Monitoring anaesthetic gas concentrations in the exhaust of the cardiopulmonary bypass oxygenator

Editor—Nitzschke and colleagues[1] recently studied sevoflurane plasma concentrations during cardiopulmonary bypass (CPB). The authors found no relationship between sevoflurane plasma concentrations and either sevoflurane concentrations in the exhaust of the oxygenator or bispectral index (BIS) values, prompting them to conclude that 'Measuring the concentration of sevoflurane in the exhaust from the oxygenator is not useful for monitoring sevoflurane administration during bypass'.

However, the authors failed to take into account the consequences of Henry's law: at a constant temperature, the amount of a given gas that dissolves in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid. Blood/gas partition coefficient changes for sevoflurane during CPB were not measured, and may have been considerable given the acute changes in blood temperature and haematocrit that routinely occur.[2] For this reason, the partial pressure in the blood remains unknown. This is the important variable, because, like all gases, inhaled anaesthetics are transported down a partial pressure gradient (not a concentration gradient), and because their clinical effects correlate with the partial pressure. The appropriate technique to use is double headspace equilibration of blood samples, as described by many previous authors, which allows simultaneous measurement of partial pressure and solubility.[3–6]

To summarize, reporting plasma concentrations without blood solubility does not allow meaningful clinical recommendations to be made. By implication, trying to find a relationship between plasma sevoflurane concentration and BIS with these data is futile. Therefore we argue that the conclusions by Nitzschke and colleagues are premature: pending further evidence, it remains reasonable practice to monitor anaesthetic gas concentrations in the exhaust of the oxygenator.

Declaration of interest

None declared.

J. F. A. Hendrickx[1]*
R. Carette[1]
P. Peyton[2]
A. De Wolf[3]
, members of www.navat.org research consortium
[1]*Aalst, Belgium*
[2]*Melbourne, Australia*
[3]*Chicago, USA*
[*]*E-mail: jcnwahendrickx@yahoo.com*

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The safety profile of neuraxial magnesium has not been properly addressed

Editor—We read with interest the recent meta-analysis by Morrison and colleagues,[1] in which the authors reviewed the effect of intrathecal administration of magnesium on the duration of spinal anaesthesia. After a thorough subgroup analysis, the authors concluded that the addition of intrathecal magnesium to lipophilic opioids with or without local anaesthetic is associated with an increased duration of spinal anaesthesia in the non-obstetric population, defined as time to first analgesic request. They also encouraged authors to perform additional randomized controlled trials (RCTs) to better define the role of intrathecal magnesium when administered with local anaesthetics alone, and more specifically, in the obstetric population.

However, we would like to raise an important issue. As stated recently in another meta-analysis investigating the analgesic efficacy of perioperative neuraxial magnesium,[2] the safety profile of this mode of administration has not been properly addressed. This previous review supported the clinical conclusions of Morrison and colleagues, demonstrating that intrathecal magnesium increased the time to first analgesic request by a mean difference of 39.6 min, reduced morphine consumption at 24 h after operation, and reduced early postoperative pain scores. Of concern, however, only four of the 18 included trials, representing a total of only 140 patients, specifically sought evidence of neurological complications. Indeed, the bolus doses used of 50–100 mg may be neurotoxic. Animal studies have demonstrated pain on injection, motor dysfunction, and histological dose-dependent changes in rabbit neurones after intrathecal doses of 0.3, 1, 2, and 3 mg kg^{-1}.[3] These doses closely mirror human doses studied on a per kilogram basis (0.7–1.4 mg kg^{-1}, based on an estimated 70 kg mass). Moreover, two case reports have described patients suffering from disorientation[4] and continuous periumbilical burning pain[5] with continuous infusion of neuraxial magnesium.

In summary, most human trials investigating the efficacy of intrathecal magnesium have failed to monitor for neurological

complications and the potential neurotoxicity of intrathecal magnesium has not been adequately addressed in animals. Morrison and colleagues rightly qualify their review with the caveat that magnesium sulphate is not currently licensed in the UK for intrathecal administration. We urge clinicians to consider these concerns. Rather than proceeding with additional RCTs to answer the questions raised by this meta-analysis, we advocate additional basic science studies to strengthen our understanding of the risk-to-benefit balance from the use of this intrathecal adjunct.

Declaration of interest

None declared.

E. Albrecht[1]*
C. Kern[1]
K. R. Kirkham[2]
[1]*Lausanne, Switzerland*
[2]*Toronto, Canada*
E-mail: eric.albrecht@chuv.ch

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Reply from the authors

Editor—We thank Dr Albrecht and colleagues for their thoughtful comments regarding our recent meta-analysis of the effect of intrathecal magnesium on the duration of spinal anaesthesia.[1] They are justified in raising concerns regarding the safety of using intrathecal magnesium and, in particular, of neurotoxicity. We did mention neurotoxicity within the Discussion section, including the study from Saeki and colleagues[2] which demonstrated the destruction of laminae V–VII at doses of magnesium 1 mg kg^{-1} or more. In contrast, a study from Chanimov and colleagues[3] demonstrated no histological differences in the spinal cord when serial intrathecal injections of up to 12.6% magnesium sulphate, lidocaine, or saline were given to rats.

Other animal studies have also shown conflicting evidence regarding neurotoxicity. In contrast to Saeki and colleagues, Simpson and colleagues[4] demonstrated that administering intrathecal magnesium before thoracic aortic cross-clamping reduced the incidence of paraplegia from spinal cord ischaemia in animals. A recent study has shown, however, that in animals, 15% magnesium sulphate given via the intrathecal route is associated with some degeneration of the mitochondria, and neuronal degenerative changes on repeated injections.[5] The trials included within our meta-analysis either used 50% magnesium[6–9] or 15% magnesium sulphate.[10] There were no reported events suggestive of neurotoxicity within these or any other studies in our meta-analysis, although undoubtedly the length of follow-up may not have been sufficient to uncover all the possible neurological effects. Given the inconsistency regarding the potential neurotoxicity, we would advocate that the safety profile of magnesium sulphate should perhaps be confirmed with further well-designed safe dose finding studies in clinical research.

Dr Albrecht and colleagues also raise the issue of disorientation after epidural administration of magnesium sulphate that was administered as an infusion inadvertently.[11] We did not investigate the effect of continuous epidural magnesium sulphate; hence, we cannot speculate as to whether the symptoms are applicable to the intrathecal route. Furthermore, the authors of the case report attributed the symptoms to a supra-therapeutic serum magnesium concentration having received 9 g in just over 1 h.

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A. P. Morrison[1]
J. M. Hunter[1]
S. H. Halpern[2]
A. Banerjee[1]*
[1]*Liverpool, UK*
[2]*Toronto, Canada*
E-mail: abanerjeeuk@gmail.com

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