Patient safety update: Safe vascular access, local anaesthetic toxicity, anaphylaxis

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QUESTIONS

Before continuing, try to answer the following questions. The answers can be found at the end of the article, together with an explanation. **Please answer True or False:**

1. **Regarding safe vascular access:**
   a. Inotropic agents must never be given via a peripheral line
   b. The risk of infection associated with a central line is unrelated to the insertion site
   c. Major complications of arterial cannulation are similar at radial, brachial and femoral sites
   d. Ultrasound is recommended as a standard of care for insertion of central lines
   e. Retained anaesthesia drugs in cannulae is only a realistic concern in paediatric practice

2. **Regarding local anaesthetic toxicity:**
   a. Local anaesthetic systemic toxicity (LAST) occurs in around 1-10 cases per 10,000 regional anaesthetics
   b. Local anaesthetic CNS toxicity always exhibits an initial excitatory phase characterised by slurred speech, perioral tingling and tinnitus
   c. Injection of LA around the brachial plexus is more likely to lead to toxicity than epidural injection of LA
   d. Blood concentration of α1-acid glycoprotein (AAG) is an important patient-related factor affecting the likelihood of LAST
   e. Symptoms and signs of LAST always occur immediately after LA injection

3. **Regarding anaphylaxis:**
   a. After a suspected anaphylactic reaction, take blood samples for mast cell tryptase and serum specific immunoglobulin E (IgE)
   b. If anaphylaxis is suspected during a surgical operation under anaesthesia, the surgical team should take responsibility for referring the patient for investigation
   c. Anaphylaxis can be both “allergic” and “non-allergic”
   d. According to current estimates, anaphylaxis would occur in around 1:10,000-1:20,000 anaesthetics
   e. A history of previous exposure is found in fewer than 50% of patients who are allergic to neuromuscular blocking drugs

Key Points

- Vascular access is the most common invasive procedure in hospital care; safe practice should be followed at all times
- Local anaesthetic systemic toxicity can be treated successfully with intravenous intralipid
- Anaphylaxis should be considered if a patient develops unexplained cardiovascular collapse or severe bronchospasm during anaesthesia

INTRODUCTION

This tutorial is based on the Patient Safety Update published by the Safe Anaesthesia Liaison Group (SALG). SALG is a professional group with a core membership including representatives from the Royal College of Anaesthetists (RCoA), the Association of Anaesthetists of Great Britain and Ireland (AAGBI), and NHS England Patient Safety. SALG's quarterly Patient Safety Updates contain learning from incidents reported to the National Health Service England and Wales National Reporting and Learning System (NRLS). The aim of SALG is to highlight potential or existing patient safety issues from patient stories, and to encourage incident reporting for the purpose of learning.

Cases reported to the NRLS database that are associated with severe harm or death are reviewed on a quarterly basis and form the basis of the SALG PSU. The text is changed very little from the reports of the clinicians involved – these are real stories. There are often common themes within the cases that influence the learning points highlighted. The aim of this exercise to is learn from the experience of others, and in that way we can all improve the care of our patients.

The cases reported are reproduced with permission from the Safe Anaesthesia Liaison Group, and were originally published on the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland websites. Further information, together with this and previous Patient Safety Updates, is available on the SALG website.[1] The information contained in this tutorial is taken from the SALG Patient Safety Updates Jan-Jun 2016 but SALG has not reviewed this publication.

Safe vascular access

"Area of very dark necrotic looking skin noted on dorsum of left foot covering significant part of upper aspect of foot. The area had previously had a cannula through which peripheral inotropic support had been given."

"CVP line removed from patient … followed by a drop in consciousness with mixed signs, both right and left weakness. The patient improved with time."

"Left hand dusky fingers with arterial line in left radial artery. Arterial line removed. Doctors aware and had documented slightly mottled hand two days earlier."

"Arterial line was removed and placed in right brachial however concerns raised over right hand led to line being removed and patient now managed without arterial line."

"A patient was being cared for in recovery after an emergency procedure. The patient was unstable and required treatment for fast AF... the patient had suddenly deteriorated approximately one minute after intravenous fluids were changed from one cannula to another. The patient was not breathing adequately, became tachycardic and hypertensive and had some abnormal limb movements. The airway was supported and the episode resolved completely after a few minutes. The patient had complete recall for the event...we suspect that there was some residual suxamethonium in the cannula used for induction of anaesthesia and that the patient had an inadvertent small bolus when the IV fluids were changed. The cannula had an extension and two ports."

Vascular access is one of the most common invasive procedures undertaken in hospitalised patients. The AAGBI published comprehensive guidelines on this topic in 2016.[2] The 'Safe vascular access guideline' notes that the use of peripheral venous cannulae for vasopressor and inotropic drugs is contentious, but suggests that if peripheral inotropes are to be used, a large vein with high blood flow and lower drug concentration is likely to be safer.

Indications for central venous access include patient monitoring, or administration of vesicant drugs, inotropes, or hyperosmolar fluids such as parenteral nutrition or if there is a requirement for long-term vascular access. Central venous catheters may be percutaneous non-tunnelled lines (for up to 7-10 days), tunnelled or totally implanted lines (used for months to years); or peripherally inserted central catheters (PICCs) (1-6 months). Risks and benefits should be considered in all cases.

Common or important complications of central venous catheters include:

- Infection
- Thrombosis, catheter occlusion
- Arterial puncture/tear
- Pneumothorax, haemothorax
- Arrhythmias
- Myocardial perforation
- Air embolism
- Retained guidewire/catheter embolism

The risk of misplacement, pneumothorax or arterial puncture is lower if ultrasound guidance is used and if the internal jugular site is used. The ideal position of the CVP tip is in the lower SVC/high right atrium. The most common way to identify the catheter tip is on a chest X-ray, although this may not identify misplacement outside a vein. The risk of infection is lowest if the subclavian or internal jugular route is used, and the femoral route should be avoided if possible. A full aseptic technique should be used to insert any central line, using a 'care bundle' and checklist.[3] The skin should ideally be cleaned with chlorhexidine in alcohol, the operator should wear gloves, gown and facemask, the patient should be fully draped, and the insertion site should be dressed with a sterile dressing. The line should be handled aseptically and should be removed when no longer required.[3] The risk of thrombosis is reduced by using the catheter with the smallest lumen required for treatment needs, and also by removing the device as soon as it is no longer needed.

Air embolism is a rare but serious risk associated with central lines, and may be fatal.[2] It is avoided by using careful technique during insertion and handling of the line. When the line is removed, the exit site should be below the heart to reduce the risk of air embolism. Air embolism should be considered in any patient who deteriorates suddenly with a central line in place, or after a central line is removed. Management includes preventing further air entry, giving 100% oxygen and optimising circulatory function with fluids, vasopressors and inotropes. Large air collections in the heart may

be amenable to aspiration via a catheter in the right atrium with the patient in the left lateral decubitus position. Prompt hyperbaric oxygen treatment may be useful if available, particularly for cerebral air emboli.

An extensive review of literature demonstrates that for arterial cannulae, serious complications such as limb ischaemia occur in <1% of cases, and are independent of the cannulation site.[2] Thrombosis risk is related to cannula diameter and so smaller cannulae are preferred. A higher incidence of occlusion has been reported when the cannula is left in place for more than 48 - 72 hours. Arterial patency can be assessed using ultrasound; the Allen test to assess ulnar collateral supply is unreliable.

There have been a number of case reports in recent years of inadvertent administration of anaesthetic drugs in recovery or on the ward when an intravenous line has been flushed. This is more likely to occur in children but has also been reported in adults.[4] A Patient Safety Alert was published by NHS England in 2014 highlighting the serious risk posed by inadvertent injection of residual anaesthesia drugs.[5] The safety alert states that all cannulae and extensions should be flushed after use and before the patient leaves the theatre and/or recovery. It is also noted that the risk of residual drugs being present is increased by having multiple cannulae in situ, or where there are extensions in place with multiple ports.

Local anaesthetic toxicty

"Axillary brachial plexus block was done. Safety precautions were followed. The patient developed the following local anaesthetic toxicity symptoms: blurring of vision, light-headedness, difficulty in swallowing and shivering. Intralipid 20% was administered IV according to the protocol. Patient felt better over the next 10-15 minutes. Planned operation went ahead uneventfully."

"Patient was scheduled for a 2nd stage brachiobasilic fistula formation, and after pre-assessment clinic review a regional anaesthetic technique was preferred due to pre-existing cardiac disease. 20ml 0.375% levobupivicaine in a supraclavicular block (US guided) failed to cover the surgical region. 135 minutes later - repeat supraclavicular block under ultrasound. 10ml 2% lignocaine, 10ml 0.5% bupivicaine + 1:200,000 adrenaline used. 15 minutes later – intercostobrachial block, landmark technique. 5ml 1% lignocaine. 75 minutes later – the patient began jerking the right arm, thought to be focal seizure activity. This was announced out loud in theatre and Intralipid was found and administered to the patient as per AAGBI protocol for local anaesthetic toxicity. Jerking ceased approximately one minute after the end of the initial bolus of intralipid."

Although cases of local anaesthetic (LA) systemic toxicity (LAST) are rare, with an estimated incidence of 1-10 per 10,000 anaesthetic blocks,[6] anaesthetists need to remain vigilant at all times and have a specific plan to manage toxicity whenever local anaesthetic drugs are given. Intravenous 20% lipid emulsion (Intralipid 20%) has been used to treat LAST successfully, described in the AAGBI safety guideline: 'Management of Severe Local Anaesthetic Toxicity.[7] Intravenous propofol in lipid emulsion is not a suitable alternative in this situation as it is associated with significant cardiovascular depression.

Classical descriptions of LAST involve a three phase cardiovascular response and a biphasic central nervous system response, but it is important to note that LAST can manifest as cardiovascular collapse without any CNS features, and may also occur some time after LA administration.

Patient factors, site and conduct of the block, and type of drug and dose injected determine the risk of toxicity.[6] Since drug toxicity is related to free peak plasma concentration, lower plasma concentrations of binding proteins such as alpha 1 acid glycoprotein (e.g. in neonates, infants and pregnancy), leads to a higher risk of toxicity. Clearance is also reduced in liver and renal failure.

Sites for LA injection differ with respect to the risk of inadvertent intravascular injection, and in the rate of systemic absorption (with the risk of toxicity classically described as increasing from subcutaneous (lowest) to brachial plexus, epidural and intercostal (highest)).

LA drugs differ in their propensity to cause CNS and cardiovascular disturbance. Lidocaine induces seizures at about 1/7 of the dose required to cause cardiovascular collapse. Bupivacaine seizures start at around half the dose required for CVS collapse.

Anaphylaxis

"A 79-year-old patient presented for hip replacement. Past medical history included hypertension, asthma, renal impairment, hiatus hernia, partial thyroidectomy, hysterectomy, anterior and posterior repairs, and a right total hip replacement. Body Mass Index (BMI) was 34.9. There were documented allergies and/or intolerances to penicillin, cephalexin, tetracyclines, indomethacin, tramadol, cipramil, sertaline, meloxicam. A spinal anaesthetic was given along with prophylactic antibiotics (teicoplanin). This takes a while to mix and so the surgeons were quite well advanced in the procedure before the antibiotic was given. A low dose infusion of propofol was running for sedation. About ten minutes after the teicoplanin injection, the patient developed a tachycardia and blood pressure was recorded as 40 mmHg systolic. The propofol infusion was stopped. The surgeons were asked to wait (no cement was in the patient) while increments of adrenaline were given and an adrenaline infusion started. The patient was noticeably red in the arms and face once the pressure was restored. The procedure was completed. The plasma tryptase was raised at around 34.6mcg/l, 25.5mcg/l then 3.4 mcg/l the next morning."

Anaphylaxis is defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction. It may be allergic (immune-mediated), where the offending drug causes Ig E-mediated degranulation of sensitised mast cells and basophils, or non-allergic, where the drug causes mast cell and basophil degranulation by direct action. [see ATOTW 324: An Update on Perioperative Anaphylaxis (2016)]

According to French and Australian data, the incidence of anaphylaxis under anaesthesia is approximately 1:10,000-20,000 anaesthetics. It has been reported that the incidence of anaphylaxis differs widely between different geographical areas, possibly as a result of different exposure to chemicals in the environment. The sixth National Audit Project (NAP) of the RCoA is currently underway and aims to provide the incidence of anaphylaxis related to anaesthesia in the UK.[8] This project will also describe common signs and symptoms of anaphylaxis. Details of care will be collated from emergency management through to allergy clinic investigation follow-up, and hopefully lead to recommendations to improve the care and outcomes of patients with anaphylaxis.

Nearly two-thirds of anaesthesia-related anaphylaxis is attributed to neuromuscular blocking agents, with latex and antibiotics being the next two most common trigger agents. Immediate management and later referral for specialist testing are described in the AAGBI guideline: Management of a patient with suspected severe anaphylaxis during anaesthesia.[9] UK guidelines from the National Institute for Health and Care Excellence (NICE) recommend taking timed samples for mast cell tryptase as soon as possible after emergency treatment has started, and a second sample within 1-2 hours, or not later than 4 hours after the onset of symptoms.[10]

Recognition of anaphylaxis under anaesthesia is often delayed as the presenting features (hypotension and bronchospasm) are common, and may be confused with other more common conditions such as blood loss or asthma. Many “mild” reactions, such as those causing urticaria or mild hypotension, are probably missed.

Incidents reported to the UK NRLS have shown that in many cases of anaphylaxis human error is an important factor as the patient is given a medicine to which they have a known and documented allergy.[8] It is important to take a meticulous history for drug allergies and adverse reactions prior to anaesthesia, and to avoid potential trigger agents.

Anaesthetists should refer patients for specialist investigation where any of the following have occurred:

- Unexplained cardiac arrest during anaesthesia.
- Unexplained, unexpected hypotension (for example a decrease of mean arterial pressure of more than 30 mmHg) that requires active treatment.
- Unexplained, unexpected bronchospasm, particularly if the bronchospasm is severe, causes a significant decrease in oxygen saturation and is relatively resistant to treatment.
- Widespread rash, flushing or urticaria.
- Angioedema

Patients who report problems during previous anaesthetics that could be due to anaphylaxis should have their old notes reviewed where possible.

SUMMARY

- Vascular access is the most common invasive procedure in hospital care. Serious complications are rare, but their occurrence can be minimised by following safe practice guidelines on site selection, cannulation technique and device removal.
- Local anaesthetic systemic toxicity can manifest as cardiovascular collapse without any CNS features, and may also occur some time after LA administration. LAST can be treated successfully with intravenous intralipid.
- Anaphylaxis should be considered if a patient develops unexplained cardiovascular collapse or severe bronchospasm during anaesthesia. In many cases of anaphylaxis human error is an important factor as the patient is given a medicine to which they have a known and documented allergy. It is important to take a meticulous history for drug allergies and adverse reactions prior to anaesthesia, and to avoid potential trigger agents.

ANSWERS TO QUESTIONS

1. Regarding safe vascular access:

a. **False**: Inotropic agents may be given via a peripheral line in an emergency situation, but it is better to use a large vein and dilute drug to reduce the risk of ischaemic damage, if possible.
b. **False**: The risk of infection is greater if the femoral route is used.
c. **True**: There is no relation between the site of arterial line insertion and the risk of major complication.
d. **True**: Ultrasound reduces the risk of complications associated with central line insertion such as inadvertent arterial puncture, and is recommended as a standard of care in the UK.
e. **False**: There have been case reports in adults as well as children related to inadvertent administration of anaesthesia drugs due to the failure of the anaesthetist to flush the line.

2. **Regarding local anaesthetic toxicity:**
   a. **True**: Recent estimates for the incidence of LAST vary between 2.5-9.8:10,000 peripheral nerve blocks and 1.2-11:10,000 epidurals.
   b. **False:** Although the classic description of LA CNS toxicity includes an initial excitatory phase, followed by a depressive phase including coma and respiratory depression, in reality toxicity can occur without these early signs.
   c. **False:** The risk of toxicity associated with different injection sites in the order from least likely to most likely is: subcutaneous injection, brachial plexus, epidural, caudal, and finally intercostal blocks (and topical anaesthesia).
   d. **True:** A low plasma α1-acid glycoprotein concentration, such as seen in neonates and infants, and pregnant patients, results in a higher concentration of free LA.
   e. **False:** A recent review of published LAST reports found that although most followed the classic description, 40% were either substantially delayed or involved only signs of cardiovascular compromise.

3. **Regarding anaphylaxis:**
   a. **False**: UK guidelines from the National Institute for Health and Care Excellence (NICE) recommend taking timed samples for mast cell tryptase as soon as possible after emergency treatment has started, and a second sample within 1-2 hours, or not later than 4 hours after the onset of symptoms. Testing for IgE outside of a specialist setting is not recommended.
   b. **False:** It is the anaesthetist's responsibility to ensure the patient is referred for investigation.
   c. **True:** Allergic reactions are immune-mediated, with antibodies to the offending drug forming on mast cells and basophils, while in non-allergic anaphylaxis the drug causes mast cell and basophil degranulation by direct action.
   d. **True**: These rates are drawn from studies in France and Australia. The incidence of anaphylaxis during anaesthesia for the UK is being investigated by the current NAP6.
   e. **True:** A previous history of specific drug exposure is not necessary for anaphylaxis to occur, especially for neuromuscular blocking drugs

REFERENCES AND FURTHER READING

1. Safe Anaesthesia Liaison Group https://www.rcoa.ac.uk/salg (Accessed 14th November 2016)
2. Bodenham A et al. Association of Anaesthetists of Great Britain and Ireland: Safe vascular access 2016. Anaesthesia 2016;71:573-585 http://bit.ly/2dtSRbP (Accessed 14th November 2016)
3. The Joint Commission. Preventing Central Line–Associated Bloodstream Infections: Useful Tools, An International Perspective. 2013. http://www.jointcommission.org/CLABSIToolkit (Accessed 14th November 2016).
4. Bowman S, Raghavan K, Walker IA. Residual anaesthesia drugs in intravenous lines--a silent threat? . Anaesthesia. 2013;68:557-61 http://onlinelibrary.wiley.com/doi/10.1111/anae.12287/epdf (Accessed 14th November 2016)
5. NHS England. Stage One: Warning Residual anaesthetic drugs in cannulae and intravenous lines. 2014. https://www.england.nhs.uk/wp-content/uploads/2014/04/psa-residual-anaesthetic-drugs.pdf (Accessed 14th November 2016)
6. Christie LE, Picard J, Weinberg GL. Local anaesthetic systemic toxicity. British Journal of Anaesthesia Education 2015;15:136–142 http://bjaed.oxfordjournals.org/content/bjaed/15/3/136.full.pdf (Accessed 14th November 2016)
7. AAGBI Safety Guideline: Management of Severe Local Anaesthetic Toxicity. 2010. http://www.aagbi.org/sites/default/files/la_toxicity_notes_2010_0.pdf (Accessed 14th November 2016)
8. AAGBI Safety drill: Management of a patient with severe anaphylaxis during anaesthesia. 2009. http://www.aagbi.org/sites/default/files/ana_web_laminate_final.pdf (accessed 14th November 2016)
9. The Royal College of Anaesthetists National Audit Projects. http://www.rcoa.ac.uk/research/national-audit-projects (accessed 14th November 2016)
10. National Institute for Health and Care Excellence. Anaphylaxis: assessment and referral after emergency treatment. 2011. (https://www.nice.org.uk/guidance/cg134/resources/anaphylaxis-assessment-and-referral-after-emergency-treatment-35109510368965) (Accessed 14th November 2016)