Correspondence

Aprotinin and renal function at cardiac surgery

EDITOR:

Fauli and colleagues [1] are to be congratulated for their investigation into aprotinin use at cardiac surgery and its effects on subclinically detected renal injury and dysfunction as estimated using beta-N-acetyl-beta-D glucosaminidase (NAG)/creatinine and alpha-1-microglobulin (alpha-1-m)/creatinine ratios, respectively. In particular, a study period of up to 40 days postoperatively is helpful.

The authors show no significant effect of aprotinin administration on NAG/creatinine ratios, suggesting that subclinical tubular injury was not increased by this agent. However, they found a dose dependent increase in alpha-1-m/creatinine ratios suggesting aprotinin-mediated tubular dysfunction [1]. This interesting observation led to the conclusion that ‘the use of high-dose aprotinin in older patients or in patients with preoperative renal dysfunction deserves more cautious consideration [1].’

Our group has considerable experience in measurement of NAG/creatinine and alpha-1-m/creatinine ratios at cardiac surgery both with [2] and without [3] cardiopulmonary bypass (CPB). Unlike Fauli’s study, which did not obtain a 48 h urinary sample, we have described, in the CPB patients, a transient second peak in urinary NAG at 48 h [2] which we call the ‘lag in the NAG’. Interestingly, this delayed peak at 48 h is found in patients undergoing their surgery with CPB, but was less pronounced at off pump CAB surgery [3], suggesting that this delayed 48 h peak in NAG is CPB specific. Moreover, in an investigation of the possible renoprotective effects of preoperatively administered methylprednisolone (MP) we found that MP significantly reduced the delayed peak in NAG/creatinine ratios at 48 h but not the early peak [4]. Had we not measured a 48 h sample we would have missed the renoprotective effect of MP, which had earlier been highlighted in the context of infra-renal ischaemia-reperfusion-mediated renal tubular injury [5]. Of particular relevance to Fauli’s study, we found that MP increased urinary alpha-1-m/creatinine ratios (subclinical renal dysfunction) at cardiac surgery in the absence of any increases in urinary NAG (subclinical renal injury). We noted that the reduction in reabsorptive function which accompanies transient tubular dysfunction (as indicated by transiently increased urinary alpha-1-m/creatinine ratios) may be renally protective through diminishing tubular work and thus oxygen demand [4]. This argument similarly applies to Fauli’s report of aprotinin-mediated temporary increases in tubular dysfunction (alpha-1-m) in the absence of increased tubular injury (NAG). Moreover, since alpha-1-m has anti-inflammatory effects [6] increased amounts in the filtrate may even be beneficial.

Clearly more studies are needed to determine if Fauli’s interesting report of transient renal dysfunction induced by aprotinin, translates into a renal protective mechanism through temporarily reducing renal oxygen demand during the perioperative period, when oxygen delivery to the kidney is sometimes compromised.

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References

3. Gormley SM, McBride WT, Armstrong MA et al. Plasma and urinary cytokine homeostasis and renal function during...

Reply

EDITOR:
We appreciate the comments and interest shown by Dr McBride and his collaborators [1] regarding our study concerning kidney-specific proteins and aprotinin at high- and low-dose regimens during coronary artery bypass grafts with cardiopulmonary bypass. We agree with all of those aspects referred to by the authors and we will try to clarify certain aspects of their comments.

The designs of the two studies [1,2] are different, with different recording times. Our results are not therefore directly comparable with those of McBride’s results concerning the renal protection of aprotinin. We measured the variables at those particular times because aprotinin exhibits prolonged adherence of up to 5–6 days to the epithelial cells of the proximal renal tubules [3]. We could not find a second peak in urinary beta-N-acetyl-beta-D glucosaminidase (NAG) at 48 h in the urine, instead, we observed a significant increase of NAG and alpha-1-microglobulin (α-1-m) at 24 h, 72 h and on the 7th day into three groups, and recovery took place between the 7th and 40th days postoperatively. Perhaps there was an increase at 48 h related with our results as well as the 72 h increase of α-1-m in all groups studied (included placebo group).

In our opinion, the increase in NAG (reflecting cellular damage) could appear first and before renal dysfunction (shown by a increased urinary α-1-m) and perhaps in this way our result could be related to those of Dr McBride [1]. This could be a temporary dose-dependant protective mechanism of aprotinin (reduction in reabsorptive function indicated by increased urinary α-1-m).

A. Fauli

References

Brachial plexus injury during anaesthesia in patients receiving cisplatin-based chemotherapy

EDITOR:
Patient positioning during anaesthesia and surgery is occasionally responsible for peripheral nerve trunk or plexus lesions, leading to neurological deficit that may persist for several weeks or months or definitely [1,2]. Most of the time patients are free of any neurological disease but occasionally, the occurrence of a postoperative deficit may allow discovery of a pre-existing neuropathy. Patients suffering from diabetes or renal insufficiency are prone to develop peripheral neuropathy but it is unknown so far if this is a risk factor for the occurrence of postoperative neurological deficit. More and more patients scheduled for surgery for cancer have been treated previously with...
protocols of chemotherapy which may induce nerve lesions, symptomatic or not. These patients could be especially at risk for postoperative neurological complications. We report two cases of transient peripheral neurological deficit following anaesthesia and surgery in patients who underwent neurotoxic chemotherapy before surgery.

Case 1
An 18-yr-old male suffered from a testicular germ cell tumour with retroperitoneal and thoracic para-vertebral node extension. He underwent firstly an orchidectomy followed by three courses of chemotherapy including bleomycin (30 mg per week), etoposide (170 mg per day over 5 days) and cisplatin (36 mg per day over 5 days) with a 21 days rest period between each course. One month after the end of the last course of chemotherapy, the patient was scheduled for laparoscopic para-aortic lymphadenectomy. Anaesthesia was induced with thiopental (300 mg) and sufentanil (20 µg) and maintained with isoflurane (0.5 minimum alveolar concentration), sufentanil and nitrous oxide 50% in oxygen. Muscle relaxation was achieved with vecuronium. The patient was placed in the supine position, the head was in a neutral position and a soft head ring was inserted under the occipital bone. The upper arms were abducted by 80–90° and the forearm was in supination. A roll was placed under the lower part of the chest to facilitate surgical access to the retroperitoneum. Carbon dioxide was inflated at 12–13 mmHg for laparoscopic surgery. The patient was intubated and maintained with controlled ventilation during surgery that lasted 4 h and extubated 15 min after the end of the procedure. In the recovery room, a complete neurological deficit of the right upper arm was rapidly noted. The motor deficit was associated with a complete sensory loss of the upper limb extending to the shoulder and a loss of reflexes. The neurological deficit recovered very slowly and 20 days later the patients were able to flex his fingers and his forearm. Electrophysiological testing was performed at that time. It displayed a nerve conduction block in C5-C6 spinal roots. A cervical magnetic resonance scan failed to document any local cause of nerve trauma or compression. The deficit recovered completely within 6 months, as demonstrated by electrophysiological testing that was normal.

Case 2
A 46-yr-old male suffered from testicular germ cell tumour that was treated by testicular ablation and three consecutive courses of chemotherapy with bleomycin (15 mg per day at days 1, 8 and 15), cisplatin (70 mg per day from days 1 to 15), vinblastine (10 mg at days 1 and 2) and etoposide (560 mg per day on days 1–3). Surgical excision of lumbar-aortic lymph nodes was planned after chemotherapy because of persisting tumour nodes on computed tomographical scan. Anaesthesia was induced with propofol (200 mg), sufentanil (20 µg) and orotracheal intubation was facilitated by atracurium (40 mg). Anaesthesia was maintained by sevoflurane and nitrous oxide 50% in oxygen and repeated injection of sufentanil as required. Patient position was the same as described in the first case. Careful attention was paid not to place the upper limb in abduction to more than 90°, but due to placement of the roll under the thorax, the upper arms position was below that of the thorax in the horizontal section. Muscle relaxation was maintained during the 4½ h duration of the laparoscopic procedure. The patient was extubated in the recovery room 10 min after the end of the surgical procedure. A bilateral motor deficit of the arms was immediately noticed. The patient was unable to grip the hands on both sides, to flex the forearms and to raise the arms. Sensory deficit in the C5-C6-C7-C8 distribution was also noted bilaterally. An electromyographical assessment was performed within the first 24 h. It documented a lack of motor activity in the deltoid, biceps brachii and brachioradialis muscles and a marked decrease in conduction velocity in the radial nerves. F-waves were delayed and their amplitudes were decreased in the four limbs. A rapid improvement in motor and sensory deficit occurred and muscle strength had recovered completely on day 6. A second electromyographical assessment was performed 20 days later. It documented a decrease in nerve velocity in lumbar, sciatic and brachial plexus nerves without conduction block. F-waves delay remained prolonged and sensory potentials amplitudes were still decreased in the four limbs.

Comments
These two cases document the occurrence of reversible peripheral nerve deficits in patients with unsuspected peripheral neuropathy. In the second case, peripheral neuropathy was asserted by the electromyographic examination performed on the first day after surgery that documented nerve conduction abnormalities in the four limbs [3]. Although the first patients did not have an early nerve conduction measurement nor than a measurement of nerve conduction in the four limbs, it is likely that he also suffered from sub-clinical chemotherapy-induced neuropathy.

Several risk factors may have contributed to transient nerve damage including stretch and compression.
related to positioning, the use of muscle relaxants and the duration of surgery. Although abduction of the upper limbs was carefully controlled, and abduction angle was less than 90°, raising the thorax above the level of the support of the upper limbs may have contributed to putting brachial plexus under traction. In addition, this position was maintained for 4 h or more and muscle relaxant could have facilitated spinal root stretching because of the loss of muscle tone. Head rotation opposite to the abducted arm or hyperextension of the neck may also facilitate root damage but a soft head ring placed under the occipital bone prevented this.

In most of the cases, peripheral nerve damage related to positioning during anaesthesia occurs in patients without any known neuropathy. Patients may also have neuropathy such as diabetic neuropathy with pressure hypersensitivity that could make them theoretically at risk to develop postoperative neurological deficit, although only two cases have been reported so far [4,5]. Chemotherapy with cisplatin and vinblastine is known to induce peripheral neuropathy [6]. Cisplatin-induced neurotoxicity is thought to be related to deposition of the drug at the level of the dorsal root and dorsal root ganglia neurons that results in apoptosis [7]. In patients with germ cell tumours, peripheral neuropathy is the most common form of neurotoxicity observed with cisplatin-based chemotherapy. Chemotherapy with cisplatin and vinblastine is also used preoperatively in patients with non-small cell lung cancer. Risk factors for the development of neural damage include high cumulative dose of cisplatin and the use of vinblastine [8]. Cisplatin neuropathy is not always reversible after discontinuation of treatment and could persist for months or years [6]. In these patients, detailed electrophysiological evaluation could predict the final neurological outcome [9] and should be performed before surgery. Such patients with pre-existing neuropathy could be prone to develop motor and sensory deficit postoperatively, related to patients positioning during surgery. This so-called ‘double-crush’ hypothesis suggests that nerves already compromised become more susceptible to injury [10]. Hebl and colleagues have described the case of a patient previously treated by cisplatin, who developed diffuse brachial plexopathy after interscalene block [11]. As previously stressed, in these two cases compression and stretching due to positioning has certainly contributed to the occurrence of sensory and motor deficit, but it is remarkable that profound and diffuse neurological deficit occurred which resembles more a toxic–metabolic aetiology such as that seen with cisplatin or vinblastine than the consequence of direct trauma which usually results in a more limited extent of the deficit [1,2].

In conclusion, the risk of neurological injury must be considered in patients treated by cisplatin and vinblastine. Electrophysiological testing could be recommended before surgery to recognize patients prone to develop such a complication.

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References

9. Argyriou AA, Polychronopoulos P, Koutras A et al. Peripheral neuropathy induced by administration of
Anaesthesia for total hip replacement in Gaucher’s disease

EDITOR:
Gaucher’s disease, the most common lysosomal storage disorder, is an enzymatic defect with consequent accumulation of undegraded glucocerebroside in cells of the monocyte–macrophage system [1]. Most patients present with enlargement of the spleen and liver resulting in hypersplenism, with thrombocytopenia generally more significant than anaemia. Skeletal involvement, particularly osteonecrosis of large joints and pathological fractures, invariably is the most significant cause of morbidity and decreased quality of life. In spite of enzyme replacement therapy, osteopaprosis and osteonecrosis continue to be clinically important. The need for total hip replacement (THR), and subsequent revision, is relatively common in these patients at a relatively young age. With regard to the anaesthetic management for orthopaedic surgery in patients with Gaucher’s disease, only one case report appears in the literature of an adult with a sub-capital hip fracture who underwent subarachnoid anaesthesia [2]. We wish to report the anaesthetic management of all cases seen in our institution for THR or revision from 1990 to 2005. Patient characteristics and perioperative data are summarized from the clinical records and presented in Table 1.

There were 14 patients, 10 males and 4 females, who underwent THR. Five of these underwent a revision. Six patients (43%) were homozygous for the mild N370S (1226) mutation; eight patients (57%) had been splenectomized; and six patients (43%) had pulmonary hypertension at the time of surgery. Fifty-three percentage of patients underwent general anaesthesia. Five of the operations (21%) were performed with preoperative platelet counts <80 × 10³ mm⁻³. Perioperative blood product transfusion was required in 68% of the operations.

All patients with general anaesthesia were orally intubated utilizing direct laryngoscopy and ventilated with tidal volume 6–8 mL kg⁻¹ and respiratory rate of 10–16 min⁻¹. There were no difficulties in airway management.

All patients were given preoperative antibiotic prophylaxis mainly with cefazidine; nonetheless, 37% experienced postoperative wound infections presenting significantly higher rates compared to similar patients in our institution (2%) and the rate reported in medical literature (0.3–2%) [3]. A wound infection was defined as one of the following: wound redness, excessive pain, tissue necrosis, local oedema, purulent discharge from the operation wound and maximal temperature >38.5 and/or white cell count >10.000. Other complications included one inadvertent spinal, one failed spinal and one patient with severe postoperative thrombocytopenia (21 × 10³ mm⁻³).

Joint replacement for patients with Gaucher’s disease is an important therapeutic intervention that dramatically reduces pain, improves functionality and increases quality of life. For patients with Gaucher’s disease, the preoperative evaluation of haematological

<table>
<thead>
<tr>
<th>Laboratory tests</th>
<th>Count (patients; 19 operations)</th>
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<tbody>
<tr>
<td>Platelets (×10³ mm⁻³)</td>
<td>164 ± 93.8 [21–325]</td>
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<tr>
<td>Prothrombin time</td>
<td>Normal</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>10.3 ± 1.1 [8.5–12.1]</td>
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<tr>
<td>Intraoperative fluids (L)</td>
<td>3.37 ± 1.47 [1.5–6.5]</td>
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<table>
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<tr>
<th>Perioperative blood products</th>
<th>Count (patients; 19 operations)</th>
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<tr>
<td>Platelets (units)</td>
<td>5 operations (26.3%) [6–16]</td>
</tr>
<tr>
<td>Fresh frozen plasma (units)</td>
<td>4 operations (21%) [2–3]</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>2 operations (10.5%)</td>
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<tr>
<td>Packed cells</td>
<td>11 operations (57.8%) [1–5]</td>
</tr>
<tr>
<td>Infection</td>
<td>7 (36.3%)</td>
</tr>
<tr>
<td>Other complications</td>
<td>Inadvertent spinal – 1; failed spinal – 1</td>
</tr>
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status is of primary concern. Many have very low platelet counts with or without abnormal platelet function [4]. Thrombocytopenia may be sufficiently severe as to preclude regional anesthesia [5]. In minor procedures (e.g., dental extractions) we have successfully used platelet transfusions immediately prior to and directly after surgery. Coagulation factor deficiencies are also common in this population and may occur independently of platelet abnormalities.

A relatively large percentage (44%) in this cohort had pulmonary hypertension at surgery. This complication reflects disease severity but we have also posited a possible connection with enzyme replacement therapy [6], so that a history of enzyme treatment does not preclude normal lung function. In these most severe cases, regional anesthesia may be preferred because of pulmonary hypertension.

In conclusion, patients with Gaucher’s disease undergoing THR may have associated medical conditions such as pulmonary hypertension and coagulopathy that complicate their anesthetic management and postoperative course. Further, they are at high risk for development of postoperative infection. We strongly recommend a multi-disciplinary approach that includes internal medicine, anesthesiology and orthopaedic surgery when planning of major orthopaedic procedures in patients with Gaucher’s disease.

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References

Cerebral oximetry monitoring during unexpected cardiopulmonary arrest and tension pneumothorax

EDITOR:
Cerebral oximetry (rSO₂) has had mixed reviews in its use as an accurate tool for determining the level of cerebral oxygenation [1,2]. We present the case of an elderly male who presented for skin grafting in whom cerebral pulse oximetry was monitored.

A 66-yr-old male presented for skin grafting to his left shin area. The area had become blackened and necrotic as a result of a blockage to a previous femorodistal bypass graft. His graft was found to be blocked on Duplex scanning and he was scheduled for a semi-elective femorodistal bypass graft. His medical background included previous myocardial infarction with subsequent three vessel coronary artery bypass graft. He was also hypertensive and had a 50-yr smoking history. He was assessed as an ASA IV.

He had an episode of melaena on the day of his admission and his surgery was postponed until a cause
could be found. An oesophago–gastro duodenoscopy revealed gastric erosions. He was transfused with packed red blood cells to bring his haemoglobin to a level of 9.1 g dL$^{-1}$. Three days later he underwent a left re-do femoro-distal graft procedure.

This was carried out under a general anaesthetic with etomidate induction and maintained with remifentanil and desflurane. The procedure lasted 7.5 h and was uneventful. During a further procedure 2 weeks later under general anaesthesia using a laryngeal mask airway, his breathing became laboured and he became hypotensive. Vasoconstrictors were administered and he required endotracheal intubation and intermittent positive pressure ventilation. It was noted on the anaesthetic chart that this was assumed to be an episode of bronchospasm. He was extubated uneventfully at the end of the procedure. Two weeks later he underwent a third debridement of his left shin, which was performed uneventfully under a spinal anaesthetic.

One week later he was scheduled to have skin grafting to his left shin as the final component of his treatment. It was decided that the procedure would again be carried out under spinal anaesthesia. The cerebral oximeter was attached at the beginning of the procedure and the rSO$_2$ was found to be 40%. This value is at the lower level of the normal range. Values for non-invasive blood pressure (130/80 mmHg), electrocardiograph (85 beats min$^{-1}$, sinus rhythm) and pulse oximetry ($S\text{PO}_2$ 98%) monitoring were normal. A 16-G cannula was inserted into the dorsum of the left hand and Hartmann’s solution infused. Spinal anaesthesia was administered in the sitting position. Using a 25-G Whitacre needle at the level of L3/L4, bupivacaine 0.5% 2.4 mL was administered using an aseptic technique. The height of the block was noted as T4 using ethyl chloride spray for cold sensation and pinprick testing for pain. Ten minutes after the spinal anaesthetic was administered, mild hypotension was noted and 9 mg of ephedrine administered with a return to normotension. Surgery commenced and proceeded uneventfully with minimal blood loss. However, 25 min into the procedure the patient complained that he felt unwell and ‘thought that he was going to die’. His breathing became laboured and he started to become bradycardic and hypotensive. About 600 µg of atropine was administered with no effect and cardiopulmonary arrest ensued. The rSO$_2$ fell promptly to less than 20 (Fig. 1). One milligram of epinephrine was administered and cardiopulmonary resuscitation (CPR) initiated and the patient’s trachea was intubated. After 3 min of CPR, a peripheral pulse was detected and a blood pressure of 170/80 mmHg obtained along with a heart rate of 130. rSO$_2$ reading immediately rose to 65% – much increased from the start of surgery. However, once again BP and rSO$_2$ began to fall and his lungs became difficult to ventilate. Chest auscultation revealed decreased air

Figure 1.
Changes in rSO$_2$ before during and after cardiopulmonary arrest and the accompanying interventions. CPR: cardiopulmonary resuscitation.
entry over both left and right lung fields. A diagnosis of a tension pneumothorax was made. Two 14-G canula were inserted at the level of the second intercostal space in the mid-clavicular line on both sides. The needle was withdrawn from the left and a 'whoosh' heard. Both NIBP and rSO₂ immediately improved (Fig. 1). A left-sided chest drain was inserted followed by a right-sided chest drain along with an arterial line, central venous catheter and urinary catheter. Surgery was completed and the patient awaited transfer to the intensive care unit (ICU). A low-dose epinephrine infusion running at 0.05 µg kg⁻¹ min⁻¹ was started to maintain a mean arterial pressure between 80–90 mmHg, the patient being sedated with a 1% propofol and morphine infusion.

The patient remained in the operating theatre for 5 h until an ICU bed became available. After 4 h, with BP, temperature, acid–base and fluid balance observations stable, the patient was extubated. rSO₂ readings during this post-arrest period were consistently greater than 60, some 50% greater than the pre-arrest picture. He was transferred to the ICU where he remained stable and was discharged the following morning. He underwent one further procedure 2 weeks later to apply the remaining skin grafts without anaesthesia. His rSO₂ was again monitored and found to be back to 40%. He continued to make a complete recovery and was discharged home 2 weeks later.

Discussion

The Somanetics INVOS® cerebral oximeter has been in use for more than 10 yr [5] as a tool for assessing cerebral oxygenation. It has been used during carotid artery surgery [4], cardiac arrest situations [5] and during cardiopulmonary bypass surgery [6]. However, their use in clinical practice remains controversial not least in part due to interpretation of the information provided. It has been demonstrated that it is possible to obtain rSO₂ readings from cadavers that are higher than in healthy alive individuals [7]. The explanation for these findings [5] is that near infrared spectroscopy reflects the balance between regional oxygen supply and demand. In dead or infarcted non-metabolizing brain, saturation may be near normal because of sequestered cerebral venous blood in capillaries and venous capacitance vessels. However, in regionally or globally ischaemic, but still metabolising brain, rSO₂ decreases because oxygen supply is insufficient to meet metabolic demand.

Studies have also shown [8] during isocapnic hypoxia in healthy persons, cerebral oxygenation as estimated by near infrared spectroscopy precisely tracks changes in measured jugular venous oxygen saturation within individuals, but the relation exhibits a wide range of slopes and intercepts. It was therefore felt that the usefulness of the device is limited to situations in which tracking trends in cerebral oxygenation would be acceptable. This was certainly true in our case where a pre-arrest reading for rSO₂ of 40% was replaced with one of 65% post-arrest. It was at least reassuring to believe that post-arrest cerebral oxygenation was not impaired and indeed had improved on the pre-arrest picture. This being manifest upon extubation of the patient who demonstrated no neurological deficit.

During this case, the use of rSO₂ provided useful information. This was not only in the pre-arrest period where an rSO₂ reading of 40% reflected the patient’s poor physical condition but also during the procedure, where BP, S₉O₂ andETCO₂ fell in parallel with rSO₂ before and during the arrest and tension pneumothorax and correspondingly rose following successful resuscitation.

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References