Obstetric epidural and chronic adhesive arachnoiditis

Editor—We read with interest the review article on obstetric epidurals and chronic adhesive arachnoiditis by Rice and colleagues. This article addresses most of the issues relevant to anaesthetists and pain specialists. However, we would like to draw attention to the complications associated with long-term use of neuroaxial opioids. The authors state that a review of the literature by a panel of experts in chronic pain relief noted that the intrathecal administration of morphine and fentanyl at clinically effective concentrations appeared to be safe. To our knowledge, there is no evidence for chronic adhesive arachnoiditis after long-term opioid administration from human or animal data. However, catheter-tip inflammatory masses (granulomas) are increasingly reported in humans receiving long-term intrathecal opioid drugs. These are sterile masses consisting of inflammatory cells attached to the catheter tip that may or may not result in spinal cord compression. Pathophysiological causes associated with their formation include:

(i) Anatomical damage to neural tissues predisposing to analgesic toxicity.
(ii) Previous or simultaneous use of other intraspinal devices such as spinal cord stimulators.
(iii) Altered regional cerebrospinal fluid dynamics (sluggish flow in the ventral thoracic region resulting in build up of a high local concentration of the drug).
(iv) Common in younger patients.
(v) Patients receiving higher dosages and high concentrations of morphine.
(vi) Hypersensitivity reaction to the catheter material itself.

There is evidence to suggest that opioids can incite an inflammatory response in the brain or spinal cord tissues. The postulated mechanisms for formation are:

(i) The mitogen-activated protein kinase cascade where morphine can act as a mitogen, thus activating lymphocyte activity.
(ii) Morphine enhancing cytokine formation, leading to an inflammatory cell response.
(iii) Opioids causing endothelial cells, granulocytes and monocytes to release nitric oxide, which in turn leads to monocyte migration in the presence of mesangial cells.

The development of an inflammatory mass should be suspected if a patient presents with progressive loss of analgesic efficacy despite dose escalation, accompanied by a change in character, quality or intensity of the pain, drug withdrawal symptoms, sensory changes (e.g. numbness, tingling, burning), hyperaesthesia, hyperalgesia, sleep disturbances, bowel and/or bladder dysfunction, myelopathy, conus syndrome, gait disturbances/difficulty ambulating, or paraparesis/paralysis.

In asymptomatic or minimally symptomatic catheter tip-associated inflammatory masses, the opioid therapy could be effectively continued by changing to a different opioid drug, substituting the opioid for an infusion of normal saline, or discontinuation of treatment, altogether along with close neurological monitoring. Catheter explantation is not necessary. Regular follow-up and maintaining an index of suspicion will permit early diagnosis and minimally invasive treatment of these masses, preventing neurological damage.

Whenever possible, positioning the catheter in the lumbar thecal sac, keeping the daily dose of opioid as low as possible, and using lower concentrations of preservative-free opioids may reduce the incidence of such inflammatory masses.

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Editor—I read with interest, but concern, the review article by Rice and colleagues. Interest because much of my working week is spent in dealing with chronic backache, and concern because the reassurance this article purports to offer to pregnant women asking about the risks of arachnoiditis after an epidural, I believe is insufficiently grounded in wisdom, or worse still, may be misleading. The thrust of the article describes the intrathecal sequelae of either epidurally or intrathecally placed solutions. Almost nothing was said of the epidural space. The implication is that if intrathecal changes cannot be detected from correct epidural placement of accepted non-toxic solution, in the presence of inconclusive studies on back pain, all must be well; women in labour can be reassured. I disagree. Epidural cannulation and catheterization gives rise to epidural fibrosis and upon this topic we are not in a position to reassure anyone.

After a number of publications reporting that repeated epidural anaesthesia is unreliable, Igarashi and colleagues assessed the cephalad spread of analgesia in 491 patients undergoing epidural anaesthesia at the L2–3 or L3–4 interspace. Patients were classified into one of three groups based on the number of previous lumbar epidural procedures: none (Group 1, n=339), one (Group 2, n=82), and two or more (Group 3, n=70). Cephalad spread of analgesia was significantly greater in Group 1 than in Groups 2 or 3, regardless of the puncture site. Examination of the epidural space took place using a flexible extraduroscope in 32 patients who were excluded from the analysis of spread. Epiduroscopy demonstrated patency in patients with no history of prior lumbar epidural anaesthesia, but in patients who had received epidural anaesthesia one or more times there were clear aseptic inflammatory changes, including proliferation of connective tissue, adhesions between the dura mater and the ligamentum flavum, and granulation tissue within the ligamentum flavum. It was concluded that epidural anaesthesia might cause aseptic inflammatory changes in the extradural space which affects the spread of analgesia.

Kitamura and colleagues divided patients into a control group of 10 who had not previously received epidural analgesia, and 8 who had epidural analgesia for 7–14 days. The epidural space was observed through a 0.75 mm epiduroscope passed through a 17 gauge Tuohy needle. Adverse reactions such as haemorrhage or congestion with engorgement were observed in four patients in the epidural group. Five in the epidural group experienced pain when the epiduroscope was passed. No such findings were found in those with a previously unentered epidural space.

Wulf and Striepling reported post-mortem findings in subjects who had received continuous postoperative analgesia before death. Infiltration of the dura and epidural tissues with lymphocytes and plasma cells was found along with bacterial contamination in 7 out of 10 patients. That these gross pathological changes in the epidural space can occur after epidural catheterization is not in doubt. But apart from probably affecting subsequent epidural efficacy, do they matter?

Crude imaging estimates of the amount of epidural fibrosis vs symptoms of back pain invariably fails, as does the relationship of

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the amount of fibrosis to the extent of direct epidural space trauma, e.g. at operation.\textsuperscript{12, 13} In the failed back surgery syndrome (FBSS), some authors have assigned chronic pain to the presence of scar tissue itself, apportioning 8–14\% of patients with a FBSS to this finding.\textsuperscript{14, 15} Others reject that pain is produced by fibrosis, using as evidence the grossly similar anatomical mass of scar between symptomatic and asymptomatic patients. This argument ignores the potential pathophysiological effects of nerve root tethering and compression.

In examining epidural scar tissue, magnetic resonance imaging is very disappointing, even with gadolinium enhancement; spinal endoscopy is far more sensitive.\textsuperscript{16, 17} Epiduroscopic changes associated with long-term backache frequently reveal the exact same changes described by Igarashi and colleagues after epidural catheterization.\textsuperscript{16, 17} There is a proliferation of connective tissue, adhesions between the dura mater and the ligamentum flavum and epidural granulation tissue. In addition, nerve roots appear either abnormally avascular or else hyperaemic and are often devoid of the normally marked, transmitted pulsation from the dural sac. Nerve roots embedded in scar tissue may be markedly tender to touch and frequently elicit from the patient exact descriptions of typical pain reproduction, the validity of which in relation to chronic pain has been confirmed in a number of clinical settings.\textsuperscript{16, 17} The dura, a heavily (anteriorly) innervated structure,\textsuperscript{18} if tethered by epidural fibrosis, can be a potent source of diffuse back pain, probably partly attributable to impairment of its ability to stretch with back and hip movements.\textsuperscript{19} Interestingly, in patients with chronic back pain after intervertebral disc degeneration with or without surgery, spinal endoscopy, despite revealing a highly abnormal epidural space, if dural puncture is made and the intrathecal space is examined, normal anatomy is nearly always found.

It is a matter of concern to me that these changes within the epidural space, which follow seemingly innocuous epidural catheterization and which are the same or very similar to changes in patients with chronic severe back pain, seem to be overlooked. Although the step of connecting these changes to long-term pain is not proven, it would appear unwise to ignore them.

It is not the purpose of this letter to attempt a review of the demographic evidence for or against chronic back pain after obstetric epidurals. There are worries\textsuperscript{20–22} that statistically and methodologically are very difficult to discount. How do you prove the non-existence of anything?

In my pain clinic, I see patients with back pain, for no identifiable reason, which follows epidural catheterization for various surgical or obstetric indications, and who attribute their problem, anatomically and chronologically, exactly to that event. In the light of the above, I find myself at a loss to either attribute their pain to the epidural or assure them they are mistaken.

The benefits of excellent afferent block in perioperative medicine, especially for unfit patients for major surgery, are central to optimal outcomes,\textsuperscript{23} and I would not wish these worries to detract from that great advance. I do, however, have concerns in using epidural anaesthesia in obstetric practice for young, healthy women with short-lived pain and a non at-risk fetus. There are alternatives to entering the epidural space.\textsuperscript{24}

I suggest that if we want to give honest information we should say something like ‘your epidural may cause scarring in your back, which might affect the quality of subsequent epidurals, but we don’t (yet) know if it could be associated with back pain’.

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Editor—We thank you for the opportunity to reply to the letter of Gulve and colleagues, and that of Richardson. We are pleased that our review article has stimulated debate on the inflammatory consequences of instrumentation of the epidural space. We believe this is an important debate to have.

We do not dispute that long-term epidural catheterization and the long-term use of neuraxial opioids can lead to the formation of inflammatory mediators and fibrosis of the epidural space. We agree with Richardson that the indisputable epiduroscopic evidence that there are inflammatory changes in the epidural space after its cannulation, both long-term\textsuperscript{16, 17} and short-term,\textsuperscript{15} is of concern. We are also aware of studies suggesting that epidural spread of local anaesthetic is unreliable on repeated epidurals.\textsuperscript{7, 25} However, epiduroscopic studies show that fibrous tissue is present in the majority of epidural spaces—many more in number than patients who have had epidural interventions, or experience unreliable epidural block.\textsuperscript{26–29} Spinaloscopy also shows asymptomatic subarachnoid fibrous structures.\textsuperscript{30} It is difficult to determine the association of these adhesions with long-term pain. We are interested that Richardson has not found abnormal intrathecal spaces in those patients found to have a highly abnormal epidural space.

It may well be that epiduroscopy is a more sensitive tool for detecting epidural adhesions in those presenting with the relevant symptomatology, but we can find no reports of the sensitivity of spinaloscopy in detecting chronic adhesive arachnoiditis. We based our definition on MRI evidence because this is a more readily available investigation and has a proven track record for detecting chronic adhesive arachnoiditis.

Our remit on writing the article ‘obstetric epidurals and chronic adhesive arachnoiditis\textsuperscript{1} was very specific—to determine whether the short-term use of epidurals (usually <24 h), as used in modern UK obstetric practice led to inflammatory changes in the subarachnoid space, which cause the syndrome chronic adhesive arachnoiditis, as defined in our article. We were unable to find any convincing evidence that this is the case. After initial concerns that obstetric epidurals may lead to long-term back pain, there are now robust prospective randomized controlled trials to show that this is not the case.\textsuperscript{21, 31}

Women request epidural analgesia during labour because they find this short-term pain unacceptably distressing, often despite using other methods of pain relief. Serious psychological sequelae can occur in women denied effective pain relief in labour.\textsuperscript{32–34} In this day and age, we feel that we have a duty to alleviate such pain with the most effective method available, when we are requested to do so. Although there is some evidence of post-cannulation inflammation and fibrosis in the epidural space, particularly with long-term use of epidurals, we still cannot find any good evidence to support the claim that short-term obstetric epidurals lead to chronic adhesive arachnoiditis.

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