Fluid shifts in anaphylaxis

EDITOR:
We read the interesting article of Dr Iannuzzi and colleagues [1] and would like to illustrate the extent of fluid shifts induced by anaphylaxis, the necessity of volume support and catecholamine therapy.

A 35-yr-old male (ASA I) presented for elective operation of the paranasal sinuses. Five minutes after induction of anaesthesia with propofol (200 mg), fentanyl (0.3 mg) and rocuronium (40 mg), the patient developed acute hypotension (systolic blood pressure below 40 mmHg), tachycardia (130 beats min$^{-1}$) and a general grey complexion. Bronchospasm did not occur. H$_1$- and H$_2$-antagonists, methylprednisolone (500 mg) and norepinephrine (titrated 1.2 mg) were given. Two arterial blood samples taken 10 and 25 min after the beginning of this acute phase revealed an elevation of haemoglobin (Hb) concentration from $15 \text{ g dL}^{-1}$ preoperatively to $19 \text{ g dL}^{-1}$ (haematocrit, from 45.0 to 59.4%), an elevation of PaCO$_2$ to 8.7 kPa (PaO$_2$ = 10.1 kPa, SaO$_2$ = 89%) and a decrease of pH to 7.19 with a base excess of $-5 \text{ mmol L}^{-1}$. This elevation of Hb concentration and haematocrit occurred because approximately 1.5 L of fluids had left the intravascular compartment (according to the formula of Nadler and colleagues [2]), although 1 L of colloidal and 2 L of crystalloids were given. Epinephrine, the preferred catecholamine in anaphylaxis [3], was not given because of tachycardia. Norepinephrine was the catecholamine of choice for cardiovascular stabilization. Skin prick testing and a leukocyte histamine release test [3] performed 6 weeks later revealed a type I allergy to rocuronium.

We want to emphasize that in anaphylaxis massive fluid shifts can occur and must be treated adequately (as was done by Iannuzzi and colleagues [1]). Furthermore, it may be of benefit to use those catecholamines that differ from epinephrine for cardiovascular therapy.

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References
Tramadol versus meperidine in the treatment of shivering during spinal anaesthesia

EDITOR:

Shivering during spinal anaesthesia is a common problem that has potentially detrimental effects for the patient including increased oxygen consumption, carbon dioxide production, lung ventilation and cardiac output, as well as a decreased mixed-venous oxygen saturation. It has also been shown to increase the metabolic rate by up to 400% [1,2].

Various drugs have been used to control shivering. Meperidine is effective with a minimum effective dose of 0.35 mg kg$^{-1}$ [3]. Tramadol, a centrally acting analgesic drug with weak opioid agonist properties, modulates central monoaminergic pathways, inhibiting the neuronal uptake of norepinephrine and serotonin [4]. It is also effective in the treatment of postoperative shivering [5]. However, both agents are associated with adverse effects, which may be reduced by using minimum effective doses. We wanted to investigate the safety and efficacy of intravenous (i.v.) low-dose tramadol compared with meperidine in the control of intraoperative shivering during spinal anaesthesia.

After obtaining approval from our hospital's Ethics Committee, we studied 60 patients of both sexes (ASA Class I–II, aged 20–60 yr) who developed severe shivering (Grade 3 or 4, on a 0–5-point scale [6]) (Table 1) during orthopaedic and urological surgery under spinal anaesthesia. Exclusion criteria were obesity, a body temperature >38.0°C, a history of alcohol abuse, or taking antidepressant or analgesic drugs.

Patients received midazolam 5 mg intramuscularly 30–45 min before anaesthesia. Hyperbaric bupivacaine 0.5% was used for spinal anaesthesia. The operating room temperature was kept at 24°C. All infused fluids and drugs were given at room temperature. Patients were randomly allocated to one of two treatment groups: meperidine 0.35 mg kg$^{-1}$ ($n = 30$) or tramadol 0.25 mg kg$^{-1}$ ($n = 30$). These doses were the minimum doses used for treatment of shivering and found to be effective in previous studies [3,7]. Before the start of surgery, the anaesthetist involved prepared two syringes containing 5 mL solution. The first syringe contained tramadol 5 mg mL$^{-1}$, the second meperidine 7 mg mL$^{-1}$. These syringes were labelled ‘1’ and ‘2’; both the investigator and the patients were blinded to the content of the syringes. The investigator who evaluated the extent of the shivering gave the injection at a dose of 0.05 mL kg$^{-1}$ and recorded the delay until the control of shivering. Both drugs were administered i.v. over 30 s. During shivering, supplemental oxygen was administered via a nasal cannula (3 L min$^{-1}$). Five minutes after the injection, treatment efficacy was assessed as no improvement (Grades 3 or 4), or improvement (Grades 0, 1 or 2). If the shivering score was Grade 3 or 4 after 5 min, the same dose was repeated, and the treatment was considered as ineffective. Arterial pressure, heart rate and sedation scores were recorded at baseline and at 5 min intervals for 15 min after the injection of the study drugs. If patients developed hypotension (systolic blood pressure <100 mmHg or a decrease from the baseline >30%), ephedrine 5–10 mg i.v. was administered. Sedation scores were estimated by using a three-point scale (0 = no sedation, 1 = mildly sedated, easily rousable, 2 = heavily sedated). The recurrence of shivering and presence of nausea or vomiting were also noted. Nausea and vomiting were evaluated by using a four-point scale (0 = no nausea, 1 = mild nausea, 2 = severe nausea, 3 = vomiting).

Patients who developed severe nausea and vomiting, metoclopramide 10 mg i.v. was administered. Statistical analysis was performed using a $t$-test, $U$-test and $\chi^2$-test. $P < 0.05$ was considered as significant.

The groups were similar in the distribution of gender, age, weight, ASA physical status and duration of anaesthesia (Table 2). There was no difference in shivering grades before the treatment. The response rates of meperidine (93%) and tramadol (90%) were similar (Fig. 1). The time to control shivering was 155 ± 64 s for tramadol and 181 ± 89 s for meperidine. Response rates and the delay for response were not different between groups. There was no difference either between the two groups in the baseline sedation scores. In both groups, there were no differences in sedation scores, arterial pressure and heart rate during the study. Shivering recurred in two patients

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical signs</th>
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<tbody>
<tr>
<td>0</td>
<td>No shivering</td>
</tr>
<tr>
<td>1</td>
<td>Palpable mandible vibration or electrocardiogram artefact</td>
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<tr>
<td>2</td>
<td>Visible fasciculation of the head or neck</td>
</tr>
<tr>
<td>3</td>
<td>Visible fasciculation of the pectoral muscles or trunk</td>
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<tr>
<td>4</td>
<td>Generalised shivering of the entire body</td>
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at 10 and 15 min after successful treatment with tramadol. No patients in the meperidine group experienced recurrence of shivering. No patient in any group required ephedrine after the injection of the study drugs. With tramadol, two patients were nauseous and none vomited. With meperidine, four patients were nauseous and none vomited; one received metoclopramide.

The effect of tramadol 0.25 mg kg$^{-1}$ i.v. on shivering during spinal anaesthesia was similar to meperidine 0.35 mg kg$^{-1}$ i.v. The selection of a drug and the dosage for the treatment of shivering must be tailored to each patient. However, tramadol may be a suitable alternative to meperidine for the treatment of intraoperative shivering.

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References


Epidural bleed and quadriplegia due to acquired platelet dysfunction unrelated to multiple spinal and epidural puncture

EDITOR:

We present a patient who developed an epidural haematoma at the cervical and upper thoracic level that resulted in tetraplegia. However, this was not due to multiple spinal and epidural punctures at the lumbar and lower thoracic level for several orthopaedic procedures over several weeks of care. A 58-yr-old male, with no previous history of bleeding disorders, presented to the orthopaedic department with a tumour of the right femur. The diagnosis of a high-grade fibrosarcoma was confirmed by an open biopsy under spinal anaesthesia. A total resection of the femur and a reconstruction with a total femur megaprosthesi was then performed under combined epidural and general anaesthesia; insertion of the epidural catheter at T11–T12 was uneventful. Patient-controlled epidural analgesia (PCEA) was initiated for relief of pain after operation. Three weeks
later, a metastasis resection of the left femur with cemented osteosynthesis was performed, with epidural anaesthesia at L3–L4. Insertion of the epidural catheter was reported to have been technically difficult, but without complications. After 4 weeks, a revision due to haematoma formation in the right leg became necessary, which was performed under uneventful spinal anaesthesia at L3–L4. Another revision, again to stop haemorrhage, was performed 3 weeks later under epidural anaesthesia at L3–L4, and again PCEA was used. Investigations by haematologists 10 days after this revision did not reveal any specific disorders of coagulation. Primary haemostatic capacity was investigated by the PFA-100® Analyser (AD-TECH Communications, Hollywood, CA, USA), which measures primary haemostasis in vitro by uniquely simulating the in vivo hemodynamic conditions of platelet adhesion, activation and aggregation; and was on two occasions with 103 and 69 s (reference value 71–118 s) for closing time by a collagen/adenosine diphosphate (ADP) probe cell and closing times of 97 and 74 s (reference value 85–165 s) for closing time by a collagen/epinephrine probe cell. This was interpreted as a normal primary haemostatic capacity without a clinically relevant decrease of platelet function. For further revision and explantation of the tumour prosthesis, regional anaesthesia was administered via the epidural catheter that had been inserted 16 days previously. Three days later, computed tomography (CT)-guided drainage of a lesion – highly suspicious for abscess and osteomyelitis in the pelvis – was undertaken. The epidural catheter was removed 26 days after insertion. Because of further haematoma formation in the right thigh and an abscess in the iliosacral joint, another revision was scheduled 2 weeks later. The right paramedian approach to the epidural space at L3–L4 using an 18-G Tuohy needle led to a loss of resistance at 6 cm, with bright red blood being withdrawn. A second puncture at L3–L4, using a lateral approach, led to a comparable incident – bright red blood was very easily withdrawn through the Tuohy needle. The quantity of blood was quite different from that seen with an ‘ordinary’ bloody tap. In the view of the patient’s condition and his clearly stated preferences, a further epidural puncture was performed at the L2–L3 level using a left lateral approach. This was uneventful, with the catheter being inserted 5 cm into the epidural space with the needle in the cranial direction. However, approximately 7 min after placement, the catheter started to drain blood. The anaesthetic was changed to general anaesthesia. For postoperative pain control, intravenous PCA was used. Owing to the bloody punctures and abnormal coagulation parameters postoperatively, the epidural catheter was left in situ, and the patient was closely monitored by the acute pain service. Two days later, motor weakness in the left leg was noted. No sensory or motor pathologies in the right leg or upper extremities were detected. The epidural catheter was removed after verification that the plasma coagulation variables and platelet count were within normal ranges. On the evening of the same day, a paresis of the left arm was documented for the first time. Acute intracranial haemorrhage was excluded by cranial CT, which revealed signs of a previous ischaemic insult in the right hemisphere. However, since a recent ischaemic insult could not be excluded, therapeutic anticoagulation with heparin was initiated with a partial thrombin time between 70 and 80 s. Two days later, the patient developed a massive retroperitoneal haematoma, which necessitated immediate surgical intervention under general anaesthesia. The patient did not recover consciousness, but immediate CT did not reveal any new pathology. Although consciousness gradually returned after 24 h, the patient was tetraplegic. Immediate magnetic resonance imaging (MRI) showed evidence of an epidural haematoma extending from C2 to T3–T4 (Figs 1 and 2). MRI of the lower spine was unremarkable. There

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**Figure 1.**
Magnetic resonance image of the cervical spine. The sagittal T2 image (TSE 3800/91) reveals a large posterior epidural collection that is mainly hypointense to cerebrospinal fluid and markedly compresses the dural sac from C2 to T3. Additionally, the spinal cord shows a long segment of abnormal increased intramedullary signal due to compression. Note small areas of increased signal within the epidural haematoma that suggest subacute blood collection (methaemoglobin) within an acute haematoma.
was no evidence of bleeding at the site where the multiple neuraxial blocks had been performed. Somatosensory and motor-evoked potentials did not elicit a cortical response. Motor and sensory function did not recover any further, and the patient was required to be artificially ventilated because of diaphragmatic paralysis. Since haemorrhage from the various surgical sites continued, requiring further blood transfusions, surgical decompression of the spinal cord was rejected. An analysis of platelet functional capacity conducted by a platelet research laboratory revealed an acquired severe thrombocytopenia with reduced fibrinogen binding and decreased CD62 and CD63 expression induced by thrombin or collagen. The expression of CD62 and CD63 reflects the secretion of platelet \( \alpha \)-granules and dense bodies, respectively. This secretion is important for strengthening the thrombus. The team of orthopaedic surgeons and neurosurgeons decided that a decompressive laminectomy for a haematoma over five segments in a patient with thrombopathy was unlikely to be successful. The patient was ultimately transferred to a centre specializing in rehabilitation after spinal cord injury, but died 5 months after the initial diagnosis of a femoral fibrosarcoma.

In this patient, there was no obvious relationship between the blocks performed and the development of an epidural bleed. It demonstrates that spinal and epidural puncture in patients with coagulopathy will not necessarily produce an epidural haematoma, and how the blame for an epidural haematoma can be erroneously assigned to needle puncture.

The incidence rate of paresthesiae and neurological injuries has been reported as ranging between 0.01 and 0.001\% [1,2]. The most devastating complication is paraplegia caused by an epidural haematoma. Three instances of paraplegia, induced by spinal haematomas, out of 18 000 epidural blocks, have been reported in patients with compromised haemostasis. Other investigators experienced no complications in 100 000 patients receiving central neuraxial anaesthesia or analgesia [3], or in 4185 patients undergoing thoracic epidural anaesthesia [4]. To avoid epidural haematoma, it is essential to observe published guidelines and recommendations [5]. In addition to evaluating the coagulation profile thoroughly, it is extremely important to take a detailed history of the patient’s preoperative medication, not forgetting enquiry about new inhibitors of thrombocyte aggregation (e.g. clopidogrel or ticlopidine), and any history of bleeding.

The recurrent bleeding disorders in this patient were apparently due to a complex acquired platelet dysfunction that could not be detected using routine general coagulation tests or with the factor analysis conducted after consultation with haematologists. Only sophisticated experimental assays, not available in clinical practice, allowed the diagnosis of the acquired thrombopathy in our patient. Heparinization to improve the possible cortical infarct might also have further impaired haemostatic capacity, leading to the epidural haematoma.

After a central neuraxial block, patients must be observed or monitored until the level of regional anaesthesia has declined by at least two segments. Special attention should be given to detecting persistent sensory or motor blocks, radicular back pain and urinary retention. If there are any clinical signs of an epidural haematoma, diagnostic and therapeutic procedures should be initiated immediately. The procedure of choice is MRI, which allows the extent of the haemorrhage to be determined. If MRI is unavailable, CT or myelography should be performed immediately. If the results are positive, an immediate laminectomy can improve the patient’s prognosis. Even though there was no direct causal relationship between the neuraxis blocks and epidural bleeding in our patient, spinal and epidural punctures should only be performed after thorough evaluation when active bleeding occurs, despite a normal coagulation profile.

**Figure 2.**
Axial T2 image (GRE 550/18/20) showing dorsolateral extension of the haematoma in the posterior epidural space markedly deforming the thecal sac. There is an anterior rim of diminished signal that is felt to represent a combination of displaced dura and haemorrhagic components at the periphery of the haematoma in a different stage of evolution.
EDITOR:
Holt–Oram (hand–heart) syndrome is a rare genetic disorder associated with structural and functional abnormalities of the heart and upper limbs. We describe a patient with limited cardiac function who successfully underwent right total hip replacement using combined spinal/epidural anaesthesia and sedation.

A 60-yr-old female presented with severe pain in her right hip. She had had two cannulated hip screws inserted 3 yr previously, after a fall, but continued to suffer pain in the right hip; the screws were scheduled to be removed followed by total hip replacement.

The patient had been born with a triphalangeal left thumb. Holt–Oram syndrome was diagnosed at 25 yr of age when she underwent repair of an isolated ostium secundum defect. Recent coronary angiography (to investigate worsening breathlessness) had demonstrated a dilated left ventricle, moderate mitral regurgitation and moderate pulmonary hypertension. No residual left-to-right shunt was noted. Contemporaneous echocardiography estimated a left ventricular ejection fraction of 27%. Because the patient had episodic bradycardia, a dual-chamber demand pacemaker was fitted. During the pacemaker insertion, left subclavian vein cannulation had been ‘difficult’. She had a fixed flexion deformity (45°) of the left elbow, in addition to the left thumb anomaly. Both radial pulses were palpable. Chest radiography was consistent with dilated cardiomyopathy, but the lung fields were clear; no Holt–Oram syndrome-related bony anomalies were seen.

Intravenous cannulation was secured and monitoring sensors applied (three-lead electrocardiogram, pulse oximeter, non-invasive blood pressure). The patient was then sedated (such that she could be roused verbally) with fentanyl 100 mg, midazolam 2 mg and ketamine 20 mg intravenously. Supplemental oxygen was provided by facemask. Under local anaesthesia, radial arterial cannulation (Seldinger method) was attempted, bilaterally. Despite both pulses being strong, the guide-wire could not be advanced more than 1 cm distal to the end of the intra-arterial needle in either wrist. However, a cannula was sited easily into the left dorsalis pedis artery. A triple lumen catheter was sited in the right internal jugular vein. Spinal anaesthesia was achieved by subarachnoid infusion of hyperbaric bupivacaine 0.5% 2 mL via a 25-G pencil-point spinal needle, inserted through a 16-G Tuohy epidural needle, at the level of

References
L1–L2. The epidural space was entered 5 cm from the skin, and an epidural catheter was sited, with 4 cm of catheter protruding into the space. Neuraxial blockade reached the level of T10.

The operation was performed with the patient in the left lateral position, suitably padded. Sedation required supplementation with midazolam 5 mg, ketamine 25 mg and fentanyl 250 µg over the 90 min of the operation. Cardiovascular stability was maintained without the use of vasopressor agents, and there were no complications arising from endoprostheses insertion using cement. Bipolar diathermy was used, in view of the patient’s pacemaker. The blood loss was 500 mL; 1250 mL of warmed Hartmann’s solution were administered (no blood was transfused or retransfused). The patient was discharged from the postoperative recovery unit to a hospital ward. The postoperative course was uncomplicated. Epidural analgesia (using bupivacaine 0.25% plain, 0–8 mL h⁻¹) was discontinued after 48 h.

Holt–Oram syndrome was first described in 1960 [1]. It is a rare disease with an estimated prevalence of 0.95/100 000 births. The gene responsible for the spectrum of anomalies is on the long arm of chromosome 12 (12q2), near both the HOX C gene (implicated in cardiac conduction pathway differentiation) and the RARγ gene (implicated in animal limb development). Recently, a series of distinct mutations of the TBX5 gene locus on chromosome 12q2 have been found in both familial and isolated cases of Holt–Oram syndrome [2]. The mutations introduce premature stop codons in the TBX5 gene product. The human TBX5 gene corresponds to the TBX5 gene in mice. TBX5 is a member of the Brachyury (T) gene family, which is responsible for limb shortening abnormalities in mice. Of cases of Holt–Oram syndrome, 15–70% are familial, with autosomal-dominant inheritance; 30–85% of cases occur in isolation, de novo. Isolated cases show greater upper limb anomaly than familial cases. The phenotypic range of heart and upper limb abnormalities is progressively more severe with successive generations of families with Holt–Oram syndrome. Upper limb anomalies are always present and are sufficient in isolation for a diagnosis of familial HOS. A diagnosis of de novo Holt–Oram syndrome requires the presence of both cardiac and upper limb abnormalities. Upper limb anomalies may be uni- or bilateral and result from the abnormal development of the embryonic radial ray. The most common anomaly is hypoplasia of the thumbs. Triphalangeal thumbs, digitalization of the thenar bones, carpal bone deformities, hypoplastic or deformed radii, severe ectromelia or phocomelia have been reported, occurring in any combination [3]. Clavipectoral hypoplasia may be present [4], which may make subclavian central venous cannulation difficult particularly if anomalies of upper limb venous drainage coexist. Other vascular abnormalities may occur, including persistent left superior cava, cerebral and renal arterial malformation, and absence of the radial artery [5]. Abnormal arterial and skeletal anatomy may make blood pressure monitoring difficult [6].

Our patient was an isolated case of Holt–Oram syndrome. The fixed flexion deformity of her right elbow was congenital, but the humerus, radius and ulna were all radiologically normal; this combination has not been reported previously in Holt–Oram syndrome. Left subclavian vein cannulation had been reported to be ‘difficult’ at the time of pacemaker insertion, possibly due to a persistent left superior cava. Radial arterial cannulation proved difficult, bilaterally. However, without the benefit of arteriography, we cannot comment on whether this was due to any Holt–Oram syndrome-related congenital radial artery malformation. Clinically and radiologically, the clavipectoral region appeared structurally normal, and passage of a right internal jugular line was uncomplicated.

Cardiac anomalies include structural abnormalities and conduction defects. Atrial septal defects (42–60% of cases) are three times more prevalent than ventricular septal defects. Fallot’s tetralogy, total anomalous pulmonary venous drainage and endocardial cushion defects are rarer. Most cardiac dysrhythmias occur in conjunction with structural abnormality. However, dysrhythmias may occur in isolation, particularly in familial cases of Holt–Oram syndrome. Sinus arrest, sinus node dysfunction, bradycardia, atrial fibrillation, atrioventricular block, bundle branch block and Wolff–Parkinson–White syndrome have been recorded and may contribute to the excess of sudden deaths observed in patients with Holt–Oram syndrome [7]. Permanent cardiac pacing may be indicated [3]. Prolonged postoperative cardiac monitoring is warranted for patients with significant cardiac anomalies.

Regional anaesthesia may be technically difficult to administer, particularly for the upper limb. However, as the sole method of providing anaesthesia, regional techniques have several benefits in the anaesthetic management of older patients with Holt–Oram syndrome. Myocardial depression, which occurs with many anaesthetic agents, is avoided. A pressor response to intubation does not occur. Consequently, there is improved cardiovascular stability, which is an important consideration in patients whose cardiac function is compromised by anatomical or conduction abnormalities. Our use of combined spinal and epidural anaesthesia had two other advantages [8]. First, sympathetic vasoconstrictor blockade facilitated a reduction in cardiac afterload (compensatory cardiac...
chronotropism was not seen in our patient). Second, provision of effective pain relief in the postoperative decreased cardiac strain. Careful administration of crystalloid before subarachnoid bupivacaine infusion avoided intraoperative hypotension, the likelihood of which was further reduced by concurrent use of ketamine as a sedative.

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References

Plateletpheresis the day before cardiac surgery and the impairment of platelet function

EDITOR:
The pathogenesis of the platelet qualitative defect after cardiopulmonary bypass (CPB) remains incompletely elucidated [1]. Theoretically, the collection of platelets before CPB followed by their transfusion immediately at the end of CPB would result in improved haemostasis. We decided to study the effect of autologous plateletpheresis the day before surgery on platelet function and mediastinal blood loss.

After institutional review board approval and written informed consent, patients scheduled for cardiac surgery were prospectively enrolled. Cardiac procedures with expected CPB longer than 2 h represented the target population. Twenty patients with normal coagulation function, platelet counts and withdrawal of antiplatelet drugs for at least 7 days before the operation were randomized for either the control group (n = 10) or the apheresis group (n = 10). The day before surgery, platelet collection was performed with a cell separator (COBE Spectra LRS®, Denver, CO, USA). The platelets were stored for 24 h in an incubator (Helmer, Nobelsville, IA, USA). Surgical procedures were performed with standard CPB techniques at moderate systemic hypothermia (32°C). Aprotinin was infused to all patients. Heparin was given at an initial dosage of 300 IU kg⁻¹, supplemented to maintain an activated coagulation time (ACT) greater than 480 s and ‘reversed’ with protamine sulphate to return ACT to baseline. Autologous platelets were infused at the end of CPB. Blood samples were collected after induction of anaesthesia (T1), after completion of CPB and protamine-induced heparin neutralization (T2), 30 min after protamine-induced antagonism of heparin and after completion of autologous platelet infusion in the apheresis group (T3), 4 h after heparin neutralization (T4) for measurements of platelet count, haemoglobin concentration and platelet aggregation. Photo-optical aggregometry was used (Platelet Aggregation Profiler-4®, Bio Data Corporation, Hatboro, PA, USA). Briefly, platelet-rich and -poor plasmas were obtained by centrifuging whole blood at 1000 and 3000 rpm, respectively. The aggregometer was calibrated. One agonist was added to platelet-rich plasma: ristocetin (Paesel Lorei®, Hanau, Germany) 1.2 mg mL⁻¹, adenosine diphosphate (ADP®; Boehringer, Mannheim, Germany) 5 μmol L⁻¹, collagen (collagen reagent Horin®, Munich, Germany) 2.5 μg mL⁻¹. In both groups, the same algorithm was applied for transfusion
requirements. Mediastinal blood loss was recorded during the second, 12th and 24th h. Continuous variables were expressed as mean ± standard deviation. Blood losses were expressed as median and interquartile ranges (25–75%). Comparisons for continuous variables between groups were made using the U-test; comparisons between the groups, for discrete variables, were made with Fisher’s exact test; a Spearman’s rank correlation test was used. P < 0.05 was considered as being statistically significant.

Patient characteristics and preoperative haematological variables were similar among patients of both groups. The control and apheresis groups did not differ significantly for the duration of CPB (137 ± 20 vs. 144 ± 36 min). In the apheresis group, a mean of 13 ± 2 × 10¹¹ platelets was collected. Mediastinal blood losses were quite similar with a median of 720 (640–975) mL during the first 24 h in the control group vs. 820 (745–885) mL in the apheresis group. No difference was noted at any time with reference to haemoglobin concentration or platelet aggregation (Table 1). Four hours after infusion of the autologous stored platelets (T4), the platelet count was not significantly higher in the apheresis group than in the control group (162 ± 50 vs. 154 ± 55 × 10¹² L⁻¹).

One of the most important findings of the study in the apheresis group was that platelet aggregation did not improve either after platelet infusion or 4 h after completion of CPB. After protamine administration, ADP and ristocetin induced-platelet aggregation demonstrated a significant negative correlation with a mediastinal blood loss at the 12th postoperative hour when patients of both groups were pooled (r = −0.6, P = 0.006 and r = −0.6, P = 0.008, respectively). In the apheresis group, Table 2 shows the evolution of the platelet function after stimulation with the various agonists. This process reduced ADP-induced platelet aggregation in the platelet storage bag immediately after the platelet collection (P = 0.01) but did not modify the platelet response when ristocetin or collagen were used. After 24 h of platelet storage, the ADP (P = 0.001) and collagen tests (P = 0.004) were markedly decreased whereas the ristocetin-induced platelet aggregation was not reduced.

Platelet dysfunction is considered the most important defect following the use of CPB [1]. Therapeutic yield intraoperative platelethephesis has been evaluated for the reduction of blood transfusion. Wajon and colleagues failed to demonstrate any reduction in transfusion requirements in the largest prospective, randomized clinical trial to date [2]. In several trials, the failure to document a reduction in mediastinal blood loss may be explained by the poor collected platelet yield [3]. In a meta-analysis of the effect of platelet-rich plasmapheresis in cardiac surgery,

Table 1. Haemoglobin concentration, platelet count and platelet aggregation.

<table>
<thead>
<tr>
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<th>Control group (n = 10)</th>
<th>Apheresis group (n = 10)</th>
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<tbody>
<tr>
<td><strong>Haemoglobin (g dL⁻¹)</strong></td>
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<tr>
<td>T1</td>
<td>11.0 ± 1.4</td>
<td>11.4 ± 1.4</td>
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<tr>
<td>T2</td>
<td>8.6 ± 1.1</td>
<td>8.8 ± 0.9</td>
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<tr>
<td>T3</td>
<td>9.1 ± 1.2</td>
<td>8.8 ± 0.7</td>
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<tr>
<td>T4</td>
<td>9.6 ± 1.8</td>
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<td><strong>Platelet count (×10¹² µL⁻¹)</strong></td>
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<tr>
<td>T1</td>
<td>206 ± 40</td>
<td>130 ± 17†</td>
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<tr>
<td>T2</td>
<td>124 ± 36</td>
<td>73 ± 18†</td>
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<tr>
<td>T3</td>
<td>131 ± 37</td>
<td>177 ± 48‡</td>
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<tr>
<td>T4</td>
<td>154 ± 55</td>
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<td><strong>Ristocetin (%)</strong></td>
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<td>T1</td>
<td>83 ± 26</td>
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<td>T1</td>
<td>87 ± 6</td>
<td>83 ± 9</td>
</tr>
<tr>
<td>T2</td>
<td>62 ± 16</td>
<td>58 ± 15</td>
</tr>
<tr>
<td>T3</td>
<td>70 ± 18</td>
<td>67 ± 15</td>
</tr>
<tr>
<td>T4</td>
<td>72 ± 11</td>
<td>66 ± 27</td>
</tr>
</tbody>
</table>

Values are the mean ± SD. T1: After induction of anaesthesia and before CPB; T2: after completion of CPB and protamine-induced heparin neutralization; T3: after autologous platelet reinfusion in apheresis group or 30 min after heparin antagonism in control group; T4: 4h after protamine administration. † P < 0.05; ‡ P < 0.01; † P < 0.001 between groups at the same time-point.

Table 2. Effects of apheresis and storage on platelet function.

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ristocetin</strong></td>
<td>89 ± 8</td>
<td>87 ± 4</td>
<td>92 ± 3</td>
</tr>
<tr>
<td><strong>ADP</strong></td>
<td>70 ± 11</td>
<td>31 ± 26*</td>
<td>17 ± 12†</td>
</tr>
<tr>
<td><strong>Collagen</strong></td>
<td>77 ± 11</td>
<td>68 ± 21</td>
<td>34 ± 28*</td>
</tr>
</tbody>
</table>

Values are the percentage of normal values. Platelet aggregation as a function of different sampling times. A: Before the start of platelet collection (baseline value); B: platelet storage bag; C: platelet storage bag after 24 h of storage. *P < 0.05; † P < 0.01; † P < 0.001 (compared with baseline value).

Rubens and colleagues suggested that platelethephesis seemed to be effective in decreasing the proportion of patients receiving homologous blood product [4]. However, the poor quality of randomized clinical trials made it difficult to determine the effectiveness of platelethephesis and to demonstrate that autologous platelet collection had a clinical protective effect. In our selected population of patients undergoing major cardiac surgery who had stopped their antiplatelet inhibitors, preoperative platelethephesis
does not decrease total mediastinal blood loss. However, mediastinal blood loss is well known to be a poor marker of true blood loss because the haematocrit value of the blood – collected into the mediastinal drainage unit – is often low and because mediastinal drainage may be incomplete [5]. In our study, platelet dysfunction after CPB remains even when a large number of platelets, collected by apheresis and free of contact with the CPB, were transfused. The effects of the plateletpheresis procedure on the platelet function are in accord with previous reports [6,7].

In conclusion, plateletpheresis the day before cardiac surgery does not decrease mediastinal blood loss or improve platelet function after CPB.

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References


