral blood flow volume in preterm neonates during the first two weeks of life. *Pediatr Res* 2005; **58**: 927–30
21. Perlman JM. Cerebral circulation and hypotension in the premature infant. In: Pearlman JM, editor. *Neurology: neonatology questions and controversies*. 2nd edition. Elsevier Saunders; 2012
22. Camfferman FA, de Goederen R, Govaert P, et al. Diagnostic and predictive value of Doppler ultrasound for evaluation of the brain circulation in preterm infants: a systematic review. *Pediatr Res* 2020; **87**: 50–8
23. de Graaff JC, Frykholm P. Ephedrine to treat intraoperative hypotension in infants: what is the target? *Br J Anaesth* 2023; **130**: 510–5
24. Szostek A-S, Saunier C, Elsensohn MH, et al. Effective dose of ephedrine for treatment of hypotension after induction of general anaesthesia in neonates and infants less than 6 months of age: a multicentre randomised, controlled, open label, dose escalation trial. *Br J Anaesth* 2023; **130**: 603–10
25. Arumainathan R, Stendall C, Visram A. Management of fluids in neonatal surgery. *BJA Educ* 2018; **18**: 199–203
26. Holtby H, Skowno JJ, Kor DJ, Flick RP, Uezono S. New technologies in pediatric anesthesia. *Paediatr Anaesth* 2012; **22**: 952–61

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