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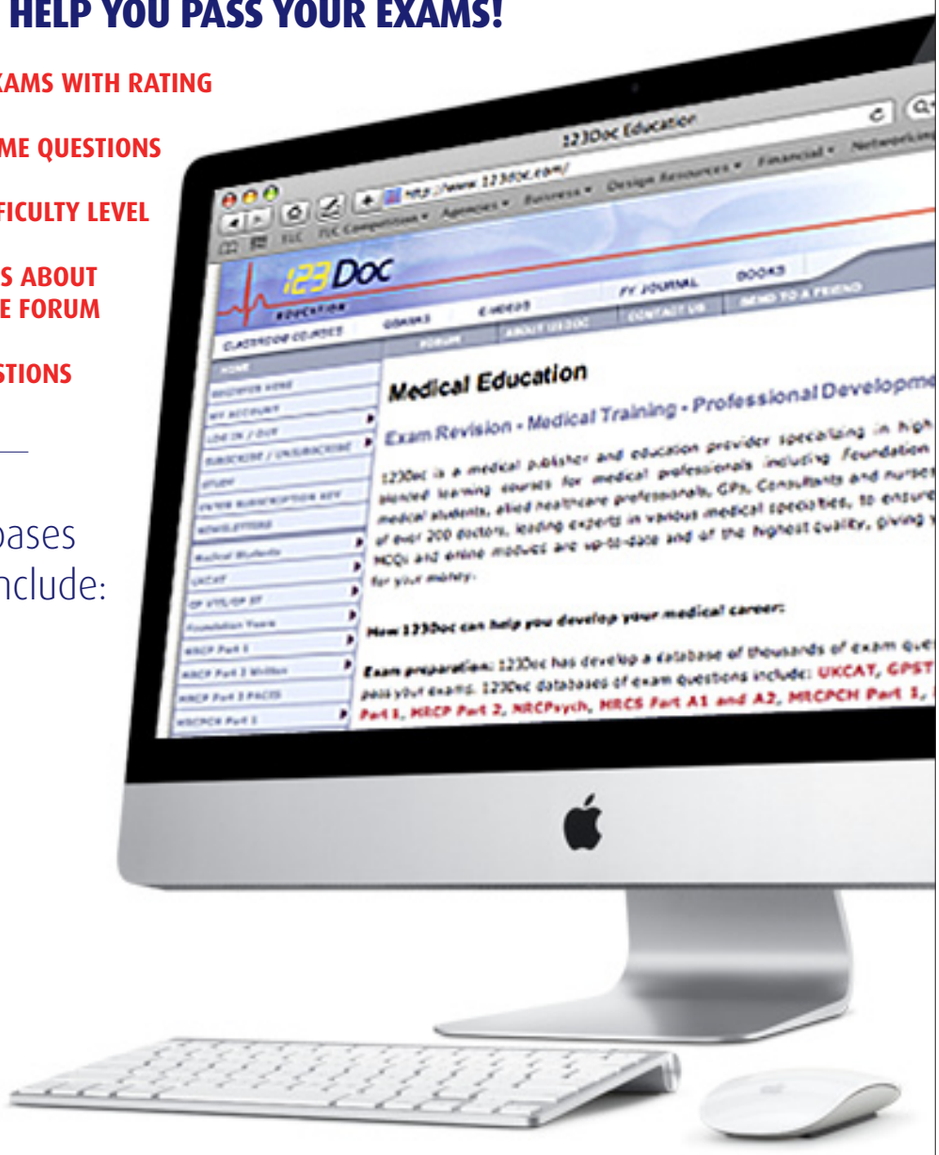

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CBD ANAPHYLAXIS

B Nzekwu, S James, R Byreddy

Abstract

Anaphylaxis is an acute and potentially life threatening condition with systemic reactions. It is a medical emergency that foundation doctors are likely to deal with. Prompt recognition and management is critical. We describe two case reports of patients that developed anaphylaxis with different presentations and progression. The first case demonstrates a patient who developed anaphylaxis under general anaesthesia and the second describes a case of food-triggered anaphylaxis.

Introduction

Anaphylaxis is an acute and potentially life threatening condition with systemic reactions. The incidence is approximately 50 to 2,000 cases per 100,000 persons and a lifetime prevalence of up to 2.0% (1) and between 1 per 10 -20,000 cases during anaesthesia (2)(3).

Anaphylactic reactions are mostly mediated through an immunological response involving immunoglobulin E (IgE) antibodies, which leads to mast cell and basophil activation and subsequent release of inflammatory cytokines. A proportion of anaphylaxis is classified as idiopathic where no identifiable cause is found. It is a medical emergency that foundation doctors are likely to deal with. Prompt recognition and management is critical.

We describe two case reports of patients that developed anaphylaxis with different presentations and progression.

Case 1

A 27 year-old female was admitted to a District General Hospital (DGH) for an elective diagnostic laparoscopy for infertility. She had no significant medical or drug history, history of atopy or known allergies. Her past anaesthetic history included an adenotonsillectomy, aged 14, which was uneventful. Airway examination was unremarkable. In the anaesthetic room, she was anaesthetised with Fentanyl 100mcg, Propofol 150mg and Atracurium 30mg (non-depolarising muscle relaxant) to facilitate tracheal intubation.

Bag mask ventilation was noted to be easy and a size 8-cuffed oral endotracheal tube was passed with a grade 1-laryngoscopy view. She was ventilated at a rate of 14 breaths per minute with sevoflurane, nitrous oxide and oxygen. She was then transferred to the operating theatre and the procedure was commenced. Prior to commencement, a prophylactic dose of intravenous Co-amoxiclav was given as per protocol for such procedures.

Approximately fifteen minutes into the procedure, her airway pressures were noted to be significantly raised with a peak pressure of 40cmH2O and was thought to be secondary to the pneumoperitoneum induced by the surgeon to aid the laparoscopy. The operating surgeon was notified and the insufflation pressure and flow was reduced. Five minutes later, with a persistent raised airway pressure, a sinus tachycardia of 150 beats per minute (bpm) was noted and a further dose of Atracurium and Fentanyl was given.

A few minutes later she developed severe hypotension of 62/38mmHg, a worsening tachycardia of 170bpm and decreased oxygen saturations (SaO2) of 85%. Inspired oxygen was increased to 100%, intravenous fluids (Hartmann's) administered and boluses of Metaraminol (sympathomimetic drug) were given up to 2mg to increase the blood pressure. No rash or urticaria was noted at this time. The hypotension and tachycardia persisted at 60/38mmHg and 174bpm respectively with worsening SaO2 at 79%.

Subsequently adrenaline (1:10000) 50mcg was given. The patient's blood pressure increased to 90/50mmHg and SaO2 increased to 94%. A presumed diagnosis of anaphylaxis was made and intravenous Hydrocortisone and Chlorphenamine was given. She required repeat adrenaline boluses to maintain her blood pressure hence a central venous catheter (CVC) was inserted in the right internal jugular vein and an arterial line in the left radial artery for monitoring with an adrenaline infusion commenced via the CVC. The procedure was abandoned and the patient transferred to Intensive Care Unit (ITU) ventilated.

She was gradually weaned off the adrenaline infusion, extubated two days later and discharged home the next day with specialist allergy service follow up where Co-amoxiclav was found to be the offending agent.

CBD ANAPHYLAXIS

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Case 2

A 56 year-old man presented to Accident and Emergency (A&E) as a precaution having mistakenly ingested a meal containing nuts. He was known to have a nut allergy with a past history of anaphylaxis for which he carried an Adrenaline auto-injector (EpiPen). His past medical history included hypertension and hypercholesterolaemia. There was no other known allergy. On examination, all his observations were found to be within normal parameters and physical examination was unremarkable. The plan was to observe him in the A&E for four hours and discharge him if he developed no new symptoms and his observations remained stable.

About two hours later, he developed tingling around his lips and slight difficulty in breathing. This subsequently worsened requiring the administration of oxygen via a non-rebreathing facemask. His SaO2 at this time was noted to be 91% despite 15L of oxygen. Within 20 minutes he had become hypotensive with a BP of 70/43mmHg and developed an audible wheeze, generalised urticaria, obvious facial swelling and worsening SaO_2 of 85%. He became unconscious very quickly and suffered a cardiac arrest. Cardiac resuscitation was commenced and an endotracheal tube inserted. He received several doses of adrenaline along with other resuscitative drugs.

Unfortunately resuscitation was unsuccessful and the patient was declared dead an hour later.

Discussion

Prompt recognition and management is of utmost importance to prevent further morbidity and mortality.

Clinical manifestations of anaphylaxis occur within minutes to hours of exposure to an allergen. However a delayed presentation can follow over a few hours.

The most common manifestations of anaphylaxis are cutaneous which include urticaria, pruritus, angioedema, flushing. Other clinical findings can be categorised into systems: Respiratory findings include dyspnoea, tachypnoea, hypoxia, wheeze, bronchospasm, stridor, rhinitis, lip or tongue swelling; Cardiovascular findings include hypotension, tachycardia, syncope, arrhythmias and cardiac arrest; Gastrointestinal findings include diarrhoea, nausea, vomiting, abdominal pains or cramps; Neurological findings include anxiety, headache, seizures and loss of consciousness.

Recognition of anaphylaxis in patients undergoing general anaesthesia can be difficult. Cutaneous signs are not easily noted and can be obscured by the surgical drapes. Ventilation, inhalation anaesthetics and the mode of ventilation can mask respiratory signs. Airway pressures can be raised as a result of a number of factors including gas insufflation, having a light plane of anaesthesia or being inadequately paralysed.

Additionally, drug-induced hypotension is quite common following induction of anaesthesia or neuraxial blockade. Hence when these manifestations present during anaesthesia, treatment is frequently given for a differential diagnosis before anaphylaxis is recognised. The first case demonstrates this and how it can easily be missed.

Other differentials that presents with signs and symptoms of anaphylaxis include vasodepressor reactions, severe asthma attacks, acute anxiety, poisoning, angioedema, hypoglycaemia, myocardial dysfunction, pulmonary embolism, foreign body aspiration and seizure disorders(5).

The second case describes a patient with food-triggered anaphylaxis. Anaphylaxis triggered by food can occur at any age. The most common food triggers are tree nuts, peanuts, shellfish, fish, milk, eggs and sesame(4).

However any food can cause anaphylaxis. It also emphasises how anaphylaxis or anaphylactic shock can have a delayed presentation following exposure to a known allergen. It can present with minor symptoms and rapidly progress to a critical situation. This was recognised and the patient was monitored for deterioration in signs and symptoms. Unfortunately, the outcome was poor though mortality from anaphylaxis is rare.

If clinically suspected, the treatment of anaphylaxis must be instigated rapidly. As a life-threatening emergency, within the initial resuscitation period, the key aim is the early administration of Adrenaline. The Resuscitation Council UK Anaphylaxis treatment algorithm outlines the chronological sequence of management steps.

Once stable, patients should be monitored in an appropriately staffed and equipped setting in case of acute deterioration. Even if initial response to treatment is good there is still a risk of early symptom recurrence. Biphasic reactions are the recurrence of symptoms within 72 hours without re-exposure to the triggering allergen(7). These subsequent reactions can vary widely in symptom severity and should be treated as for the initial presentation.

Given the underlying pathophysiology of anaphylactic reactions, timed blood samples for mast cell tryptase levels are required to confirm diagnosis. Ideally the first sample should be taken as soon as possible with caution not to delay initial resuscitative care. A second sample taken within 1-2 hours from onset of symptoms and a third after 24 hours for baseline mast cell tryptase levels should be obtained (6).

Prior to discharge, information regarding the signs and symptoms and action to take if anaphylaxis recurs should be thoroughly discussed with patients and their families, as well as informing their GP. Individual consideration for the need of an Adrenaline auto-injector along with a demonstration of correct technique of use is recommended. All patients should be referred for review at a specialist allergy centre to identify the specific allergen in order to reduce the risk of future events and enhance patient education.

CBD ANAPHYLAXIS

B Nzekwu, S James, R Byreddy

These cases along with discussion highlight the challenges clinicians face with recognising anaphylaxis and the importance of rapid resuscitation and management.

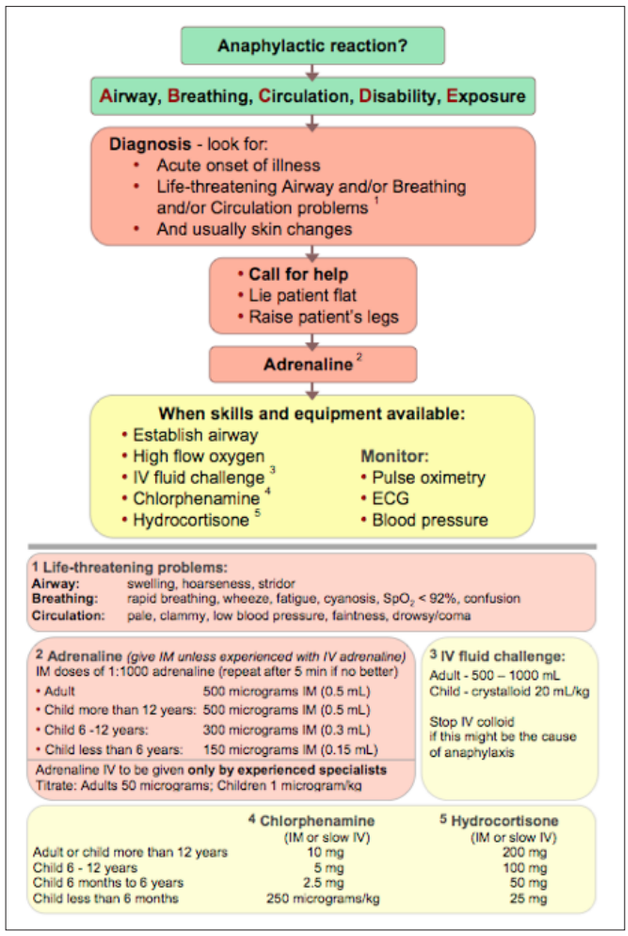

Figure 1. Anaphylaxis algorithm produced by the Resuscitation Council UK. 2008(6)

Test Yourself

1. From the following signs and symptoms, anaphylaxis usually presents with:

a. Hypotension
b. Tachypnoea
c. Urticaria
d. Stridor
e. Any of the above

2. Which of the following is NOT used in the initial management of suspected anaphylaxis?

a. Intravenous crystalloid fluids
b. Corticosteroids
c. Oxygen
d. Adrenaline (Epinephrine)
e. None of the above

3. What is the concentration of adrenaline given for intramuscular route?

a. 1:10000
b. 1:100
c. 1:1000
d. 1:100000
e. 1:1

4. Which group of immunoglobulins have a significant role in the development of anaphylaxis?

a. IgA
b. IgD
c. IgE
d. IgG
e. IgM

5. Which of the following needs to be completed in patients with a suspected severe anaphylactic reaction?

a. Provide patient information and support and notify the GP
b. Timed serum samples sent for mast cell tryptase
c. Referral to a specialist allergy service
d. Considered for an adrenaline auto-injector
e. All of the above

Answers

1. Answer is E.
The presentation of anaphylaxis can be varied as multiple systems can be affected. It must be noted that minor signs and symptoms can rapidly worsen resulting in a medical emergency. Correlation between relevant preceding history and progression of clinical picture will aid in the suspicion of, and therefore timely management of anaphylactic reactions.

2. Answer is B.
Corticosteroids have a delayed onset of action and do not relieve the initial symptoms of anaphylaxis. Corticosteroids prevent prolonged reactions and recurrence in the resuscitative period. They are useful for preventing anaphylaxis that can re-occur within 24 hours of the initial appropriate management (biphasic anaphylactic reactions).

CBD ANAPHYLAXIS

B Nzekwu, S James, R Byreddy

3. Answer is C.

In severe shock, the muscles may not be well perfused and adrenaline administered via the intramuscular route might not be adequately absorbed making the intravenous route more appropriate. Slow intravenous adrenaline (concentration of 1:10000) should be administered and by clinicians experienced in its use. A dose of 50mcg (0.5ml of 1:10000) is given initially with repeat boluses if needed titrated to response.

4. Answer is C.

The majority of anaphylactic reactions are a result of large amounts of pre-sensitized IgE antibodies binding to high-affinity (Fc) surface receptors on basophils and mast cells. Upon subsequent exposure to the allergen, the binding of the antigen to the IgE primed mast cells leads to degranulation releasing histamines, leukotrienes and other chemical mediators that result in the clinical presentation of anaphylaxis.

5. Answer is E.

Patients receiving emergency treatment for suspected anaphylaxis should be referred to a specialist allergy service and an adrenaline auto-injector given as an interim measure. Prior to discharge, patients should be given information on anaphylaxis and what to do should a reaction recur. The patient's GP should be informed.

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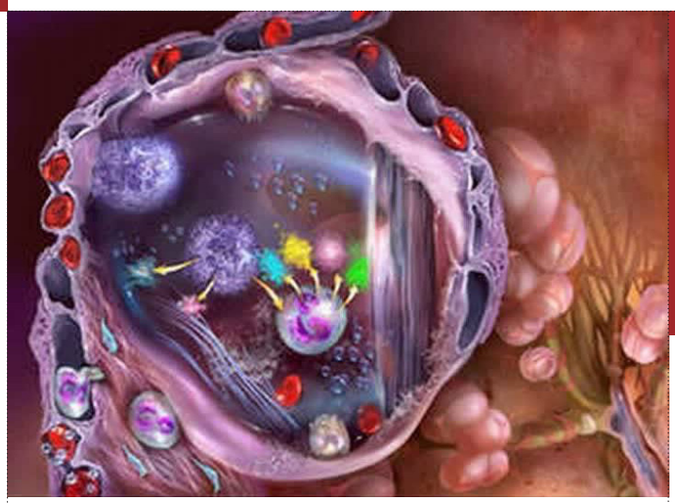
ARDS: WHEN BASIC MANAGEMENT FAILS, WHAT HAPPENS NEXT...

H Swinburne-Cloke, AR Davies, L Burrows



ARDS: When basic management fails, what happens next...
Patient Management

Abstract

Acute respiratory distress syndrome (ARDS) is an acute, diffuse, inflammatory lung injury. (1) The causes can be either primary (direct) or secondary (indirect), and commonly include pneumonia or sepsis.

Basic management focuses on achieving adequate oxygenation. Three main strategies are employed; lung protective ventilation (low tidal volumes), high PEEP (positive end expiratory pressure) and permissive hypercapnoea.

ARDS can prove to be refractory to basic management strategies and therefore extensive research has been carried out into more advanced techniques. One such intervention includes nursing the ventilated patient in a prone position. This is a relatively new technique with an increasing evidence base.

Whilst working on the Intensive Care Unit (ICU), we came across a young trauma patient who developed ARDS secondary to fat emboli from a femoral fracture. He deteriorated rapidly despite maximal ventilatory support. An improvement was only demonstrated after proning the patient.

In this article, we discuss the patient's management and reflect upon the new interventions that are being developed to manage ARDS; a condition that continues to carry a high mortality rate.

Case Report

A previously fit and well 19 year old male, Mr X, presented in the emergency department as a major trauma call after crashing his moped into a lamp-post at 30mph. An initial trauma CT revealed bilateral femoral fractures but no other injuries. He was taken straight to theatre for intra-medullary (IM) nail fixation.

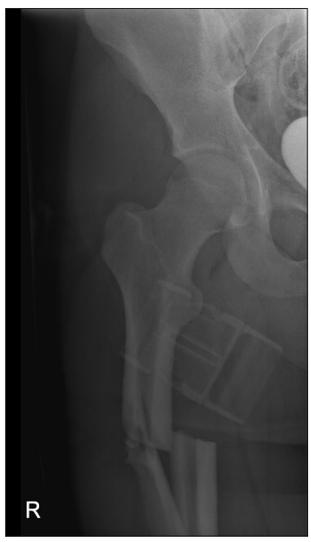


Figure 1

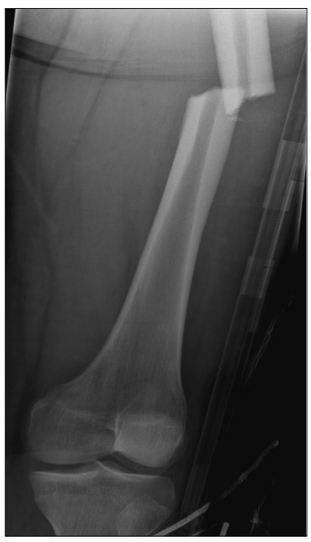


Figure 2

Twenty-four hours post-IM fixation, Mr X desaturated to 70% on room air. Despite the application of 10 litres of oxygen via a non re-breathe mask, he remained hypoxic (PaO_2 9.9kPa). His chest x-ray (CXR) was clear and a CT Pulmonary Angiogram excluded pulmonary embolus. However, the images were suggestive of multiple small fat emboli. He was transferred to ICU with a diagnosis of type 1 respiratory failure. (Hypoxaemic respiratory failure: PaO2 is less than 8kPa (60 mm Hg) with a normal or low $PaCO_2$).

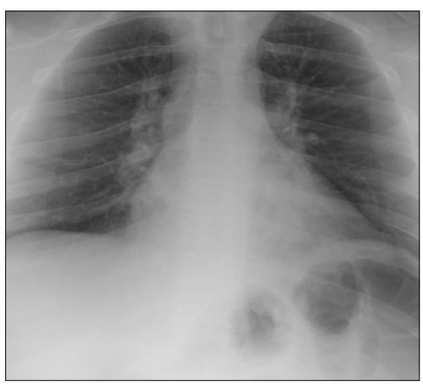


Figure 3

ARDS: WHEN BASIC MANAGEMENT FAILS, WHAT HAPPENS NEXT...

H Swinburne-Cloke, AR Davies, L Burrows

Initially, he maintained his saturations at 95% on high flow oxygen, (Fraction of inspired oxygen (FiO_2) 0.55) and chest physiotherapy, with only occasional episodes of desaturation (as low as 84%). However, over the next 48 hours his oxygen requirements continued to increase up to 100%, whilst only maintaining oxygen saturations of 89%. He began to tire and a portable CXR revealed bilateral pulmonary infiltrates consistent with ARDS. The decision was made to intubate and ventilate. He was managed on volume controlled ventilation (synchronized intermittent mandatory ventilation- SIMV) using lung protective ventilation with a PEEP of 12 cmH_2O and FiO_2 of 0.55.

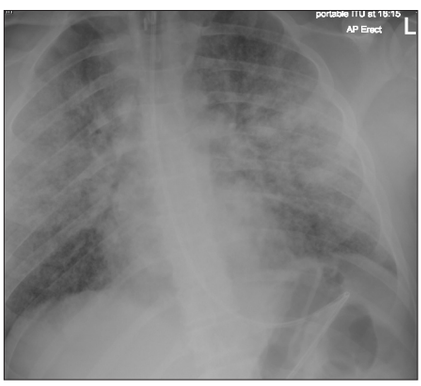


Figure 4

Initially, adequate oxygenation was maintained but over the next 24 hours his condition began to deteriorate. To achieve a PaO_2 of only 11.5kPa, his FiO_2 had to be increased to 0.7 . A repeat CXR showed progression of his pulmonary infiltrates. He fulfilled the criteria of moderate ARDS; acute onset hypoxia of respiratory origin, PaO_2/FiO_2 ratio of 16.4 kPa (123 mmHg), bilateral opacities on his CXR and PEEP 12 cmH_2O. Despite maximal therapy,

Mr X continued to deteriorate and the decision was made to use prone ventilation. He was turned prone for 18 hours at a time, before returning to the supine position.

Within 48 hours his FiO_2 requirements to maintain adequate oxygenation dropped to 0.45, but he remained dependent on high levels of PEEP. Proning was used as an intervention for 3 days; he was extubated after 5 days.

This appeared to improve Mr X's oxygenation. He was discharged from ITU 3 days post-extubation. He made a full recovery and was discharged from hospital a few days later with no residual deficits.

Discussion

ARDS is an acute, diffuse, inflammatory lung injury (1) which can be caused by direct injury to the lung (primary) or secondary to severe systemic illness. Severe lung damage and release of mediators of inflammation cause increased pulmonary vascular permeability, increased lung weight and a loss of aerated tissue. (1) This is often associated with multi-organ failure.

Causes of ARDS

Primary	Secondary
Pneumonia – bacterial or viral	Sepsis
Severe Chest Trauma (Pulmonary contusions)	Acute pancreatitis
Inhalation of vomit (aspiration), smoke or toxic chemicals	Transfusion Related Acute Lung Injury (TRALI)
Drowning	Burns

Figure 5

ARDS is a spectrum of disease that can present in severe forms on the ICU, but many milder cases may be present on the hospital wards. However, most patients in the moderate-severe category require mechanical ventilation. It is diagnosed using the Berlin definition below (1).

ARDS

	Mild	Moderate	Severe
Timing	Acute onset within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Hypoxemia	PaO_2/FiO_2 201–300 with PEEP/CPAP ≥ 5	PaO_2/FiO_2 ≤ 200 with PEEP ≥ 5	PaO_2/FiO_2 ≤ 100 with PEEP ≥ 10
Origin of Edema	Respiratory failure associated to known risk factors and not fully explained by cardiac failure or fluid overload. Need objective assessment of cardiac failure or fluid overload if no risk factor are present		
Radiological Abnormalities	Bilateral opacities*	Bilateral opacities*	Opacities involving at least 3 quadrants*
Additional Physiological Derangement	N/A	N/A	$V_{E\,Corr}$ > 10 L/min or C_{RS}<40 ml/cmH_2O

*Not fully explained by effusions, nodules, masses, or lobar/lung collapse; use training set of CXRs; $V_{E\,Corr} = V_E \times PaCO_2/40$ (corrected for Body Surface Area)

Figure 6 (1)

ARDS: WHEN BASIC MANAGEMENT FAILS, WHAT HAPPENS NEXT...

H Swinburne-Cloke, AR Davies, L Burrows

In ARDS there are a number of basic management strategies involving lung protective ventilation; low tidal volume (6ml/kg), plateau pressure < 30cmH_20, the use of PEEP and permissive hypercapnoea. (Allowing the carbon dioxide level to rise above normal levels to facilitate low tidal volume ventilation).

In ARDS, lung compliance is lower, which causes higher pressures to be required to deliver the same tidal volume on a ventilator. This increases the risk of ventilator associated lung injury, including a higher risk of pneumothoraces. The use of lung protective ventilation (tidal volume of 6 ml/kg) has been demonstrated to reduce mortality from 40% to 31% and also reduce the length of time a patient spends on a ventilator. (3) Lung protective ventilation is therefore a cornerstone in the management of ARDS.

The use of PEEP in the management of ARDS is controversial. Patients will typically have a high requirement due to the extent of alveolar collapse. Theoretically, a high PEEP would increase alveolar recruitment and thus improve oxygenation. However, trials have produced mixed results, with some showing no improvement in mortality (4). A more recent meta-analysis suggests that a high PEEP is beneficial in terms of mortality in patients with moderate-severe ARDS (5), hence Mr X was put on higher levels of PEEP.

The mortality rate in ARDS is high, with figures as high as 67% quoted in some studies (6). ARDS has also been shown to be refractory to basic management strategies, therefore extensive research has been carried out on alternative techniques. The following table demonstrates current strategies; those in blue having a greater evidence base.

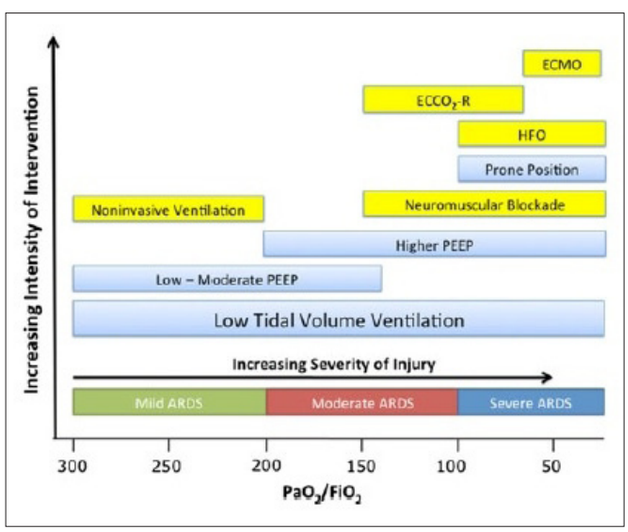


Figure 7 (1)

There is also some evidence to support the use of muscle relaxation in early severe ARDS for the first 48 hours (7). If these strategies fail, prone positioning is considered.

Proning is thought to improve ventilation-perfusion matching, which is a significant problem in ARDS; the degree of lung collapse and amount of blood flow are greatest in the same place: the dependent portions of the lung i.e. there is no oxygen getting to the areas with highest blood flow. When a patient is proned, the previously collapsed alveoli begin to re-open, but the blood flow to that area remains unchanged (being independent of gravity), thus improving oxygenation.

Initial trials had not shown a benefit in mortality; however, they included patients with only mild ARDS and were often proned for short periods of time (6-8 hours). (8) Complications such as pressure sores also reduced enthusiasm for the technique. However, there is now sufficient evidence to support its use. (9)

In the PROSEVA study (10), they randomised patients with severe ARDS (PaO_2:FiO_2<150 in this case) and proned patients for at least 16 hours. Those who were proned had a decreased 28 days mortality (16% vs 33%) with a p-value of <0.001. There was no difference in adverse outcomes between the 2 groups; in fact there was a lower incidence of cardiac arrest in the prone group. (10)

Although proning does not work for all patients and there are a number of contraindications (e.g. raised intra-cranial pressure, haemodynamic instability, recent abdominal surgery), it has proven to be a useful adjunct in patients with severe refractory hypoxaemia. It appeared to be a very useful technique for the management of refractory hypoxia in Mr X.

Lastly, should treatment have failed in this case, he would have been referred to a specialist respiratory centre for ECMO (Extra-Corporeal Membrane Oxygenation). An example of the current referral pathway is demonstrated below:

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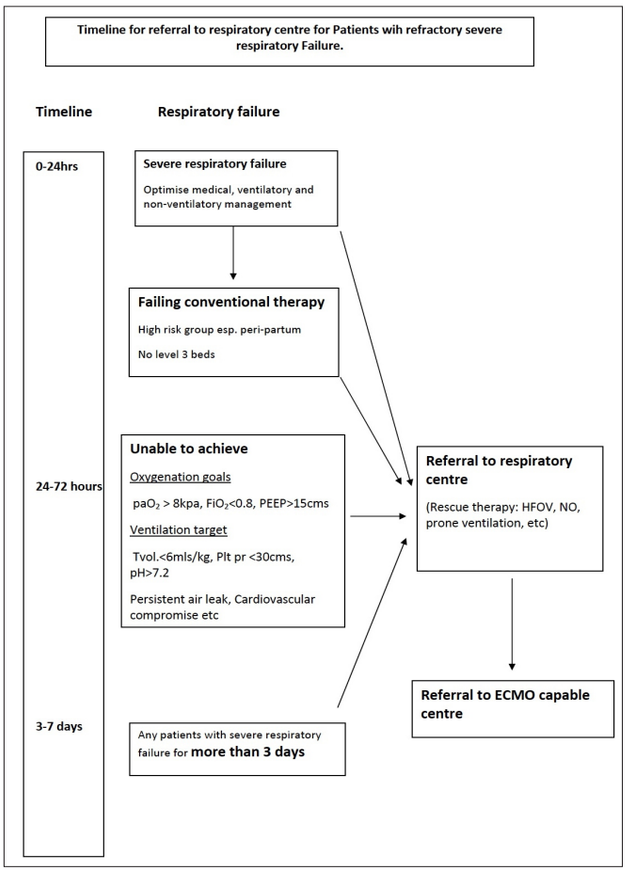

Figure 8 (11)

MCQs

1) What is the best strategy for ventilation in a patient with severe ARDS?

a. High tidal volume, high PEEP and permissive hypercapnoea
b. Low tidal volume, high PEEP and permissive hypercapnoea
c. Low tidal volume, low PEEP and normocapnoea
d. Low tidal volume, high PEEP and normocapnoea
e. High tidal volume, low PEEP and normocapnoea

2) Which of these is not a known cause of ARDS?

a. Myocardial Infarction (MI)
b. Pancreatitis
c. Fat emboli
d. Sepsis
e. Pneumonia

3) Which of the following cases would fit the criteria for moderate ARDS?

a. A 75 year old female develops worsening shortness of breath after being admitted to hospital with pneumonia. She is found to be hypoxic with a PaO_2/FiO_2 of 170 mmHg and her chest xray reveals unilateral changes consistent with pneumonia.
b. A 48 year old year man is admitted with necrotising fascitiis and septic shock. A chest xray reveals extensive bilateral opacification. His PaO_2/FiO_2 is 88 mmHg. He is intubated and requires ventilation with a PEEP of 12cm H_2O.
c. A 67 year old lady is admitted to the ICU with severe acute pancreatitis. She is intubated and ventilated with a PEEP of 7cm H_2O due to type 1 respiratory failure. A chest xray reveals bilateral pulmonary infiltrates and her PaO_2/FiO_2 is 130 mmHg.
d. A 58 year old is admitted to ICU after becoming acutely short of breath following a blood transfusion. He is intubated and ventilated with a PEEP 3 cmH2O. His PaO_2/FiO_2 is 165 mmHg. A chest X-ray reveals bilateral pul-monary changes.
e. An 88 year old female is admitted following a neck of femur fracture. She deteriorates rapidly on day 1 post-operatively, requiring high flow oxygen on the ward. Her PaO_2/FiO_2 is 266 mmHg. A chest xray shows changes con-sistent with ARDS.

Answers

1. The answer is B.
Low tidal volume, high PEEP and permissive hypercapnoea. Lung compliance is reduced in ARDS and therefore normal tidal volumes require higher pressures, which would increase the risk of ventilator associated lung injury. A high PEEP increases the oxygenation by increasing alveolar recruitment. Both permissive hypercapnoea (12) and high PEEP are associated with reduced mortality as part of lung protective ventilation.

2. The answer is A.
Myocardial infarction. Although heart failure as a result of an MI can often mimic ARDS, in particular the appearance on CXR, it is not a recognised cause. Pneumonia is an example of a primary cause, and is one of the commonest causes of ARDS. Pancreatitis, sepsis and fat emboli are all known secondary causes of ARDS, sepsis being the most common secondary cause.

3. The answer is C.
To fulfill the moderate criteria, a patient must have a PaO_2/FiO_2 ratio of 101-200 mmHg, with a PEEP of 5 or more. There must be bilateral opacities on the chest xray, and the onset must be within a week of a known clinical insult.

ARDS: WHEN BASIC MANAGEMENT FAILS, WHAT HAPPENS NEXT...

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CASE BASED DISCUSSION: ENHANCED RECOVERY AFTER ORTHOPAEDIC SURGERY

D Hewson, S Jassim, S Sarkar

Case Based Discussion: Enhanced Recovery After Orthopaedic Surgery
Patient Management

Abstract

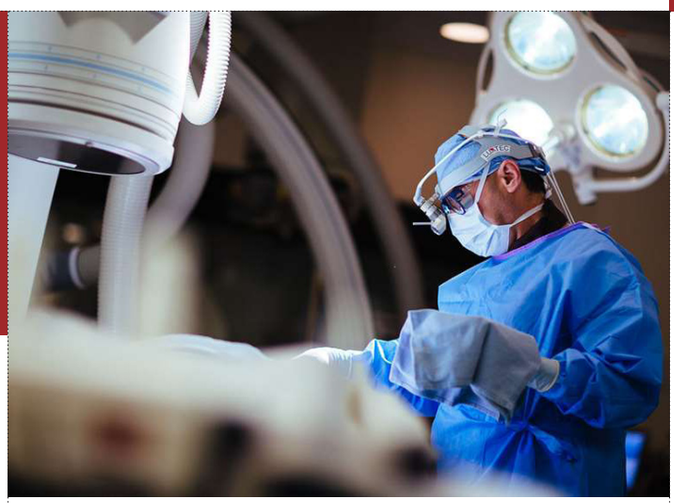
A 77 year-old man presents for elective major joint surgery. He has concerns that major surgery will not be feasible due to the disruption it will cause to his caring responsibilities for his wife, who suffers from severe dementia. His peri-operative pathway is described and the principles of enhanced recovery after orthopaedic surgery are explained. These give him the best chance to return to optimal function as soon as practicable within current perioperative practice.

Case History

A 77 year-old man, Mr N, is referred by his general practitioner (GP) to the orthopaedic surgeons due to chronic, progressive left knee pain relieved by rest. He has a hypertension controlled with lisinopril and is intolerant of aspirin due to gastric irritation. He also takes paracetamol, tramadol, bisoprolol, simvastatin and clopidogrel regularly. He is a fulltime carer for his wife, who has severe dementia. His knee pain is disabling in this regard because he finds it difficult to assist his wife with her basic care needs.

On examination he has evidence of osteoarthritis in his hands and his knees. His left knee has a slight varus deformity with reduced range of movement and significant joint crepitus. Weightbearing plain radiographs confirm tri-compartmental loss of joint space with sclerosis and osteophytosis. The patient is counseled regarding the diagnosis of osteoarthritis. Given the severity of his functional loss a total knee replacement is suggested to him as a suitable treatment. The patient has concerns regarding his ability to care for his wife in the post-operative period. The surgical team address this by explaining the enhanced recovery pathway after orthopaedic surgery.

Mr N is given an appointment at a pre-operative assessment outpatient clinic. He fills out a medical health questionnaire that reduces duplications of questioning by staff. A nurse specialist undertakes a medical assessment to determine his suitability for surgery and identify modifiable risk factors. The nurse records his pulse rate, blood pressure, oxygen saturations, weight and height. She takes blood for full blood count, renal function, serum group and save and records an electrocardiogram (ECG). He is given verbal and written information about the surgery, anaesthetic and recovery process. He is asked to continue physiotherapy exercises to improve quadriceps strength up until surgery because these will assist with post-operative joint function.



A medical plan is made regarding pausing his clopidogrel for the perioperative period. He is invited to the 'joint school' where he meets other patients to learn about pre- and post-operative exercises and realistic expectations of the immediate postoperative period. Mr N is admitted to a surgical pre-admission lounge on the day of surgery.

He is instructed that he can eat until 2am and continue drinking water until 6am on the day of his admission. He is given a high calorific drink to take on the evening before surgery and on the morning of surgery. Before surgery his procedural consent is rechecked and operative limb marked. He is reviewed by the anaesthetist who explains his anaesthetic technique. He is given 300mg of gabapentin and 1g of paracetamol pre-operatively.

A few hours later, Mr N is brought to the theatre complex and the World Health Organisation perioperative safety checklist is commenced. A 16G peripheral venous cannula is inserted, monitoring commenced and a single-shot spinal anaesthetic of 2.5ml levo-bupivacaine performed. The anaesthetist then performs a saphenous nerve block using an ultrasound-guided sub-sartorial canal approach. Gentamicin 2mg/kg and flucloxacillin 2g are administered as antibiotic prophylaxis.

Surgery proceeds uneventfully and during the operation Mr N is given 8mg ondansetron, 1g tranexamic acid and 1litre of intravenous balanced crystalloid solution. He received a target-controlled infusion of propofol 1% for intra-operative sedation, titrated to effect. He remains responsive to verbal commands and is able to maintain his airway patency throughout. The surgeon infiltrates 3mg/kg of ropivacaine in a targeted fashion to the posterior joint capsule and to the subcutaneous tissues around the knee joint.

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Post-operatively Mr N is admitted to the elective orthopaedic unit and prescribed regular paracetamol 1g q.d.s., 300mg gabapentin t.d.s. for a maximum of 5 days, slow-release oral morphine 20mg b.d. for 3 days and two further doses of antibiotic prophylaxis. Regular antiemetics (ondansetron 4mg tds) and aperients (senna and lactulose) are prescribed too. He is prescribed immediate–release oral morphine solution 0.3mg/kg as required. He is prescribed enoxaparin 40mg subcutaneous once per day while in hospital, to be followed by a 14 day course of rivaroxaban for venous thromboembolism prophylaxis.

His analgesic regime allows mobilization physiotherapy to commence on the afternoon of surgery and daily thereafter. He is discharged on the second post-operative day. To assist with the care of his disabled wife Mr N, together with his GP, arranged a short course of respite care while he continued to recover at home from his surgery.

Discussion

Enhanced recovery after surgery (ERAS), also known as fast track surgery, is the use of multimodal perioperative interventions to decrease post-surgical organ dysfunction and complications and thereby improve post-operative recovery. The principles of ERAS have been adapted and applied to patients undergoing a wide variety of surgical procedures including colorectal1, day-case, vascular, cardiac surgery and orthopaedic surgery. ERAS encompasses clinical domains across the peri-operative period.

Patient Education & Support

Patients who are well informed about their treatments, and actively engage in their surgical and recovery process, are likely to recover sooner and more fully than those who are not (2,3). Mr N was counseled at several points in the pre-operative period, given written information to reinforce his consultations and invited to a multidisciplinary joint school. This is sometimes referred to as prehabilitation.

Pre-operative assessment

Identifying appropriate patients for ERAS is vital. Surgical units should develop multidisciplinary, locally agreed criteria for patient selection and ensure these are disseminated and understood by primary care colleagues to ensure suitable patient referral. A governance framework is necessary to monitor the success of the programme once it is implemented.

Patients should undergo multidisciplinary pre-operative assessment with referral to relevant sub-specialty colleagues if pre-optimisation of medical co-morbidities is thought possible. Ideally these should be addressed in primary care prior to surgical referral. Investigations should be limited to those whose results are likely to change subsequent management or to establish baseline values in those patients with particular risks (4).

Peri-operative management

Peri-operative anaesthetic management is specifically focused on facilitating early mobilization. Patients should be admitted on the day of surgery to a dedicated elective area. To minimize physiological disturbance fasting times are kept to a minimum and patients are given calorific drinks to take prior to surgery. Analgesia is commenced in the pre-operative period. Spinal anaesthesia provides excellent operative conditions, contributes to post-operative analgesia and avoids the risks associated with general anaesthesia.

It is often supplemented with conscious sedation, in this case using a pharmacokinetic-modeled, titrated infusion of propofol. In order to reduce post-operative opioid consumption, the spinal is additionally supplemented with a motorsparing nerve block of the femoral nerve at its saphenous component, together with high-volume low-concentration peri-articular infiltration of local anaesthetic (5).

Regional anaesthesia has been shown to offer improved analgesia with fewer side effects compared to systemic analgesics administered as part of a general anaesthetic6. Tranexamic acid and antibiotics are given toreduce bleeding and infection risks respectively. Intra- and post-operative analgesia is multimodal for all patients and consists of oral non-opioid agents, adjuvant analgesics such as gabapentin and long acting opioids. Venous thromboembolism risk reduction can now be undertaken with oral agents and mechanical prophylaxis in addition to traditional subcutaneously delivered heparins.

Post-operative care

The aim is to mobilize the patient on the same day as surgery. Patients should be encouraged to eat and drink normally as soon as practicable after their surgery. Post-operative intravenous fluid administration should be reserved for those patients with specific medical indications since routine fluid supplementation is clinically unnecessary and can impede post-operative mobilization. Indications such as unexpected deterioration in renal function or inability to drink due to ongoing nausea should be managed on a case-by-case basis.

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Physiotherapy, nursing and occupational therapy specialists focus on the post-operative phase in returning the patient to mobility and providing the patient with the tools to return to their homes as easily as possible (7).

Close liaison with primary and social care services is sometimes required to ensure successful discharge from hospital. Patients are discharged with clear pathways for re-assessment and readmission, should they encounter unexpected problems during the at-home phase of their recovery.

Conclusion

ERAS cannot be applied to all patients undergoing orthopaedic surgery, but the principles described above will facilitate the perioperative pathway for all patients undergoing all major surgery. The most important aspects of ERAS care can perhaps be summarized as preoperatively: to optimize medical comorbidities; intra-operatively: to minimize the physiological stress of surgery; and post-operatively: to engage with the multidisciplinary team to assist recovery.

MCQ 1

The following are true of orthopaedic enhanced recovery programmes:

1. Patients require multidisciplinary pre-operative assessment to determine suitability and physiological optimisation.

2. General anaesthesia is precluded because it delays recovery from theatre and mobilization on the ward.

3. American Society of Anaesthetist Grade 3 and 4 patients are not suitable for inclusion in enhanced recovery programmes.

4. Pre-operatively general practitioner should refer patients for consideration of surgery but have no role to play in pre-optimising patients for surgery.

5. Spinal anaesthesia in this setting requires the insertion of a urinary catheter to assist micturition post-operatively.

Orthopaedic enhanced recovery pathways are designed to facilitate early, safe discharge from hospital following major orthopaedic surgery. Interventions are applied across healthcare specialties to support early mobilization after joint surgery. Anaesthetic techniques, such as general or regional anaesthesia are tailored with this goal in mind and often regional anaesthesia provides superior outcomes in this setting. In some circumstances (for example in the presence of a contra-indication to regional anaesthesia) general anaesthesia can be delivered in an orthopaedic enhanced recovery context.

Patients of any physiological and medical background can be considered for inclusion in an enhanced recovery programme, including those who could be classified as ASA 3 or 4. Primary care has a key role to play in the treatment of modifiable chronic diseases prior to surgery, since the optimisation of conditions such as hypertension and diabetes reduces the risk of post-operative complications that delay recovery. Spinal anaesthesia does not routinely require insertion of a urinary catheter in this setting.

MCQ 2

The following are true in the pre-operative work-up of a patient for total knee replacement under an orthopaedic enhanced recovery programme:

1. All patients require an electrocardiogram to identify occult pre-existing heart disease.

2. Patients cannot undergoing anaesthesia if their pre-operative systolic blood pressure exceeds 180mmHg.

3. Patients with type 1 diabetes will always require a sliding scale in the operative period.

4. Clopidogrel, at any dose, should be stopped 7-10 days prior to surgery.

5. In the absence of cardiac co-morbidities a haemoglobin of less than 80g/l is a reasonable transfusion trigger.

Pre-operative tests should always be focused on assisting clinical decision-making for specific patients. Electrocardiograms are not required in all patients and they are an insensitive identifier of occult cardiac disease. Patients with diabetes will not always require a sliding scale in the peri-operative period unless their surgery interferes with their usual ability to eat and drink and receive subcutaneous insulin.

Clopidogrel is a potent, irreversible anti-platelet agent that inhibits clot formation. It should always be stopped in the elective setting, although in the presence of recently inserted coronary arterial stents it may be necessary to institute an alternative, more easily reversible, anticoagulant. There is ongoing debate about appropriate transfusion triggers in the setting of elective orthopaedic surgery, a trigger of less than 80g/l is sensible in most patients presenting for joint arthrodesis.

CASE BASED DISCUSSION: ENHANCED RECOVERY AFTER ORTHOPAEDIC SURGERY

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Answers

Question 1

1. T 2. F 3. F 4. F 5. F

Question 2

1. F 2. F 3. F 4. T 5. T

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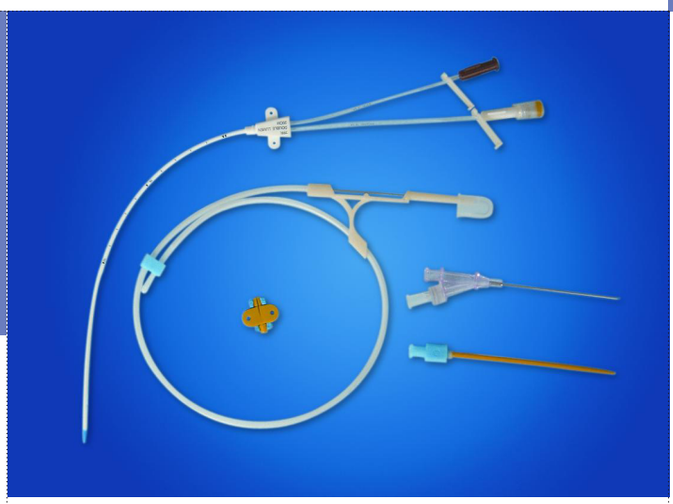
INSERTION & CARE OF CENTRAL VENOUS CATHETERS

DP Fraser, E Bradley, BJ Jenkins

Insertion & Care of Central Venous Catheters
Practical Procedures



Introduction

A central venous catheter (CVC) is a device that is inserted into the superior vena cava. Central venous catheterisation was first performed in 1929 and is now common practice in a variety of health care settings (1). Although CVCs may be inserted by any doctor who has been trained and competency-assessed, the majority are inserted by anaesthetists and intensivists to be used in the high dependency setting. Knowledge of the indications and care of CVC lines is, however, essential knowledge for any foundation doctor.

History

The patient was 79 years old, and had an emergency laparotomy for perforation of the large bowel due to a ruptured diverticulum. The CVC was inserted in the anaesthetic room of an operating theatre prior to surgery. The aim was to infuse inotropic drugs via the CVC during surgery and on the high-dependency unit following surgery. It would also provide a route for intravenous feeding as required. Because of the requirement for infusions of drugs and feeding, a multi-lumen CVC was inserted into the right internal jugular vein.

Indications

The majority of CVCs are inserted for therapeutic purposes that include the administration of potent or IV drugs with high osmolality that cannot be given through peripheral venous cannule. Common examples include inotropes such as noradrenaline and dopamine (in an intensive care setting), total parenteral nutrition infusions and chemotherapy agents (1,2,3). CVC insertion techniques are also used for the placement of haemofiltration catheters in renal failure and the placement of temporary cardiac pacing wires. Poor peripheral access is another common indication in conditions such as obesity, chronic intravenous drug use etc. where suitable veins may be difficult to locate (1,2,3).

The diagnostic role of central venous pressure measurement has declined in recent years. Historically, CVCs were inserted for measurement of central venous pressure to aid the assessment of fluid status, but central venous pressure has been proven to be a poor indicator of intravascular status and fluid requirements (1).

CVCs may also be useful in patients requiring repeated blood sampling, but peripheral venepuncture is preferred to reduce the risk of line infection (1).

Contraindications

There are no absolute contraindications to CVC insertion and the procedure may be lifesaving. However, there are numerous conditions that increase the risk associated with placement (2).

Anatomical variation can limit the success of insertion and/or increase the risk of complications. Patient conditions that may affect anatomy include morbid obesity, congenital abnormalities, and local problems such as burns or tissue infection at the intended site of CVC insertion (1,2). Patients with hyperinflated lungs, either due to chronic obstructive pulmonary disease or mechanical ventilation are at increased risk of developing a pneumothorax. Patients with pre-existing pneumothoraces should not have CVC lines placed on the contralateral side because of the risk of a second pneumothorax (1,2).

Although coagulation disorders increase the risk of haemorrhage during CVC placement, with careful site selection and good technique, complications due to haemorrhage can be kept to a minimum (2). As haemorrhage from the subclavian vein cannot be easily controlled by direct pressure, the subclavian vein is usually deemed unsuitable for CVC insertion in patients with bleeding diatheses (2).

Anatomy

CVCs can be inserted into the internal jugular, subclavian or femoral veins. This article focuses on insertion into the internal jugular vein, as it is the most popular site. Traditionally, insertion has been performed “blind” by using surface anatomical markers in the neck (“landmark technique”). Utilising knowledge of the vascular anatomy, the physician would palpate the carotid artery, aiming the needle close to but lateral to the pulse, between the heads of the sternocleidomastoid muscle at the level of the cricoid cartilage.

INSERTION & CARE OF CENTRAL VENOUS CATHETERS

DP Fraser, E Bradley, BJ Jenkins

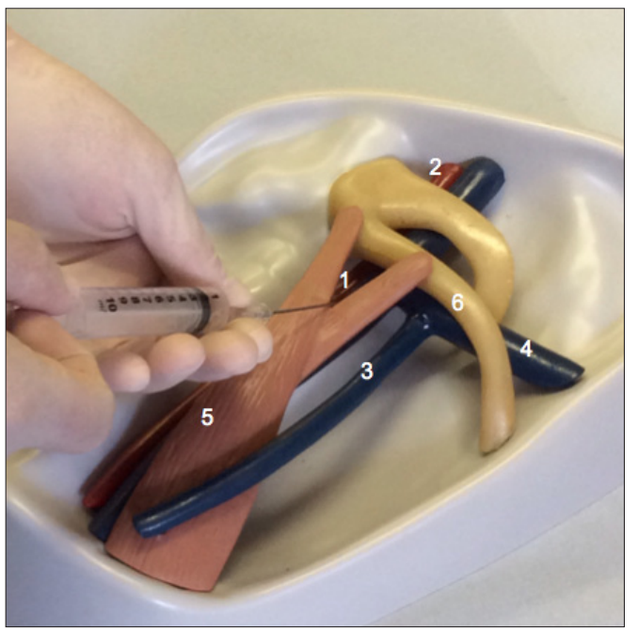


Figure 1: Anatomy of the major neck veins showing insertion site for CVC into the internal jugular vein (1). Also pictured: common carotid artery (2) external jugular vein (3) subclavian vein (4) sternocleidomastoid (5) clavicle (6).

Due to increased risk of failure and complications this technique has been largely replaced by ultrasound-guided insertion, which is now the recommended method (3). In up to 5% of patients, the internal jugular vein is not found in the expected anatomical location (anterolateral to the common carotid artery), so a landmark technique would be expected to fail in these patients (4).

The use of an ultrasound probe allows the physician to identify any anatomical variation in the position of the internal jugular vein and to insert the needle into the internal jugular vein with direct visualisation.

Procedure

Continuous electrocardiographic monitoring and pulse oximetry is required during insertion. The equipment needed is shown in Figure 2.

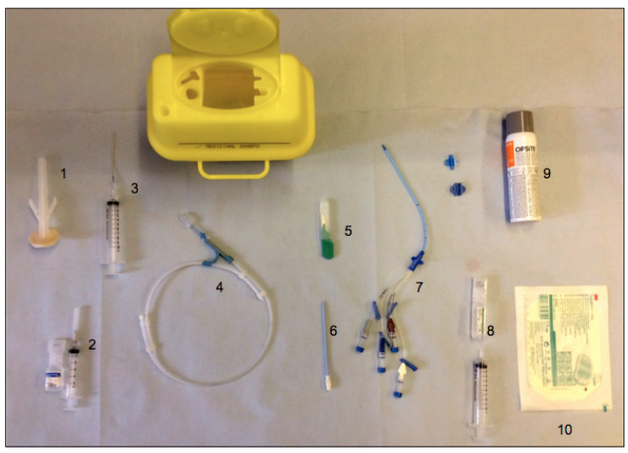


Figure 2: Equipment required for CVC insertion. 1) Chlorhexidine swab 2) Local anaesthetic 3) Needle and syringe 4) Guidewire 5) Scalpel 6) Introducer 7) CVC line 8) 0.9% slaine flush 9) Aerosol spray dressing 10) Dressing Not pictured: Sterile drape, sutures for securing line.

The patient is positioned in the Trendelenburg position, with feet up and head down in order to increase neck vein size and make insertion easier. The ultrasound probe is used to identify the relevant landmarks in the neck such as the muscles, trachea, carotid artery and the internal jugular vein. The internal jugular vein is seen as a compressible large vessel lateral to and partially overlying the carotid artery.

Because of the high internal pressure, the carotid artery is visualised as a round vessel whereas the internal jugular vein is less regular in shape. The right internal jugular vein is preferred over the left, as it is a short route to the superior vena cava and is usually easier for right-handed operators. Asking the patient to perform a Valsalva manoeuvre may aid identification of the internal jugular vein, as it causes an increase in venous pressure, making it easier to distinguish the carotid artery from internal jugular vein .

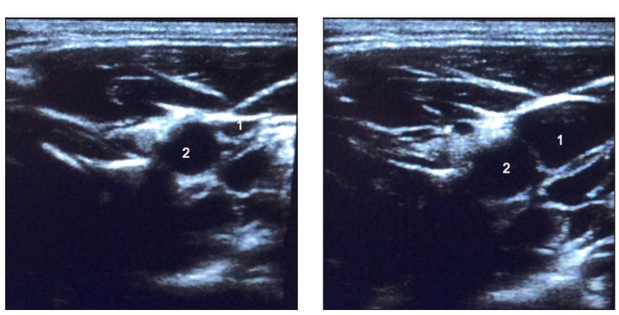


Figure 3: Ultrasound showing the anatomy of the neck on the left side. 1) internal jugular vein 2) common carotid artery. The internal jugular vein is pictured before (left) and during (right) a Valsalva manoeuvre.

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Figure 4 demonstrates the insertion procedure. Full aseptic technique is required. The area is cleaned followed by sterile draping. Sterile gown, cap, mask and gloves should be worn, and the ultrasound probe enclosed in a sterile sheath. Local anaesthetic is used to infiltrate the venepuncture site and is also required for suturing the catheter in place following insertion.

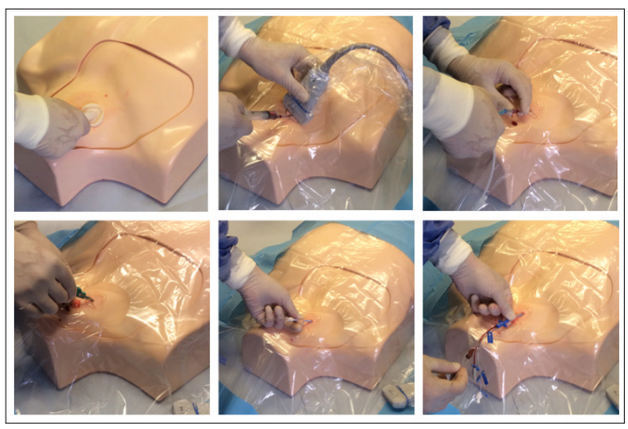

Figure 4: Insertion of CVC into internal jugular vein. From top left, in order: 1) cleaning of site 2) insertion of needle into internal jugular vein with ultrasound guidance 3) insertion of guidewire 4) incision with scalpel 5) dilation of entry site 6) insertion of CVC into jugular vein over guidewire.

A Seldinger technique for catheter insertion is usual. Under ultrasound guidance the operator advances a needle attached to a small syringe into the desired vein, holding the needle at 45 degrees to the skin and typically aiming towards the ipsilateral nipple to avoid carotid artery puncture. The syringe is inserted whilst continuously attempting to aspirate until blood is visualised in the barrel of the syringe, then the syringe is removed leaving the needle in place.

A J-ended guidewire is threaded through the needle into the vein, then the needle is removed leaving only the wire in place. A small incision is made at the site of puncture followed by a dilator to widen the insertion point. The catheter is then railroaded over the wire into the vein. Once the catheter is correctly positioned (15cm for right internal jugular, 18 cm for left at skin) the wire is removed, the catheter aspirated and flushed with 0.9% sodium chloride and then the whole catheter sutured in position. The skin is then cleaned with topical antiseptic, and after drying dressings are applied to maintain sterility at the point where the catheter enters the skin (1,2).

Complications

CVC insertion is not without risk, with up to 15% of insertions resulting in complications (1,2). Complications of central venous catheterisation can be divided into immediate and delayed, then further subdivided into mechanical, embolic and infectious (1). Strict attention to insertion technique, aided by an informed and calm patient helps to facilitate safe catheter placement (2).

Arterial puncture, pneumothorax and haematoma are the most common immediate mechanical complications associated with insertion (3). The intended site of catheter tip placement should be close to the junction of the superior vena cava and right atrium, and this should be confirmed by X-ray. Arrhythmias are a common complication during insertion due to the guidewire or catheter inadvertently entering the right heart (2).

Air embolism may occur at any point during the lifetime of the line, and can be related to poor technique during insertion, use of the line or line removal (1). To reduce the risk of air embolism during insertion it is vital that the needle hub is covered with a finger when readying the guidewire. Similarly, the CVC ports should remain clamped when not in use (2).

Catheter-related infection is a delayed complication of insertion. A diagnosis of CVC blood stream infection should be considered in patients with signs of systemic infection in the absence of another identifiable source (1). Organisms commonly implicated in CVC colonisation and infections are staphylococcus aureus, S epidermis, enterococci and Candida spp (1).

Care of CVC lines

Following insertion, the date, operator route and all other relevant information about catheter placement should be recorded in the patient notes. The catheter is marked to indicate length of insertion, which also should be recorded and monitored in the patient notes. A chest X-ray should be obtained to confirm correct placement and to exclude a pneumothorax (1,2).

Patients should be routinely monitored for signs of complications. Aseptic technique should be used when accessing the CVC. Catheter ports should be decontaminated using antiseptic swabs before and after any infusion, and only accessed when absolutely necessary. To avoid further infection risk, the CVC port should not be used to take routine blood samples if suitable peripheral access is available (2).

Regular flushes with 0.9% sodium chloride should be used to minimise the risk of thrombosis, and all connections should be secured to minimise risk of infection and air emboli (1).

It is vital that the insertion site is frequently and carefully assessed for signs of infection. Tenderness, heat, erythema, exudate and swelling around the line may indicate local infection. When combined with a fever the possibility of catheter-related blood stream infection (CR-BSI) should be considered. If this is the case, blood cultures should be taken and removal or re-siting of the catheter is required. This should be performed with the head in a dependent position if the neck has been used as the site of insertion (2). Treatment with antibiotics should be started if appropriate, and the tip of the catheter sent for microscopy, culture and sensitivity (1,2).

To limit the risk of infection CVC lines should also be removed when no longer required for patient management.

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Conclusion

Central venous catheters are commonly used medical devices but are not without associated complications or risk. They should not be inserted without clear clinical indication. Foundation doctors should be aware of the associated complications, be able to recognise them and act accordingly.

MCQs

Question 1: Out of the following, which are common complications associated with CVC insertion? Tick all that apply.

A. Arterial puncture
B. Thrombosis
C. Catheter-related bloodstream infection
D. Pneumothorax
E. Cardiac tamponade

Question 2: A 65 year old male patient is receiving total parenteral nutrition via a percutaneously inserted central venous catheter sited in the right internal jugular vein. He becomes febrile and tachycardic seven days after CVC insertion and the CVC is suspected as a source of infection. Which of the following organisms are most likely to have colonised the central venous catheter? Tick all that apply.

A. Staphylococcus Aureus
B. Candida spp.
C. Pseudomonas Aeruginosa
D. Coagulase-negative Staphylococci
E. Group A streptococci

Answers

Question 1: Correct answer: A, C

Catheter related blood stream infections are the most common complication of CVC insertion and have been estimated to occur in 4.3% to 26% of cases (5). A diagnosis should be considered in patients with signs of systemic infection in the absence of another identifiable source. To reduce the risk of infection strict aseptic technique should be adopted during insertion of the line and when accessing the thereafter. Arterial puncture is the next most common complication, but should be less than 5% when ultrasound guidance is used.

Question 2: Correct answers: A, B, D

The most common organisms causing catheter infection in percutaneously inserted central venous catheters are, in order, coagulase negative staphylococci, staphylococcus aureus, candida species and enteric gram-negative bacilli (6).

Although pseudomonas aeruginosa can be implicated in central venous catheter infections, it is more common in peripherally or surgically inserted lines than percutaneously inserted lines. Group A streptococci are not commonly associated with CVC infection.6

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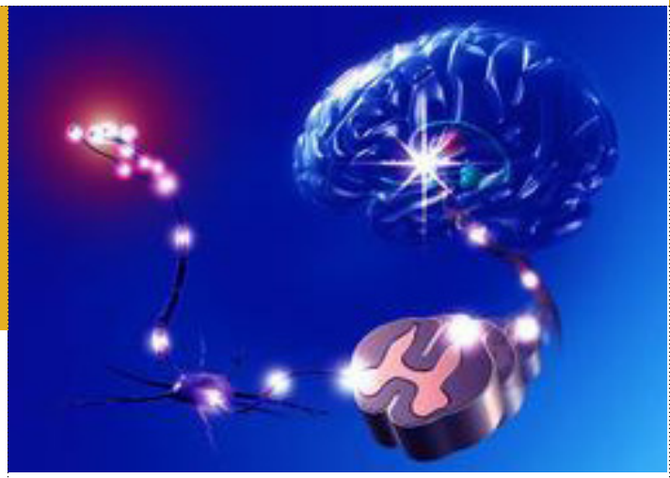
PAIN PATHWAYS & POINTS OF ACTION OF COMMON ANALGESICS: PARACETAMOL, NSAIDS & OPIOIDS

TM de Vries, GS Anil Kumar

Pain pathways & points of action of common analgesics: Paracetamol, NSAIDs & opioids
Good Clinical Care



Abstract

Pain is a sensory and emotional experience, which is a reaction to (potentially) harmful mechanical, thermal or chemical stimuli. Sharp pain is conducted through relatively fast Aδ fibres to the spinal cord, where it ascends in the neospinothalamic tract to the thalamus. From there it is transmitted to the somatosensory cortex and provides mostly temporal and spatial localisation of pain. Dull pain is transmitted through the slower C fibres to the spinal cord and ascends in the paleospinothalamic pathway to different areas in the brain stem. Dull pain is important for 'feeling' the pain and it also plays a role in the body's analgesia system.

Common analgesia exert their effect at different levels in these pain pathways. Opioids bind to receptors in the central nervous system, blocking the transmission of pain and stimulating the body's analgesia system. Their central point of effect causes a number of side-effects, however, including respiratory depression, nausea and vomiting. Non-steroidal anti-inflammatory drugs act peripherally by inhibiting the enzyme cyclo-oxygenase to produce prostaglandins, leading to decreased stimulation of pain receptors. The antipyretic effect of NSAIDs is due to its central inhibition of prostaglandin synthesis. Paracetamol's mode of action is a yet unclear, but may be due to COX-3 inhibition.

The current analgesia prescribing guidelines according to the WHO pain ladder are based on these different modes of action to provide optimal pain relief while minimising side-effects.

Pain

Pain is commonly defined as a sensory and emotional experience associated with real or potential injuries, or described in terms of such injuries (1). It is a subjective feeling, the severity of pain being expressed in terms of how the person experiencing it describes it, rather than in the degree of actual associated (potential) injury. It is meant as a protective mechanism, causing a person to withdraw from the source of pain as well as to facilitate learning from the experience in order to avoid the harmful stimulus in the future.

Mechanisms of pain

Pain is elicited by a mechanical, thermal or chemical pain stimulus which excites free nerve endings: the pain receptors. These pain receptors can consist of plexuses dispersed over wide areas stemming from one or two nerve fibres, or can be shaped like a dense spiral from a single fibre.

They are widely present in the skin, mucosa, membranes, deep fascias, connective tissues of visceral organs, ligaments and articular capsules, periosteum, muscles, tendons and arterial vessels (2), but are much less represented in other deep tissues. Pain receptors do not adapt to pain stimuli; as a matter of fact some receptors do show an increased sensitivity to continuing stimuli.

Pain is conducted through two types of nerve fibres, the Aδ and the C fibres (3). Aδ fibres are myelinated fibres 2-5 µm in diameter which conduct electrical impulses quickly, at 40 m·s-1. They are responsible for fast or sharp pain. Slow, chronic or dull pain is transmitted through C fibres, which are smaller (<2 µm) and unmyelinated and therefore only conduct impulses at a speed of 2 m·s-1. Larger Aδ fibres are mostly associated with the conduction of touch but play a role in stimulating inhibitory interneurones (4).

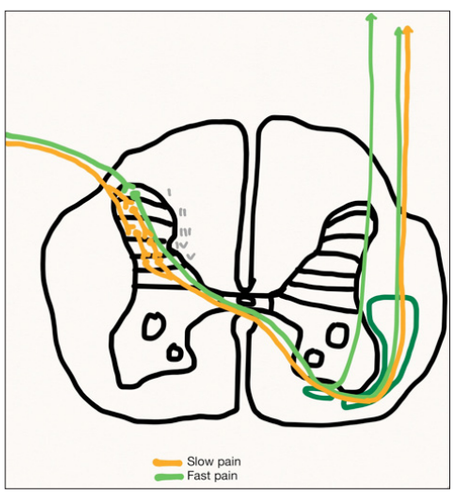


Figure 1: Transmission of fast and slow pain in the spinal cord. Fast pain is transmitted with Aδ fibres to lamina I in the dorsal horn and ascends in the neospinothalamic tract. Slow pain is transmitted with C fibres to lamina II and III of the dorsal horn and, after transmission through a number of interneurons, ascends through the paleospinothalamic pathway.

PAIN PATHWAYS & POINTS OF ACTION OF COMMON ANALGESICS: PARACETAMOL, NSAIDS & OPIOIDS

TM de Vries, GS Anil Kumar

Aδ fibres transmitting fast pain enter the spinal cord and terminate in the lamina marginalis, also known as Rexed lamina I of the dorsal horn. Here they excite second-order neurons, which cross to the contralateral side and ascend through the neospinothalamic tract in the anterolateral column (see figure 1). They terminate mostly in the thamalus as its name gives away. There, the pain signals are processed within the ventrobasal complex together with tactile stimuli from the dorsal column-medial lemniscal tract (see figure 2) (3).

The thalamus is the main point of transmission of information to the cortex. The lateral system of the thalamus transmits impulses to the somatosensory cortex and is involved in the sensory-discriminative processing of pain, providing spatial and temporal localisation of pain, as well as the evaluation of pain intensity. On the other hand, the medial system projects to limbic structures including the insula and the anterior cingulate cortex, where it influences the emotional, affective, attentional and memory responses to pain (2).

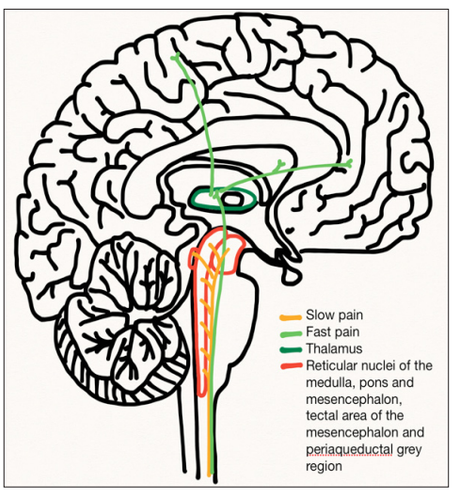


Figure 2: Transmission of slow and fast pain in the brain and brainstem. Fast pain is transmitted through the neospinothalamic tract to the thalamus, where it branches out to the somatosensory cortex as well as to the limbic system (insula and anterior cingulate cortex). Slow dull pain is transmitted through the paleospinothalamic pathway, ending in the reticular nuclei of the medulla, pons and mesencephalon, the tectal area of the mesencephalon and the periaqueductal grey region around the aqueduct of Sylvius.

Dull pain is hardly localised. It mainly has a cognitive-affective effect, which leads to a behavioural response. It is transmitted by C fibres which synapse with one of more interneurons in the Rexed lamina II and III of the dorsal horn, the substantia gelatinosa. These interneurons in turn synapse in lamina V with long axons that ascend in the anterolateral tracts and form the paleospinothalamic pathway.

These neurons end in three main areas of the brain stem: (a) the reticular nuclei of the medulla, pons and mesencephalon, (b) the tectal area of the mesencephalon and (c) the periaqueductal grey region around the aqueduct of Sylvius. This last area is involved in an analgesia system, which transmits inhibitory signals though the dorsolateral columns to the dorsal horns of the spinal cord (3).

Other spinal cord pathways also exist, such as the spinohypothalamic tract, which might be involved in integration with the autonomic nervous system, leading to neuroendocrine autonomic, but also motivational-affective and alert responses to pain (2).

In general the intensity of pain is thought to be more closely related to the rate of tissue damage as opposed to the amount of damage that has already happened (3). Pain quality depends on the location of the stimulus in the body. Whereas a stimulus arising from the skin might cause a sharp highly localised pain, pain from muscle will cause a more aching and less localised sensation. Low intensity stimuli from viscera initially cause sensations of fullness and nausea and only lead to pain if there is widespread activation of pain receptors.

Pain modulation

Pain impulses are modulated in different ways, one of these being through descending inhibitory pathways, which basically function as feedback loops. The most important descending inhibitory pathway is the periaqueductal grey area around the aqueduct of Sylvius in the brain. Stimulation of this area results in potent suppression of pain impulses in the dorsal horn, leading to profound analgesia. The periaqueductal grey area activates the nucleus raphe magnus and the locus coeruleus.

The nucleus raphe magnus is a region in the medulla which is also a descending inhibitory pathway in itself. It synapses in lamina II of the dorsal horn where it activates inhibitory neurons through serotonin release. The last of the main pathways is formed by the locus coeruleus, which is situated in the pons. Its noradrenergic neurons act both through presynaptic inhibition of primary afferents by preventing neurotransmitter release, and through postsynaptic inhibition caused by hyperpolarisation of the membrane.

Besides descending inhibitory pathways, an endogenous opioid system exists. Endorphins, encephalins and dynorphins inhibit pain transmission by binding to opioid receptors, which cause hyperpolarisation of the membrane as well as preventing neurotransmitter release through calcium channel blockade.

Inhibition of pain transmission also occurs locally in the spinal cord. This is caused by local lateral inhibition when there is a concurrent activation of Aβ fibres from touch stimuli originating from the same body region. This has been named the Gate Control Theory and explains how an action such as rubbing the skin around a painful area can diminish the pain sensation (8).

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Chronic pain

Chronic pain continues after an injury has healed or may even exist without any clearly identifiable cause (7) and can be diagnosed from six weeks after a trauma (9). It is in part caused by central sensitisation at the dorsal horn level, which happens through activation of NMDA receptors after repeated C fibre stimulation (8). Sustained Aδ stimulation or peripheral nerve injury can also result in long-term loss of inhibitory activity, while changes in synaptic architecture in the dorsal horn because of nerve injury can lead to Aβ fibres reorganising to synapse with dorsal horn nociceptive neurones in lamina II (9).

Autonomic nervous system

Due to connections with medullary centres and the hypothalamus as described above, pain can have visceral and neuroendocrine effects, including changes in ACTH and vasopressin secretion (9).

The opposite can also occur, in the sense that sensory neurones can have an increased sensitivity to adrenergic stimuli and proliferation of sympathetic nerve endings can lead to pain. This is termed sympathetically maintained pain and is a form of neuropathic pain, and may play a role in complex regional pain syndrome (9).

Points of action of common analgesics

Opioids

Opioids are all naturally occurring and synthetic morphine-like substances that stimulate opioid receptors. Opioid receptors are presynaptic inhibitory G-protein coupled receptors, which decrease excitability of the cell and decrease neurotransmitter and pain transmission by closing voltage gated calcium channels, decreasing cAMP production, stimulating potassium efflux out of the cell and hyperpolarising the membrane (5).

There are four types of opioid receptors. The μ opioid peptide (MOP) receptor, identified through morphine and hence named after it (the μ refers to morphine), can be found in sensory and motor perception and integration areas of the brain, as well as in the periaqueductal grey (where it has a role in the descending inhibitory pathway described above) and in the spinal cord (on the afferent neurones in the dorsal horn). MOP receptor stimulation causes analgesia, but also a wide range of side-effects as seen in table 1.

The KOP receptor is named after ketocyclazocine and does not cause respiratory depression; however, it may have MOP-receptor antagonistic effects. DOP receptors, originally found in the vas deferens of mice, may be involved in mood and movement next to analgesia. Finally, the nociceptin/orphanin FQ peptide receptor, or NOP receptor, produces hyperalgesia at lower doses and analgesia at higher doses. NOP receptors may lead to longer lasting analgesia and play a role in preventing morphine tolerance (4)(5).

Receptor type	Location	Effects
MOP	Throughout CNS, incl. cerebral cortex, basal ganglia, spinal cord, PAG	Analgesia Respiratory depression, bradycardia, reduced peristalsis, euphoria, meiosis
KOP	Brain Spinal cord	Analgesia Sedation, meiosis
DOP	Brain	Analgesia Respiratory depression
NOP	Brain Spinal cord	Anxiety, depression, appetite modulation

Table 1: This table shows the different opioid receptors, including their location throughout the central nervous system (CNS) and their effects. PAG: periaqueductal grey.

NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) exert their function by inhibiting the cyclo-oxygenase enzyme (see diagram 1). Cyclo-oxygenase is responsible for converting arachidonic acid to thromboxane, prostacyclin and prostaglandins. Thromboxane is formed in platelets and causes vasoconstriction and platelet aggregation. Prostacyclin does the opposite by causing vasodilatation and inhibiting platelet aggregation. Prostaglandins have various effects. These include decreasing gastric acid secretion, increasing gastric mucous secretion, vasodilatation, platelet aggregation, uterine contraction and bronchoconstriction.

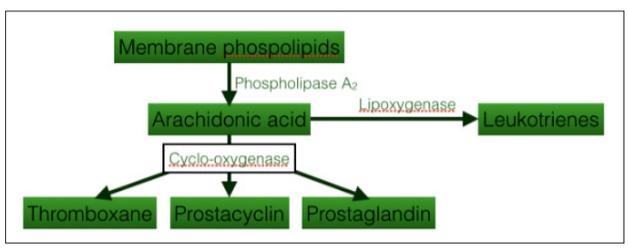

Diagram 1: Prostaglandin synthesis.

NSAIDs have anti-inflammatory effects due to their reduced prostaglandin PGE_2 and $PGF_2\alpha$ synthesis and are antipyretic due to central inhibition of prostaglandin synthesis. However, the main side effects, including gastric ulceration, also stem from prostaglandin synthesis inhibition. Reduced thromboxane production leads to decreased platelet function and therefore increased bleeding risk. Moreover, accumulation of arachidonic acid may lead to increased production of leukotrienes which causes bronchoconstriction and might provoke an asthma attack in susceptible patients.

Cyclo-oxygenase has two isoenzymes, COX-1 and COX-2. COX-1 is found in most tissues and plays a role in the control of renal blood flow, the secretion of the gastric mucosal barrier and the production of thromboxane. COX-2 is an inducible enzyme which is mainly activated by tissue damage and causes an inflammatory response. However, it is also responsible for prostacyclin production, which explains why selective COX-2 inhibitors show increased complications related to increased platelet aggregation, vasoconstriction and thromboembolism.

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Paracetamol

Paracetamol is sometimes classified as an NSAID due to its analgesic and antipyretic effects, but it has not been shown to act by inhibiting cyclo-oxygenase. Its mode of action in unclear and might be related to inhibiting prostaglandin synthesis in the central nervous system (sometimes referred to as COX-3 inhibition). It does not cause gastric irritation, but has the potential to cause liver failure, if overdosed, by saturating the hepatic conjugation pathway. This pathway is responsible for converting a highly toxic metabolite of paracetamol, N-acetyl-p-aminobenzoquinone imine, which is normally only present in small amounts, to a harmless substance.

Peri-operative pain management

An analgesic strategy should be planned preoperatively, taking into consideration the anticipated severity of the pain, the potential side effects, as well as patient factors, including patient expectations and underlying medical conditions. This might include the analgesia described above, with or without the use of local anaesthetics in the form of regional of local blocks, and/or adjuvant drugs, such as ketamine, clonidine, amitriptyline, gabapentin and pregabalin (10).

In some cases, the analgesic strategy may not only aim to reduce perioperative pain, but also to prevent long term pain syndromes, such as phantom limb pain after amputation. In that particular case, a combination of regional nerve blockade and/or adjuvant drugs may be effective, although their exact role is uncertain (11).

Conclusion

Pain is a subjective sensation that protects the body from harmful stimuli. It is transmitted through a fast pathway, mainly responsible for localisation and intensity of pain, and through a slow pathway, which is mostly responsible for emotional/affective and behavioural responses to pain.

Analgesia act at different levels within these pain pathways. Combining analgesia from different categories can therefore help to reduce the total dose of analgesia and of opioids specifically. It is generally recommended to prescribe pain killers according to the World Health Organisation (WHO) analgesic ladder (6), starting with mild analgesia with a low side effect profile such as paracetamol, subsequently adding NSAIDs, followed by mild and then stronger opioids, according to the patient's need. Regional or central nerve blockade and/or adjuvant drugs influencing the pain pathways in different ways may also be useful.

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POST-OPERATIVE DELIRIUM

A Levins, R Dolan

Post-Operative Delirium
Patient Management

Abstract

We present the case of an 84 year old female who had a fractured neck of femur and developed acute confusion following administration of opioids. Her confusion resolved but it posed a challenge for the anaesthetic team.

Delirium is well defined and common in occurrence and a good understanding is required at all levels, across all specialties. This paper will look into more detail at the risk factors, clinical assessment and treatment of delirium. We shall also look at the specific anaesthetic challenge posed by this patient.

Case History

An 84 year old female had a fall at home resulting in a shortened and externally rotated right leg. Her relevant medical history included: hypertension, hyperlipidaemia, mild aortic stenosis (Aortic valve area: 1.6cm^2) with no impediment to her activities of daily living, which she completed independently. Of note, she had no dementia, no psychological disorders and her cognition was normal.

On arrival of the paramedics, she was given morphine as a first line analgesic and was transported to hospital. On arrival to Accident and Emergency, she was noted to be confused with a reduction in her mental state (Abbreviated Mental Test (AMT): 6/10). She was pre-operatively managed with fluids and supportive measures and listed for a right hemi-arthroplasty. Over the course of the night, it is noted that her confusion diminished as the morphine wore off and in the morning, she had returned to her pre-morbid baseline (AMT: 10/10).

Upon consulting the anaesthetist pre-operatively, she stated that she would not like to undergo a general anaesthetic or sedation due to her concerns regarding confusion and delirium upon awakening.

Ultimately, she underwent an uneventful procedure under a regional technique. An ultrasound guided femoral nerve block was performed with lignocaine and adrenaline and a femoral nerve catheter was inserted for pain relief post-operatively. She then underwent a spinal anaesthetic with strict cardiovascular monitoring and haemodynamic regulation. During the procedure, she needed no sedation and this helped to maintain her level of cognition.

She developed no further episodes of delirium during her admission and was discharged without incident.

Discussion

Within this case are four aspects we wish to focus on. Firstly, are the risk factors of delirium; secondly, is the clinical assessment of a confused patient; thirdly is a focus on treatment and the fourth focus is on clinical judgement.

Risk Factors

Delirium, as defined in the Diagnostic and Statistical Manual of Mental Disorders (5th edition), is a syndrome of many different causes characterised by confusion and short term memory loss that is acute in onset and fluctuates. Key features include: a change in mental status, a reduced awareness of the surrounding environment and a disturbance in attention.

These features may be associated with symptoms affecting perception (hallucinations), cognition (disorientation, memory dysfunction) or behaviour (hypoactive, hyperactive). It is important to note that although many of the above characteristics are also associated with psychological disorders (such as schizophrenia or psychoses), to be diagnosed with delirium, there must be an organic cause (1).

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Delirium has one of the largest lists of aetiologies, encompassing many specialities and disciplines. Broadly, delirium may be induced by a medical condition, substances and the withdrawal of substances, multi-factorial or unclear. Table 1 displays a brief list of risk factors for delirium and post-operative cognitive dysfunction and is by no means, exhaustive and highlighted are the risk factors that our patient demonstrated.

Delirium	Post-Operative Cognitive Dysfunction
Patient Characteristics	Administration of sedatives or narcotics
Male	Rectal or bladder catheters
Increasing Age	Sensory impairment
Pre-Existing Cognitive deficits	Central venous catheters
Depression	Electrolyte disturbances
Dementia	Age >70
Cognitive impairment	NG feeding or TPN
History of delirium	History of depression
Functional Impairment	Cardiogenic or septic shock
Poor oral intake	Acute or chronic renal failure
Functional dependence	History of cardiac failure
Immobility	History of stroke or epilepsy
History of falls	Drug overdose or use of illicit drugs within 1 week
Sensory Impairment	Transfer from a nursing home
Drugs	Malnutrition
Alcohol and other substance withdrawal	Acute or chronic liver disease
Polypharmacy	History of thyroid disease
Narcotics	HIV/AIDS
Sedative	Acute pain
Anticholinergics and drugs with anticholinergic effects (steroids, digoxin, diuretics, cyclizine etc.)	Infection
Medical Conditions	Hypotension
Severe acute or chronic illness	
Multiple co-morbidities	
Electrolyte disturbances	
Chronic renal and/or liver failure	
Neurological disease including stroke	
Trauma	
Terminal illness	
Pain	
Infection	
Hypotension	

Table 1: Identified risk factors for the development of delirium and post-operative cognitive dysfunction (2,3).

When we say "Emergence delirium", it is typically referred to as a subset of substance delirium secondary to medications given for or whilst under general anaesthesia. When we say "Post-Operative Delirium", it is usual that the patient emerges unaffected from their anaesthesia but develops a delirium of unknown aetiology within 24-48 hours.

Incidence of post-operative cognitive dysfunction is estimated to be approximately 25% in patients over 60 years old at 1 week, decreasing to 10% at 3 months and 1% prolonged at 2 years (4).

Clinical Assessment

The clinical assessment of delirium is an important skill for all clinicians to obtain. It is a skill that is frequently utilised and crosses many medical and surgical specialties.

Clinical examination of the confused patient may prove inconclusive, with little in the way of signs available however, a thorough examination may provide some insight as to a possible cause. An increased heart rate and blood pressure may be suggestive of pain as the culprit, whereas a low blood pressure and a pale colour may be indicative of hypovolaemia.

The most commonly used tool for assessment is the Mini-Mental State Examination (MMSE) which is an assessment with thirty questions and a score less than twenty four indicative of a cognitive impairment. A more simplified version of this is the Abbreviated Mental Test, which is scored out of ten and the Abbreviated Mental Test-4.

The CAM-ICU is a tool that is validated for the use on ICU in mechanically ventilated patients as well as none ventilated ones. Recently, there has been the 4-AT piloted as an even more simplified test for cognitive dysfunction and studies are ongoing with this tool (5).

Treatment

Delirium doesn't have a specific pharmacological or non-pharmacological treatment as the management is centred on prevention and treatment of causative factors. Should the patient's delirium pose a hazard to the patient's self or staff, haloperidol or another such agent may be indicated, depending on hospital protocol. Figure 1 details a proposed treatment algorithm (6-12).

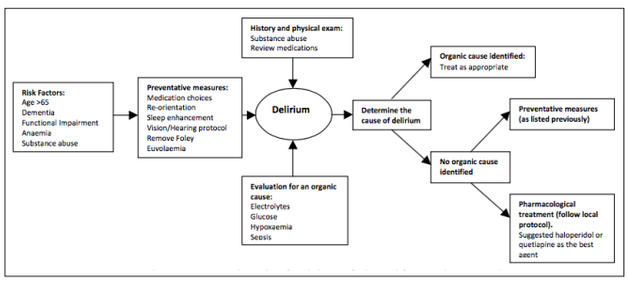

Figure 1: A proposed management algorithm for delirium (adapted from Robinson and Eiseman, algorithm for post-operative delirium) (13)

Clinical Judgement

Anaesthesia is a speciality that is unique; there is rarely one single route to anaesthesia. Medication choices, surgical intent and patient's wishes all need to be looked upon before a decision is made.

In this case, we had a patient who needed a repair of hip fracture and for this; there are two routes of anaesthesia that could have been administered: general anaesthesia or a regional technique (such as spinal anaesthesia). The patient herself expressed a desire not to undergo a general anaesthetic due to her concerns about post-operative confusion and delirium.

Regional anaesthesia would be an appropriate alternative however; it should be undertaken with caution in patients who have a history of aortic stenosis or other such cardiac abnormalities. Regional anaesthesia causes dramatic shifts in blood pressure and so, strict cardiovascular and cognitive monitoring is required.

Another consideration for regional anaesthesia is the position required of the patient to perform it: spinal anaesthesia is usually conducted with the patient sitting or lateral with the affected side down. This is sometimes painful to achieve and so, a further nerve block may be considered.

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A further issue with this case was the confusion that developed following opioid administration and so, analgesia in the post-operative phase would need to be considered. A regional anaesthetic and a nerve catheter would provide some analgesia post-operatively.

An example of an ideal anaesthetic is one that the patient and anaesthetist decide upon and maintains not only cardiovascular and respiratory haemostasis but also provides a homeostasis for the brain and optimises cognition.

Conclusion

Delirium is a common disorder that is well defined and has multiple risk factors and potential causes. The mainstay of its treatment is prevention and poses a clinical challenge as there is no definitive test or examination for it. Anaesthesia is a unique specialty and, to achieve an ideal anaesthetic, homeostasis must be attained for many organ systems, including the brain and cognition.

Test Yourself

Q1: Which one of the following statements is correct?

1. Delirium is an infrequent complication of critical illness.

2. The assessment tools available have not been validated for use in patients who are mechanically ventilated.

3. Hypoactive delirium is common.

4. Benzodiazepines should be the first line agents for treatment of agitation and delirium in Intensive Care patients.

5. Prophylactic haloperidol has been shown to prevent the onset of delirium.

Q2: Which of the following is NOT a recognised cause for delirium in the elderly patient?

1. Hyponatraemia

2. Urinary Tract Infection

3. Pain

4. Paracetamol

5. Atropine

Q3: Which of the following is NOT a recognised risk factor for delirium?

1. Age >65

2. Female gender

3. NG intake

4. Immobility

5. Chronic hepatic impairment

Q4: Which of the following would be the first line management for delirium?

1. Lorazepam 0.5 mg IV

2. Haloperidol 0.5 mg PO

3. Lorazepam 1 mg PO

4. Quetiapine 25 mg PO

5. Prevention and management of causative agents

Q5: In a patient who develops delirium, which of the following would you do FIRST?

1. CT head

2. Discontinue medications

3. A full blood panel

4. Arterial blood gas

5. Bedside examination

Answers

Q1 - 1. False.

Delirium is a common complication of critical illness although the exact incidence remains unknown. Some studies have reported incidences of over 80% whilst a review carried out in our mixed ICU detected delirium in over 30% of the patients at some stage of their admission.

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Q1 - 2. False.

The CAM-ICU assessment method has been validated for use in mechanically ventilated patients.

Q1 - 3. True.

Hypoactive delirium is the second most common form of ICU delirium after mixed hyper- and hypoactive delirium. Pure hyperactive delirium is uncommon.

Q1 - 4. False.

Benzodiazepines should be avoided in this setting if possible. They have a documented role in the treatment of delirium caused by alcohol or benzodiazepine withdrawal but administration to other patient sub-groups is an independent risk factor for delirium development.

Q1 - 5. False.

Haloperidol is the first line agent for the treatment of delirium but there is no evidence to support a role for its prophylactic use.

Q2 - 1. False.

Metabolic disturbances are a recognised cause for delirium in all patient age groups, but the elderly are especially susceptible.

Q2 - 2. False.

Infection is a recognised cause for delirium.

Q2 - 3. False.

Pain is a recognised cause for delirium.

Q2 - 4. True.

Paracetamol, independently, is not a recognised cause for delirium. On the background of chronic or acute hepatic failure, it may cause confusion however, as an independent risk factor, it is not recognised.

Q2 - 5. False.

Anticholinergic drugs are a recognised cause for delirium.
A useful mnemonic to remember the causes for delirium is: DIMTOP
Drugs (sedatives, narcotics, anticholinergics, etc)
Infections (UTI, chest, wound, etc)
Metabolic (hypo and hyper-calcaemia, natraemia, kalaemia, phosphotaemia, magnasaemia, glycaemia)
Oxygen (hypoxia and/or hypercarbia)
Psychiatric and Pain

Q3 - 1. False.

Age >65 is a large, recognised risk factor for the development of delirium.

Q3 - 2. True

Statistically, males are more likely to develop delirium than females.

Q3 - 3. False.

NG intake and TPN are both implicated in the development of delirium.

Q3 - 4. False.

Immobility is a recognised risk factor of delirium.

Q3 - 5. False.

Chronic and acute renal and hepatic impairment are all implicated in the development of delirium.

Q4 - 1. False.

Although benzodiazepines are sedative agents, they can cause paradoxical agitation in some patients and are not the first line pharmacological treatment for delirium.

Q4 - 2. False.

Haloperidol is recommended as the first line pharmacological treatment but is not the first line management for delirium.

Q4 - 3. False.

See answer 1

Q4 - 4. False.

Studies have been performed into quetiapine as a useful alternative to haloperidol in the pharmacological treatment of delirium, however, it is not the first line management of delirium.

Q4 - 5. True.

First line management of delirium is to treat the causative agent and attempt to prevent delirium from setting in. This includes ensuring orientation aids are easily visible and available, that the patient has their hearing aids/ glasses on and that the sleep cycle is optimised. Ensure that any pain, infection and hypovolaemia are treated and look into possible causes.

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Q5 - 1. False.

Although you may consider an intracranial pathology as the cause for delirium, it certainly should not be the first test performed without an indication (i.e. sudden collapse, blown pupil, neurological symptoms). It may be useful to consider further into the disease progression should the patient not be improving.

Q5 - 2. False.

A medication review is useful and some patients may benefit from discontinuing certain drugs however there are two things to consider here. Firstly, the patient may be established on some of these medications and a sudden withdrawal may be equally likely to cause delirium as the drug itself. Secondly, if the patient has been on the drugs for a prolonged period of time and there has been no change to the dosing schedule, then it is not the most likely cause for the delirium and other causes should be excluded first.

Q5 - 3. False.

A full blood panel would be useful and would certainly rule out (or diagnose) some of the more common causes for delirium however, it takes time for results to come back and answers may not be as readily available as some of the other options on the list. It would be prudent to perform a full blood panel if indicated, but it would not be the first thing you would do.

Q5 - 4. False.

An arterial blood gas provides useful information about oxygenation and some electrolyte results and it would be beneficial to obtain one if needed however, it would not be the primary action taken.

Q5 - 5. True.

A bedside examination will provide you with useful information that will tailor your next actions. Whether your patient has an abnormal pupil or neurological signs is something you will only find on examination. Whether your patient is cyanotic and needs an ABG is something you will only find by performing a bedside examination. An examination is certainly not the diagnostic test in this situation but will be the first action you take to help you tailor your next steps.

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PULSE OXIMETRY

S Pratt, D Karunaratne, C Karunaratne

Abstract

Pulse oximetry is used to measure the arterial oxygen saturation of haemoglobin (SaO_2). This measurement is achieved through the use of spectrophotometry and plethysmography. Spectrophotometry is used to measure the saturation of haemoglobin and is based on the principle that oxygenated haemoglobin and deoxyhaemoglobin have peak absorbencies for light at different wavelengths (in accordance with the Beer-Lambert Law). Plethysmography is used to distinguish the oxygen saturation of arterial blood from the remaining tissues and is based on the phenomenon that the intensity of light measured by the pulse oximeter varies with the cardiac cycle.

Pulse oximetry is now used in routine clinical care due to its ease of use, cost effectiveness and non-invasive properties, but doctors should be aware of the common pitfalls and limitations of the pulse oximeter which may be deceptive in specific clinical situations and hence are vital to recognise.

Introduction

Pulse oximetry is undoubtedly one of the greatest medical inventions, providing instant life-saving patient information non-invasively and cost-effectively. Pulse oximetry measures the arterial oxygen saturation of haemoglobin (SaO_2 or SpO_2, written as a percentage) which can be remembered through this simple equation:

SaO_2 (%) = 100 x saturated haemoglobin/total haemoglobin

SaO_2 values can give an estimation of the partial pressure of oxygen in arterial blood (PaO_2) as demonstrated by the oxyhaemoglobin dissociation curve (Figure 1) (1).

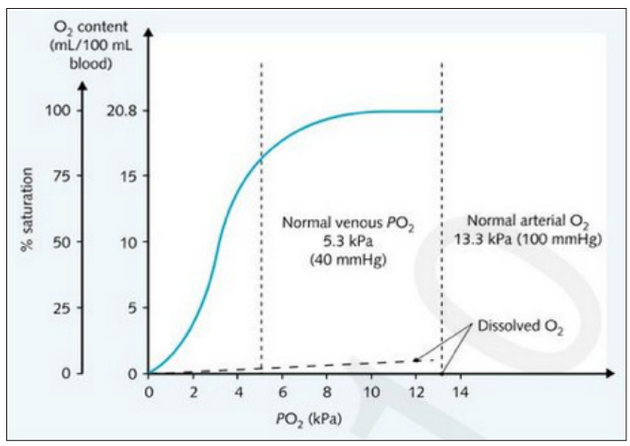

Figure 1: Oxyhaemoglobin dissociation curve.

The percentage saturation of haemoglobin (measured by the pulse oximeter) corresponds to a partial pressure (PO_2) of oxygen. An important point illustrated on this graph is that a saturation reading of 90% represents a PO_2 of about 8KPa (60mmHg) and risk of progression to severe hypoxia due to the steepness of the curve at this point. Therefore it is a common mistake to think that a reading of 90% is actually high.

Hickin S, Renshaw J, Williams R. Perfusion and Gas Transport. In: Horton-Szar D (ed.) Crash Course Respiratory System. 4th edition. China. Elsevier Mosby; 2013. p52

Although the concept of pulse oximetry has been around since the late 1930's (2), it was not introduced into standard care in hospitals until the 1980's, when in 1987 it began to be used in U.S. operating theatres, and from then onwards in recovery areas and neonatal units.

Prior to this, evaluation of oxygenation relied on clinical examination and invasive blood gas sampling. However, identifying hypoxaemia using clinical observation of cyanosis has been shown to be inaccurate, both being influenced by observer and patient variables, and having been demonstrated to not become apparent until oxygen saturations fall below 80% (the presence of 5g of deoxygenated haemoglobin per 100cc capillary blood) (3,4).

PULSE OXIMETRY

S Pratt, D Karunaratne, C Karunaratne

When pulse oximetry was initially founded, it used the principle of transillumination to measure oxygen saturation. This relies on the phenomenon where blood changes colour as haemoglobin becomes saturated with varying quantities of oxygen. Therefore, the blood will absorb a varying amount of light depending upon its degree of saturation.

However, it was not until later on that the principle of isolating the pulsatile component was introduced. This calls upon the fact that there are changes in the intensity of light according to the variation of arterial blood volume in the tissues. This variation of blood volume is due to the mechanics of the cardiac cycle. The pulsatile signal allows measurement of the haemoglobin saturation of arterial blood only eliminating measurements of other tissues and artifacts.

This article further explains the physical principles utilised in the function of the modern pulse oximeter and discusses its current clinical use, as well as its limitations.

Principle

The principle of pulse oximetry is based on both spectrophotometry (measurement of haemoglobin oxygen concentration) and plethysmography (measurement of arterial pulsatile changes).

Spectrophotometry is used to measure the saturation of the haemoglobin, and is based on the Beer-Lambert law. The Beer-Lambert law describes the relationship between the concentration of a solution and the amount of light trans-illuminated through it. It requires the knowledge of a few variables: The length of the light transmission path; the wavelength of the light; and the absorbance of the substance at the specified wavelength. This is demonstrated by the following formulae (5):

I trans = I inc – A

A = DCE

I trans = intensity of transmitted light

I Inc = Intensity of incident light

A = absorption

D = distance light is transmitted (path length)

C = concentration of solute (haemoglobin)

E = extinction coefficient of the solute (a constant for a given solute at a given wavelength)

Each solute has a specific extinction coefficient for absorption of light at a specific wavelength. Thus the concentration of a solute can be measured by knowing the incident light and the light transmitted, at a known wavelength. Where there is more than one solute, the concentrations can be measured by using different wavelengths of light with different extinction coefficients for each solute.

Applied to haemoglobin, oxygenated haemoglobin and deoxyhaemoglobin have peak absorbencies for light at different wavelengths. Deoxygenated haemoglobin has a peak absorbency at a wavelength of 660nm (red light) and oxygenated haemoglobin has a peak absorbency at a wavelength of 940nm (infrared light).

The pulse oximeter transmits light at wavelengths 660nm and 940nm from light emitting diodes (LEDs) through the tissue to a detector, and from this can measure both the amount of oxygenated haemoglobin and deoxygenated haemoglobin. The ratio of the two concentrations is then converted into a percentage of oxygenated haemoglobin – the saturation reading.

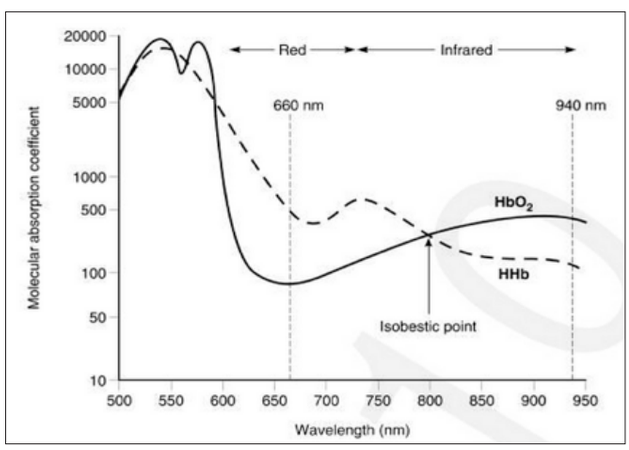

Figure 2: Absorption spectra of oxyhaemoglobin and deoxyhaemoglobin (5).

The different absorption of the two wavelengths of red light and infra-red light allows a calculation of the ratio of oxyhaemoglobin to deoxyhaemoglobin. Both oxyhaemoglobin and deoxyhaemoglobin have the same molecular absorption coefficient at the wavelength of 805nm and this is called the isobestic point.

Scott S. Clinical Measurement and Monitoring. In: Aitkenhead AR, Moppett JK, Thompson JP, Smith G (eds.) Smith and Aitkenhead's Textbook of Anaesthesia. 6th edition. China. Churchill Livingstone; 2013. p344

To distinguish the arterial blood of which we wish to measure the oxygen saturation from the rest of the tissue, the pulse oximeter uses plethysmography. As mentioned before, the intensity of light measured by the pulse oximeter varies with the cardiac cycle. Therefore, the absorbance of the light from the pulsatile arterial blood produces an alternating current (AC) signal to the microprocessor.

PULSE OXIMETRY

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This is in contrast to the constant absorbance of the light from other haemoglobin containing tissues (e.g. venous blood) which produces a direct current (DC) signal. There is an increase in intensity of light caused by inflow of arterial blood, so the microprocessor subtracts the DC signal from the AC signal, allowing it to measure just the absorption from the pulsatile arterial component.

Clinical Uses & Interpretation

The pulse oximeter is non-invasive, versatile, compact and relatively cheap, and can therefore be used in a variety of settings and situations. Pulse oximeters are used widely throughout secondary care, in some areas of primary care, and in the pre-hospital setting by emergency medical responders such as paramedics.

They can be used for individual spot checks to aid both diagnosis and monitoring in areas such as A&E, hospital wards, outpatient clinics, general practices, and home visits. They can also be used continuously, to aid both diagnosis and monitoring. They are useful in diagnosing conditions such as sleep apnoea, and are used for continuous monitoring (as part of the early warning score, EWS) in high dependency and intensive care units (including neonatal intensive care units), and peri-operatively (where they are part of the minimum monitoring as set by the AAGBI) (6) as well as in recovery areas(7). The pulse oximeter is also useful for guiding oxygen therapy, especially in patients with COPD with type 2 respiratory failure where specific target saturations of 88-92% are recommended and require strict adherence to.

The pulse oximeter has either a clip or an adhesive wrap-around (for babies and infants) to attach it the body part being used for monitoring. This is usually a finger or a toe, but other small body parts such as an ear lobe can be used. It is neither too uncomfortable nor painful which is a great advantage of its use, especially in the paediatric population.

When the pulse oximeter is used for continuous monitoring, the monitor's display provides the information in a waveform, and allows the interpretation of information other than just the haemoglobin oxygen saturation. The waveform displayed is the AC signal from the arterial pulsatile component. The pulse rate can therefore be deduced from this. Early detection of some arrhythmias (e.g. atrial fibrillation) can also be gained by the observation of an inconsistent waveform with the variable cardiac output with every heart beat.

The difference in signal between systole and diastole provides information about the perfusion of the body part where the pulse oximeter is placed. The waveform provides a volume against time graphical representation of this, almost mimicking an arterial pressure waveform(8). A tall waveform with a dicrotic notch indicates good perfusion and a flat smooth wave indicating poor perfusion.

The steepness of the upstroke in the waveform can indicate ventricular contractility, the amplitude of the wave can indicate stroke volume and the downslope can indicate preload(9,10). Information about the circulatory volume status can therefore be gained, although this is not quantifiable(10). It should be kept in mind that the perfusion of different tissues is expected to differ - the ear lobe is expected to be less well perfused than the finger.

Pitfalls & Limitations

Despite the usefulness of the pulse oximeter, it does have a number of limitations that need to be considered during its use (2,7,11).

Dyshaemoglobins

Carboxyhaemoglobin (haemoglobin bound with carbon monoxide) is present in blood in very small amounts in healthy individuals, but rises following smoke inhalation and exposure to high levels of inhaled carbon monoxide. It can be as high as 10% in heavy smokers. Carboxyhaemoglobin has a higher affinity to haemoglobin than oxygen, preventing the binding of oxygen. Carboxyhaemoglobin absorbs light at a wavelength of 660nm at a similar rate to oxygenated haemoglobin, therefore making it indistinguishable from oxygenated haemoglobin to a pulse oximeter and causing falsely high saturation readings. Carboxyhaemoglobin does not absorb much light at a wavelength of 940nm.

Elevated methaemoglobin (occurs when the ferrous component of the iron is oxidized to its ferrous state) levels can be congenital or can be acquired - for example, from certain drugs. Methaemoglobin has a higher affinity for oxygen than normal haemoglobin and does not release it at its destination site - the tissues. Methaemoglobin absorbs equal amounts of light at wavelengths 660nm and 940nm, with a ratio of pulsatile and non-pulsatile absorbencies of the two wavelengths being 1 at saturations of 85%. When high levels of methaemoglobin are present the saturation will read at 85% despite whether the actual saturations are above or below that. If either carboxyhaemoglobin or methaemoglobin are suspected, arterial blood gas sampling must be performed in order to correctly identify this.

Foetal haemoglobin accounts for about 20% of the haemoglobin of neonates. Absorbencies of wavelengths of light at 660nm and 940nm for the foetal haemoglobin in its oxygenated and reduced state are the same as those for adult haemoglobin, and pulse oximetry can therefore be reliably used in neonates.

Poor perfusion

When tissue perfusion is low, the signal (AC) to noise (DC) ratio is reduced, reducing the pulsatile signal that is required to distinguish the arterial component from other tissues and the accuracy of the saturation reading is therefore reduced. Poor perfusion is commonly caused by hypotension/hypovolaemia, peripheral vascular disease, cold extremities and proximal blood pressure cuff inflation. To increase perfusion and gain a more accurate reading, moving the oximeter probe to a different site, warming the patient's extremities, and increasing the circulating volume can be attempted.

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Ambient light

Ambient light in the ranges of that emitted by the LEDs (red light is included in the range of visible light emitted by room lighting) can not be distinguished from that emitted by the oximeter if received by the receiving plate, and can lead to inaccurate readings.

Movement artifact

Often patient movement can be confused with arterial pulsations by the pulse oximeter and lead to inaccurate readings, or the movements are erratic and the pulse oximeter recognizes this it may stop reading. This can be a particular problem when patients are shivering, when patients are distressed or confused, and when transporting patients. Some methods have been introduced to reduce the problem of motion artifact: The pulsatile waveform can be synchronized with the 'R' wave of the ECG, allowing the pulse oximeter to distinguish between arterial pulsations and motion artifact; and the lengthening of the time period over which the pulse oximeter averages out the movement to enable it to reject occasional motion artifact. However, the latter causes prolonged delay in the reading being given which can lead to a delay in detection of acute hypoxia.

Electrical artifact

Electrocautery used during surgery can interfere with the pulse oximeter used for anaesthetic monitoring. The pulse oximeter can either count these interferences as pulsations leading to a falsely decreased saturation reading, or can recognise them as electrical interference and hold its functioning when it is present. The pulse oximeter should be placed as far away as possible from the site where electrocautery will take place to reduce this electrical interference.

Dyes

Colours - particularly blue, black and green - can cause interference with the received light and lead to falsely reduced saturation readings. These can include nail varnish and injected dyes such as the methylene blue used for lymph node sampling in breast cancer surgery.

Low saturations

The data used to interpretate the information gained from the pulse oximeter into saturation readings was gained by taking samples from healthy human volunteers that were subjected to hypoxic gas mixtures to a limit of 80% oxygenated haemoglobin saturations. Readings provided by the pulse oximeter below 80% are therefore unreliable as they are calculated not measured. Saturations of 70% are generally taken as the lowest acceptable reading.

Limitations of information

As well as remembering what the pulse oximeter is measuring, it is also important to remember what it isn't measuring. It only measures the percentage of saturated haemoglobin and not the partial pressure of oxygen within the blood. As well as being unable to detect a low partial pressure of oxygen, it is unable to detect a high partial pressure of oxygen. There are times when a high partial pressure of oxygen can be harmful (e.g. free radicals from prolonged hyperoxia and patients with chronic obstructive pulmonary disease requiring a hypoxic state to maintain their respiratory drive). In patients with profound anaemia, whilst their haemoglobin may be reasonably saturated, the delivery of oxygen to the tissues may not be adequate.

The pulse oximeter does not measure partial pressure of carbon dioxide within the blood, and therefore does not assess the adequacy of ventilation in any way. In anaesthesia, if ventilation is lost all together, it will be significant time before the oxygen saturations will drop and be picked up by the pulse oximeter. In order to assess ventilation, expired gas sampling or blood gas sampling is required.

Summary

Pulse oximetry is a valuable tool in modern medicine, but it should be remembered that it is only a tool and it should be used to support diagnosis and monitoring alongside good clinical judgement and other diagnostic tools where indicated. It does not replace the value that arterial gas sampling can bring to a clinical situation, but can reduce the times where it may be necessary. The pulse oximeter can provide information other than just the saturation of oxygenated haemoglobin, such as valuable non-invasive information on the circulatory status, and perhaps in the future this information will be quantified and its use brought into clinical practice. When used appropriately and paying consideration to its limitations, the pulse oximeter is invaluable in providing quick and efficient diagnostic and monitoring information and is essential in everyday clinical practice.

Test Yourself

1. The physical principle of pulse oximetry

A. Spectrophotometry

B. Spectroscopy

C. Spectrodiametry

D. Spectrosonometry

E. Spectronanometry

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2. Pulse oximetry is inaccurate in

A. Non-smoking adults

B. Heavy smokers

C. Neonates

D. Young children

E. Elderly patients

3. The pulse oximeter reading is unreliable

A. Below 85%

B. Below 90%

C. Below 92%

D. Below 70%

E. Below 80%

4. The pulse oximeter reading could be interfered by

A. Electricity

B. Noise

C. Anaesthetic gases

D. Oxygen

E. Injected medication

5. The most important advantage of the pulse oximeter

A. The pulse oximeter gives accurate figures of the oxygen saturation

B. Prompt detection of hypoxia and prompt treatment

C. Continuous measurement of oxygen saturation

D. Could be use in high risk patients

E. Readily available in all departments in any hospital

Answers

1. Spectrophotometry

Spectrophotometry is a method to measure how much a chemical substance absorbs light by measuring the intensity of light that passes through a sample solution. Spectrophotometry is used to measure the oxygen saturation of haemoglobin, and is based on the Beer-Lambert law. The Beer- Lambert law describes the relationship between the concentration of a solution and the amount of light trans-illuminated through it.

In pulse oximetry, through light emitting diodes (LED) light is emitted though blood in two different wave lengths, 660nm (red light) and 940nm (infra-red light). Oxyhaemoglobin absorbs more red light and deoxyhaemoglobin absorbs more infrared light. Depending on the concentration of oxyheamoglobin to deoxyhamoglobin in blood, ratio of absorption of red light and infra-red light will be different. This will be picked up by the photodetector and gives us as a percentage value as oxygen saturation.

2. Heavy smokers

In heavy smokers carboxyhaemoglobin levels can be high as 10%. Carbon monoxide has a high affinity for haemoglobin than oxygen, preventing the binding of oxygen. Carboxyhaemoglobin absorbs light at a wavelength of 660nm at a similar rate to oxyhaemoglobin, therefore making it indistinguishable from oxyheamoglobin to a pulse oximeter and causing falsely high saturation readings.

Foetal haemoglobin accounts for about 20% of the haemoglobin of neonates. Over the years foetal haemoglobin gradually declines and at two years it almost disappears from the circulation. Absorbencies of wavelengths of light at 660nm and 940nm for the foetal haemoglobin in its oxygenated and reduced state are the same as those for adult haemoglobin, and pulse oximetry can therefore be reliably used in neonates and young children.

3. Below 70%

Calibration of the pulse oximeter was done on volunteers down to saturation of 80% with extrapolation below 80%. It is generally regarded, below 70%, pulse oximeter is inaccurate. Some machines deliberately blank the display below 70%.

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4. Electricity

Electrocautery used during surgery can interfere with the pulse oximeter. The pulse oximeter can either count these interferences as pulsations leading to a falsely decreased saturation reading or can recognise them as interference and hold its function. The pulse oximeter should be placed as far away as possible from the site where electrocautery will take place.

Methylene blue injected for diagnostic purposes can cause interference with the received light and could lead to falsely reduced saturation readings.

5. Prompt detection of hypoxia and prompt treatment.

The pulse oximeter is very quick to detect hypoxia. This enables clinicians to take prompt actions to rectify hypoxia with supplementary oxygen therapy or supporting inadequate ventilation. This makes the pulse oximeter unique piece of equipment in hospital or outside the hospital setting. Early detection and treatment of hypoxia has reduced cardiac arrests in hospitals.

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RECOGNITION, ASSESSMENT & MANAGEMENT OF THE UNWELL PATIENT ON THE WARD

A Malik, V Shenoy, YY Choo

Abstract

Patients go to the hospital because they feel unwell. However, whilst in hospital, a patient who has been stable on the ward may acutely deteriorate and become critically unwell.

Early recognition of the severity of the situation, careful assessment of the patient, prompt management using a systematic ABCDE approach, and effective communication between team members are the four main pillars to safely manage the unwell patient on the ward. The ultimate aims are the rapid stabilization of the unwell patient, the prevention of further deterioration, and the appropriate escalation of the patient's care.

Most patients who become acutely unwell on the ward show signs of deterioration many hours before their acute decompensation. This may be due to the progression of the primary condition which brought them to a hospital, due to their pre-existing co-morbidities or due to a new problem they have developed since admission.

The ability to recognise the early signs of deterioration and manage them accordingly is the key to improvement of the patient's outcome and survival. Physiological signs indicating a patient's deterioration include: reduced oxygen saturations, tachypnoea, hypotension, tachycardia, reduced level of consciousness and increased temperature. These parameters are documented by the nursing and allied healthcare professionals in the patient's observation chart and form a part of the NEWS (national early warning score) system.

News System

The NEWS system is a nationally standardised track-and-trigger system published by a working party created by the Royal College of Physicians in 2012. It is based on 6 physiological parameters, namely respiratory rate, oxygen saturations, temperature, systolic blood pressure, pulse rate and level of consciousness.

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A score is allocated for each of these 6 parameters and once a certain score is breached, an action will then be triggered. It is an extremely useful surveillance tool to help in the early recognition of the acutely unwell or deteriorating patient on the ward. (1)

During a shift you may be called by a nurse from a ward stating a patient's NEWS score and asking you for a review. You should always enquire about the values for all recorded parameters. To interpret them correctly you need to take the patient's age, the presence of co-morbidities, current drug treatment and the magnitude of the change from baseline values into account. A brief history from a nurse would also be helpful.

Avoid prolonged interrogations as this will delay the patient from getting the treatment. Always prioritise your jobs, don't just add the patient to your 'list'. Sick patients need to be seen first. Remember, hypoxia and hypotension will lead to hypoxic brain damage, acute kidney injury, cardiac ischaemia and eventually cardiac arrest. If you are unable to see the patient within 10-15 minutes, give instructions over the phone e.g. commence oxygen, fluids, and contact your senior colleague immediately asking for help. This patient's care is your responsibility.

Patient Assessment – ABCDE Approach

The ABCDE approach entails an assessment of airway, breathing, circulation, disability and exposure. It is organised in that order not only because it is simple to remember but also in order of priority, as an airway problem will kill the patient before a breathing problem which will in turn kill the patient before a circulation problem. (2)

When conducting an assessment it is very important to remember that you are not alone and that your senior colleagues are there to help. It is better to inform them about the sick patient earlier rather than later.

When approaching a patient, you can start off with a simple question like "How are you?" This simple question will establish whether your patient has a patent airway, if they are breathing and also if there is any brain perfusion. (3) If you do not get any response, then you should check for any signs of life. If these are not present, then the current resuscitation council guidelines for a cardiac arrest should be followed. (2, 3)

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Basic monitoring such as pulse oximetry, ECG and continuous non-invasive blood pressure monitoring should be commenced at this stage if they are not already in place. Intravenous access should be secured using 2 large bore (14 or 16 gauge) cannula and blood samples taken for full blood count, urea and electrolytes, clotting screen, blood cultures (if indicated), group and save or cross-match if haemorrhage is suspected. An attempt should be made to elicit some history from the patient. If the patient's condition or patient's exhaustion is making it impossible, the information can be obtained from medical notes, nurses or relatives. The assessment as detailed below should follow.

A – Airway

• Look for signs of airway obstruction:

- Stridor indicates obstruction at the larynx.
- Snoring occurs when the tongue obstructs the oropharynx.
- Gurgling sounds indicate presence of secretions (vomitus, saliva, blood) in the oropharynx.
- Wheeze indicates bronchial obstruction as seen in acute asthma attack or left ventricular failure with acute pulmonary oedema.
- A completely obstructed airway is rare and is characterized by paradoxical movement of the chest and abdomen with no detectable movement of air at the mouth.

• Employ airway manoeuvres to open the airway: head-tilt-chin-lift, jaw thrust. Suction any vomitus/ blood, remove dentures. If obstruction persists, use airway adjuncts e.g. Guedel airway, nasopharyngeal airway.
• Apply a non-rebreathe face mask with reservoir bag and attach to high flow oxygen (15litres/min). In acute respiratory failure, the PaO_2 should be kept as close to 13 kPa as possible, but at least above 8 kPa or 90% saturation on a pulse oximeter. (3)

This approach may need to be modified when the patient has type II respiratory failure as a result of chronic obstructive airways disease (COPD). In such cases, oxygen should be given to keep oxygen saturations within the individualised target range. Local protocols should be followed. (4) If you are not familiar with them then a target PaO_2 of 8 kPa (60 mmHg) or 90% saturation (SaO_2) on pulse oximetry is a good starting point.

Remember: *Airway obstruction is a medical emergency and if not corrected immediately, senior help should be requested as a matter of urgency and a cardiac arrest call should be activated.*

Top tip: *You can assess the patient's level of consciousness simultaneously. If the patient tolerates jaw thrust or has a minimal response to it (painful stimulus), this indicates a low level of consciousness. Toleration of Guedel airway means that airway protective responses are abolished and patient may need tracheal intubation for airway protection.*

B – Breathing

• Look for signs of respiratory distress by assessing:

Effort: *respiratory rate (normally 12-20/min), use of accessory muscles, pattern of breathing, and signs of exhaustion such as inability to complete sentences.*

Efficacy: *oxygen saturations, chest expansion.*

Effect of respiratory inadequacy on other organs:

- *heart rate – bradycardia is a pre-terminal sign*
- *skin colour – cyanosis is a late sign*
- *mental status.*

Life-threatening conditions like tension pneumothorax, massive haemothorax, acute severe asthma and pulmonary oedema should be looked for, recognised and treated immediately. (3)

• Listen – Auscultate the chest bilaterally to assess the air entry, look for added sounds like wheeze, crackles, and crepitations.
• Feel the position of the trachea and palpate the chest looking for surgical emphysema or crepitus – signs of a pneumothorax until proven otherwise. Percuss the chest looking for hyper-resonance (pneumothorax), or dullness (effusion, consolidation).
• Take an arterial blood gas to assess the adequacy of respiratory effort. Oxygen saturations may be normal especially if a patient is receiving oxygen. However, it is not possible to assess the level of carbon dioxide in the patient's blood from the pulse oximetry. High levels of carbon dioxide, leading to respiratory acidosis, indicate that the patient's ventilation is inadequate.

This may be due to a variety of reasons such as partial airway obstruction, low level of consciousness or exhaustion. High levels of carbon dioxide with respiratory acidosis warrant some form of respiratory support e.g. non-invasive ventilation (NIV) or intubation and positive pressure ventilation. The choice depends on the clinical situation and level of acidosis. Intensive care specialist advice needs to be sought.

C – Circulation

• Look at the colour of the limbs, especially hands and feet, and feel their temperature at the same time. Cold limbs which are mottled, pale or blue indicate circulatory failure.
• Check peripheral and central pulses for rate, quality and regularity. Weak, feeble pulses suggest a poor cardiac output. This could be due to cardiac failure or hypovolaemia. A bounding pulse may indicate sepsis.
• Measure the capillary refill time (CRT). It is assessed by applying cutaneous pressure for five seconds on a fingertip held at heart level (or just above) and counting the time it takes for capillary refill after the pressure has been released. The normal value for CRT is usually less than two seconds. (3)

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- Check the blood pressure. This should be interpreted in the light of patient's age and co-morbidities. Systolic blood pressure of a 100 may be entirely normal in a young person but grossly abnormal in an elderly person with a history of hypertension.
- Patient's level of consciousness and urinary output will tell you whether these organs are adequately perfused. Accept a minimum urinary output of 0.5ml/kg/hr.
- Ensure good IV access is secured, relevant blood samples have been send urgently, and that the laboratory technician has been informed and is expecting them (especially important during the night). Take a venous blood gas if an arterial sample hasn't been taken as a part of respiratory assessment. Base deficit, lactate and sodium bicarbonate are the markers of the metabolic component of acid-base balance. They will give an indication of the level of tissue hypoperfusion.
- Ask yourself if your patient is in shock? Signs of hypovolaemic, obstructive or cardiogenic shock include tachycardia, hypotension, slow capillary refill time, cold and pale peripheries, oliguria and reduced level of consciousness or agitation. The patient may have warm peripheries and a bounding pulse in septic shock. (5)
- Is your patient septic? Sepsis is very common and early recognition, rapid intervention and timely escalation will save your patient's life. The Sepsis Six care bundle needs to be initiated, within an hour, for all patients who are suspected to be septic. This includes high flow oxygen, bloods cultures and consideration of source control, intravenous antibiotics, intravenous fluid resuscitation, haemoglobin check, serial lactates, and hourly urine output measurement. (9)
- If hypovolaemia is suspected (pale, mottled and cold peripheries in a tachycardic patient), give a rapid fluid challenge (over 5-10 minutes) of 500 ml of warmed crystalloid solution if the patient is normotensive, and 1 litre if the patient is hypotensive. Use smaller volumes (e.g., 250ml) for patients with known cardiac failure and use closer monitoring (listen to the chest for crepitations after each bolus). (3) Always assess the effect of your interventions. Fluid challenge can be repeated but if it fails other means of supporting the circulatory system should be considered e.g. vasopressors or inotropes.
- In surgical patients, always exclude haemorrhage. Look at the surgical drains; examine all body cavities looking for occult blood loss. Early surgical intervention may be the only way to save the patient's life.

D – Disability

- Use the Glasgow Coma Scale (GCS) or AVPU scale. Examine the pupils for size and reaction to light.
- Hypoxaemia, hypercapnia and hypotension leads to low GCS; they should have been treated at this stage.
- Low level of consciousness could be a result of primary brain pathology, metabolic or endocrine disturbance, or an effect of a drug.
- Inspect drug chart for opioids or benzodiazepines administration and consider the antidotes.
- Check blood glucose level to exclude hypoglycaemia. If blood glucose level is below 3 mmol/l, give 25-50 ml of 50% glucose solution intravenously.

- Perform neurological examination looking for focal neurology. Could the patient be post-ictal?
- Nurse the patient in the left lateral position as he/she may not be able to protect his/her airway and will be at risk of airway obstruction or aspiration.
- Patients with GCS of 8 or less may need tracheal intubation for airway protection.

E – Exposure

- Full body exposure and examination should take place remembering to respect the patient's dignity and also prevent any heat loss. The aim is not to miss anything.
- Inspect indwelling catheters, lines, surgical wounds, and scars. Remove dressings and bandages, and look for any source of infection.
- Post-op patients will need urgent senior surgical review.

Never hesitate to call for extra help if there is a life-threatening problem that needs to be addressed immediately, or if you feel overwhelmed by the situation.

Remember

- Legibly describe all your examination findings, treatments administered and response to them in the patient's notes. All entries need to be dated and timed.
- Write down your working diagnosis and considered differentials.
- Review blood results and scans as soon as they become available.
- Prescribe fluids and drugs, and make sure that they have been administered.

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Communication

To ensure that our patients get the best possible care we need to be able to communicate effectively. A very simple but effective tool that is highly recommended and commonly used in hospitals is the SBAR communication model. It was first developed by the military (5) and has been recommended by the Royal College of Physicians of London for use during the handover of care of patients that are unwell or at risk of deterioration. (6)

SBAR is an acronym for situation, background, assessment and recommendation. It is useful to highlight the important information in an organized and succinct manner when we are handing over the care of an unw ell or deteriorating patient to our colleagues.

Situation: *Describe the demographics of the patient and the events thus far.*

Background: *Describe the patient's past medical history, and also any other reasons that may contribute to his/her diagnosis.*

Assessment: *Assess the current condition of the patient including observations of vital parameters, any relevant blood test results or investigations. Try to make a working diagnosis and consider potential differentials.*

Recommendation: *Plan of what needs to be done for the patient and how urgently. Escalation to senior colleagues if patient deteriorates. (1)*

Summary

An acute illness usually develops insidiously with signs of deterioration in the patient's condition being evident for many hours before the acute decompensation and failure of respiratory, cardiovascular and neurological systems.

Early recognition, careful systematic assessment and management using the ABCDE approach, and effective communication will keep the acutely unwell or deteriorating patient safe while awaiting the senior doctor's help with definitive diagnosis and treatment. Always remember that you are not alone. Don't be afraid to ask for senior help early, even if it is just for advice or reassurance that what you are doing is correct.

Senior colleagues prefer to know about an unwell patient sooner rather than later so remember to involve them early and update them regularly. They will be able to offer guidance, advice and support. Junior doctors who adopt an ABCDE structured approach to assessing and managing the unwell patient will find that being asked to review an acutely unwell or deteriorating patient on the ward will not be so daunting and stressful a task after all.

Self Assessments

1. You are the F1 doctor on call for general surgery and you are asked to review a patient on the ward. Mrs Smith, aged 42, has had a laparoscopic cholecystectomy today. She is usually fit and well. The nurse informs you that the patient is scoring 5 on the NEWS chart. Your assessment using an ABCDE approach:

A – The patient is able to answer your questions.

B – Respiratory rate is 22 and oxygen saturations are 97% on oxygen 2L/min. There are mild crepitations bilaterally.

C – Heart rate is 110bpm and blood pressure of 90/60 mm Hg, capillary refill time is 3 seconds, her peripheries are cold to touch. 2 wide bore cannulas are present and bloods has been taken

D – Slightly drowsy but orientated, pupils are equal and reactive. Temperature is 35.9°C and blood sugar is 7 mmol/L.

E – Her abdomen is tense and tender to touch.

2. What will be your next step?

A: Start 1 litre fluid challenge, call the lab to request 4 Units of Packed red cells, call your registrar to request urgent review.

B: Start 1 litre fluid challenge and ask the nurse to call you when it is finished, call the lab to request 2 Units of blood, call your registrar to inform him about the patient.

C: Start 500ml fluid challenge, call the lab to request 2 Units of Packed red cells, call your registrar to review the patient.

D: Start 250ml fluid challenge, call the lab to request 4 Units of Packed red cells, ask the nurse to call your registrar.

2. You are asked to review an 85 year old gentleman on the ward who was admitted today. He has been 'off legs' over the past few days. He is known to have well controlled hypertension. He is independent and lives with his wife. Your assessment:

A – The patient is talking but is confused.

B – Respiratory rate 28 breaths/min, oxygen saturations are 90% on room air and you apply 15L/min oxygen via non-rebreathing face mask; you are unable to examine his chest due to the agitation.

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C – Heart rate is 120 bpm irregularly irregular, blood pressure 85/60 mmHg, capillary refill time 3 seconds; hands are warm to touch; urine output over the last 3 hours is 15ml; cannula in-situ

D -GCS of 13 (E4 V4 M 5), pupils are equal and reactive. Temperature is 38°C and blood sugar is 12 mmol/L.

E – No rashes.

3. What will be your next step?

A: Give 1 L fluid challenge, administer antibiotics according to hospital guidelines, take bloods including cultures and arterial sample for lactate, inform your registrar.

B: Give 1 L fluid challenge, take bloods including cultures and arterial sample for lactate, prescribe antibiotics according to hospital guidelines, ask your registrar for urgent review.

C: Give 1 L fluid challenge, take bloods including cultures and arterial sample for lactate, prescribe antibiotics according to hospital guidelines and ensure the nurse administers them immediately, ask your registrar for urgent review.

D: Give 1 L fluid challenge and repeat it if there's no response, take bloods including cultures and arterial sample for lactate, prescribe antibiotics according to hospital guidelines and ensure the nurse administers them immediately, ask your registrar for urgent review.

Answers

1) Correct answer: A

This is a haemorrhagic shock until proven otherwise. Patient needs oxygen, appropriate fluid challenge, senior review and blood because she will be going to theatre to stop the bleed.

2) Correct answer: D

This is a septic shock. Sepsis six pathway needs to be completed within 1 hour: high flow oxygen, blood sampling including blood cultures and lactate, IV antibiotics and fluids, and catheterization for fluid balance monitoring. Patient needs urgent senior review. (8)

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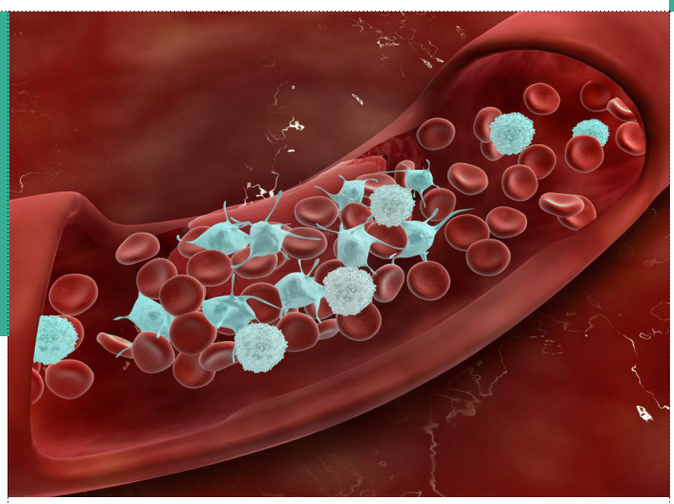
UPDATE ON NOVEL ORAL ANTICOAGULANTS

J Williams, N Sharawi



Update On Novel Oral Anticoagulants
Teaching & Training

Abstract

The novel oral anticoagulants - dagibatran, apixaban and rivaroxaban are licensed for use for a number of indications in the UK and are being increasingly used in patients to prevent and treat thromboembolic disease. Experience with these agents and their complications is still limited.

As these agents become more integrated into clinical practice, it is imperative that junior doctors develop a good awareness of their pharmacological properties as well as how to manage bleeding associated with their use.

Introduction

The novel oral anticoagulants (NOACs) came about to overcome some of the limitations of warfarin which has been the mainstay of treatment in the management of thromboembolic disease (VTE) and Atrial Fibrillation (AF) for over five decades.

Warfarin has a narrow therapeutic window, requires continuos monitoring, has inter-patient variability and along with multiple drug and food interactions has led to multiple challenges in relation to compliance and its safety profile. These drawbacks along with an increased understanding of the coagulation cascade have led to newer oral anticoagulant therapies that block procoagulant activity.

Which NOACs are available for use?

There are three main NOACs approved for use in the UK: Dagibatran etexilate (Pradaxa) - the most well-established, Rivaroxaban (Xarelto) and Apixaban (Eliquis). Edoxaban is still under consideration for approval.

What are their licensed indications in the UK?

The National Institute for Health and Care Excellence (NICE) encourages clinicians to consider the use of the new oral anticoagulants (NOAs) for their approved indications as an alternative to warfarin while taking into account the specific patient factors and risks. (1-10)

Dagibatran, rivaroxaban and apixaban are all licensed for the:

- *prevention of venous thromboembolic events in adults who have had elective total hip-replacement or knee-replacement surgery*

- *prevention of stroke and systemic embolism in adults with non-valvular atrial fibrillation and one or more cardiovascular risk factors*

- *treatment of deep-vein thrombosis and pulmonary embolism, and prevention of their recurrence, in adults*

Rivaroxaban has additionally recently been approved for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome (ACS) with elevated cardiac biomarkers when it is co-administered with aspirin alone or with aspirin+clopidogrel/ ticlopidine.

How do the NOACs work?

The NOACs work further along the coagulation pathway than warfarin and inhibit a single clotting factor to produce overall effect.

Dagibatran etexilate is a pro drug that is converted to dagibatran by non specific esterases in the liver and plasma. It is a direct thrombin (Factor II) inhibitor leading to potent anticoagulation.

Apixaban and Rivaroxaban are both factor Xa inhibitors therefore work on both extrinsic and intrinsic pathways.

Edoxaban is also a factor Xa inhibitor.

Their overall result is blocking fibrin production and thus clot formation.

UPDATE ON NOVEL ORAL ANTICOAGULANTS

J Williams, N Sharawi

MINOR BLEEDING eg epistaxis, bruising

- conservative measures – local haemostatic measures
- consider omitting subsequent dose

↓

MAJOR BLEEDING

- primary resuscitative measures
  - assess and manage A, B and C continuously
  - establish adequate IV access (at least 2 large bore cannulae)
  - maintain BP and urine output (helps eliminate drug)
- consider activated charcoal (if <2h since ingestion) and Tranexamic Acid
- stop bleeding: local compression or surgical intervention
- restore intravascular volume and replace deficiencies
  - IV fluids (eg colloids)
  - packed red cells (aim Hb > 80g/dL)
  - Fresh frozen plasma (FFP)
  - Platelets
- consider dialysis (dagibatran)
- serial assessment FBC, U&E and clotting
- maintain normothermia (optimise clotting factor function)

↓

LIFE THREATENING BLEEDING

Consider coagulation factor replacement

- prothrombin complex concentrate (PCC) : 25µ/kg
- activated prothrombin complex concentrate
- recombinant factor VIIa (rFVIIa)

Figure 1

What are the pharmacokinetic properties of the NOACs?

The NOACs reach their peak plasma concentrations around 4 hours following ingestion. Their effects are determined by their plasma concentration rather than the inhibition of clotting factor synthesis therefore their anticoagulant effects occur quicker than with warfarin.

The half-life of dagibatran is 12-17h, rivaroxaban 7-11h and apixaban 9-14h. These however may be prolonged in renal impairment. Cessation of the drug results in return to baseline coagulation status relatively quickly.

Dagibatran is mostly excreted unchanged by the kidneys (85%) whereas about one-third of rivaroxaban and one-quarter of apixaban are eliminated by this route. (11-13)

What are the main side effects associated with their use?

Bleeding is the most serious side effect that can seen with the use of any anticoagulant including NOACs.

- Dagibatran has a strong association with dyspepsia and other GI symptoms and therefore should be avoided in patients with gastrooesophageal reflux disease.

- Rivaroxaban is also associated with GI symptoms but this is not reported as frequently as with dagibatran. Other side effects include hypotension, dizziness, headaches, pain in the extremities, renal impairment and rash.

- Apixaban can cause nausea, bruising and anaemia. (11-13)

What are the benefits of the NOACs vs Warfarin?

- Multiple well-designed large trials were used to investigate the NOACs efficacy and safety profiles and the general findings are that they are at least comparable to standard treatment in terms of efficacy for their licensed indications and have comparable or improved rates of bleeding events including intracerebral haemorrhages.

Exceptions are the trials for AF where increased rates of GI bleeding was found however mortality was reduced by 10%. For management of ACS, Rivaroxaban was shown to significantly reduce the rate of the cardiovascular death, non-fatal MI or stroke compared to standard treatment. An increased rate of major bleeding was seen but no there was no difference in the incidence of fatal bleeding. (1-10)

Their onset and offset of effects are quick - they work directly on clotting factors rather than block time-dependent clotting factor synthesis as a result their actions are rapid in onset. As a result of this there is no need for bridging therapy as parenteral enoxaparin is used until warfarin's anticoagulant effects are optimal. Similarly with a relatively short half life each of around 12h thus cessation of NOACs will result in a quick return to baseline physiology. (14)

UPDATE ON NOVEL ORAL ANTICOAGULANTS

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• Their reliable and stable pharmokinetics allow for once or twice daily dosing. NOACs do not require monitoring or continuous dose titration as warfarin does as they produce a consistent and predictable dose-repsonse.(15)

• There are fewer known drug interactions - although it is believed that more may manifest as more patients become established on long-term anticoagulation with them. (11-13)

What cautions need to be taken in patients using NOACs?

• Noncompliance may increase thromboembolic risk - Patients should be warned about the importance of adhering to dosing regimen. This is particularly important especially for once daily dosages - the half-life of the NOACs is approximately 12 hours. Missing a single dose can have a significant impact on trough levels and result in suboptimal anticoagulation.

• Renal impairment may increase bleeding risk - NOACs should be used cautiously in renal impairment especially dagibatran which depends fully on the kidneys for excretion. Factors such as dehydration, hypovalemia or coadministration of medicines affecting the kidney may alter NOAC clearance from the body and therefore increase anticoagulant effect. More frequent monitoring may be indicated and doses may require adjustment or withholding after discussion with a Haematologist.

• NOACs are not licensed for use in severe renal impairment. Dagibatran is contraindicated in patients with creatinine clearance <30mL/min as it is predominately excreted unchanged via the kidneys. Apixaban is the safest option for use in patients with renal impairment. (16)

• Drug interactions: All three agents are substrates of P-glycoprotein and co-administration with medicines that inhibit (eg Verapamil) or induce (eg phenytoin) this pathway can increase of decrease the blood level concentrations of the NOACs. Caution should be taken especially with the use of NOACS whilst co-medication with anti-epileptics, macrolide antibiotics, antifungals and anti arrhythmic drugs.

How is bleeding managed in patients taking NOACs?

Bleeding is one of the main concerns with the use of the NOACs and there remains limited experience with its management. To date there are no antidotes to reverse the actions of the NOACs unlike warfarin which can be reversed by vitamin K. Junior doctors should familiarise themselves with local guidelines for the management of bleeding on NOACs.

A careful history and examination is crucial. Ascertaining when the last dose was taken and the dosing regime is very useful as one can estimate when anticoagulant effects can be expected to resolve. Knowledge of comorbidities such a renal or hepatic impairment and use of other anticoagulants can also help determine the individual patient's bleeding risk.

The patient should be assessed using an Airway, Breathing and Circulation approach. A prolonged capillary refill time, tachypnoea, tachycardia, hypotension, oliguria and altered conscious level are all signs that could indicate hypovolaemia as a result of significant blood loss and would warrant more aggressive management.

Blood should be taken to assess haemoglobin, platelet count, renal, liver and clotting function. Note that a normal clotting function does not mean that the patient is not at risk of further blood loss. Impaired renal function may be associated with prolonged anticoagulant effects. In the absence of renal impairment it could be expected that normal haemostasis will return within 12-24 hours of the last dose. In the case of impaired renal function this may take 48 hours or more to be achieved and as such bleeding may be prolonged.

Following assessment, bleeding can be categorised into minor, major and life-threatening bleeding which is a clinical judgement demonstrating degree of concern and influences the management. (16)

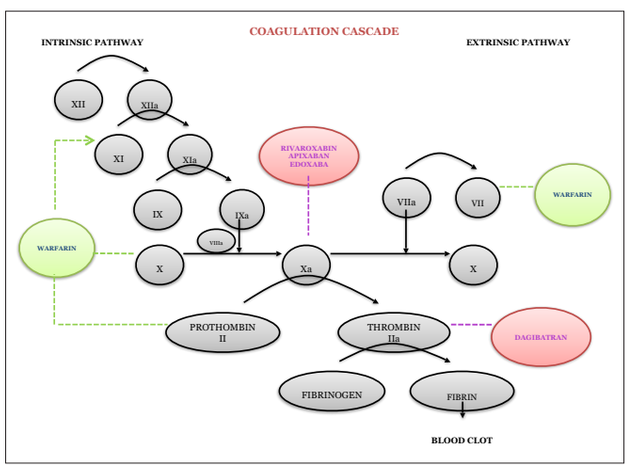

Figure 2

UPDATE ON NOVEL ORAL ANTICOAGULANTS

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Minor bleeding

It is important to remember that these agents have short half-lives and "watching and waiting" may be appropriate in the case of minor controlled bleeding. Local haemostatic measures may be all that is required. Oral activated charcoal may be considered if time of ingestion is less than two hours and can reduce absorption of the drug. Decisions to omit a subsequent dose should take into consideration the risk of thrombosis in the individual patient and should involve senior colleagues and a Haematologist.

Major bleeding

Management of significant bleeding should begin with the measures mentioned above. Subsequent doses of NOACs should be withheld until bleeding has settled and following discussion with the Haematologist. The airway should be effectively protected, supplementary oxygen should be given and adequate intravenous access should be established followed by intravenous fluid resuscitation. Management in an Intensive Care environment with haemodynamic monitoring should be considered early.

Management of major bleeding (and life-threatening bleeding) is supportive and can be categorised as shown below:

- *measures to stop bleeding e.g. surgery, endoscopy*

- *measures to help reduce drug levels in the circulation: activated charcoal and haemodialysis*

- *measures to restore circulatory volume: intravenous crystalloids, colloids, blood*

- *measures to correct anaemia, thrombocytopaenia and coagulopathy: red cells, platelets and coagulation factors respectively*

- *measures to reduce fibrin breakdown (Tranexamic Acid 1-1.5g 6-8 hourly during bleeding)*

- *measures to enhance haemostasis: Prothrombin C concentrate, activated prothrombin C concentrate, recombinant Factor VIIIa (life-threatening bleeding only)*

Throughout resuscitation the patient should be repeatedly assessed to detect response to the measures employed by assessing ongoing blood loss, their circulatory status (as mentioned above) and also haemoglobin and coagulation parameters.

Life threatening bleeding

In the event of life-threatening bleeds, the pro-haemostatic agents Prothrombin Complex Concentrate (PCC), Activate Prothrombin Complex Concentrate (aPCC) and Recombinant Factor VIIa (rFVIIa) should be considered although the evidence supporting their use is limited.

These agents are prothrombotic and their use is to be only considered as a last resort because of the risk of precipitating thrombotic events.

How can we monitor the activity of NOACs?

The lack of necessity for blood monitoring is one of the proposed benefits of these agent however not being able to measure blood levels of the drugs is a major concern. In the hospital setting there are a number of instances whereby assessment of coagulation and bleeding risk of patients on NOACs may be desirable such as in the case of bleeding, in a patient with acute renal impairment or around the period of an invasive procedure/surgery. (17-18)

Noac	Preferred method	In an emergency
Dabigatran	*Ecarin clotting time* *Dilute thrombin time*	*Activated partial thmoboplastin time (aptt)*
Rivaroxaban	*Anti-factor xa*	*Prothrombin time (pt)*
Apixaban	*Anti-factor xa*	*Dilute prothrombin time (dilute pt)*

Table 1: Laboratory tests to monitor NOACs.

Tests in current use provide a qualitative rather than a quantitative assessment of bleeding risk and the preferred tests are not available in most institutions. APTT may be used with dabigatran.

The ideal test for the factor Xa blockers, rivaroxaban and apixaban, is an anti-factor Xa assay, however, in an emergency, PT and dilute PT can be used for rivaroxaban and apixaban respectively. Prolonged coagulation times may be useful in detecting ongoing anticoagulant effects but a normal coagulation profile does not confirm that this effect has completely worn off. (18)

What about patients on NOACs who need a procedure?

In these instances, the risk of bleeding with the proposed intervention vs the risk of thrombosis should be taken into account in conjunction with the patient's renal function and the urgency of the intervention.

Epidural and spinal anaesthesia as well as lumbar punctures would be considered interventions with a high bleeding risk. It is recommended that the NOACs are stopped 24 hours before surgery procedure with a low bleeding risk, and between 48 hours and 96 hours before surgery with a high bleeding risk.

In the case of significant renal impairment longer delays may be necessary for elective cases especially with dabigatran and laboratory testing should be considered to determine the residual effects of the agents. (19-20)

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For high bleeding risk cases and emergency cases where the last dose is not known, blood and blood products should be easily accessible. If bleeding occurs intraoperatively consider easily use of blood products. Life- threatening bleeding should be addressed as in figure 2. Regional anaesthesia should be avoided.

Conclusion

We can expect to see NOACs being used considerably more over the next few years in the management of patients with atrial fibrillation, post orthopaedic surgery, venous thromboembolism management and in acute coronary syndromes. There are multiple features of these agents that make them favourable to warfarin and other standard treatments, however the lack of ability to monitor their plasma levels and lack of a reversal agent especially in the event of bleeding are concerns shared by many clinicians.

An awareness of their general pharmacokinetic properties can help improve confidence with looking after patients on NOACs on a day-to-day basis including managing major complications such as bleeding. With no antidote available, the management of bleeding is supportive following a careful history and examination to determine degree of blood loss and the patient's individual bleeding risk.

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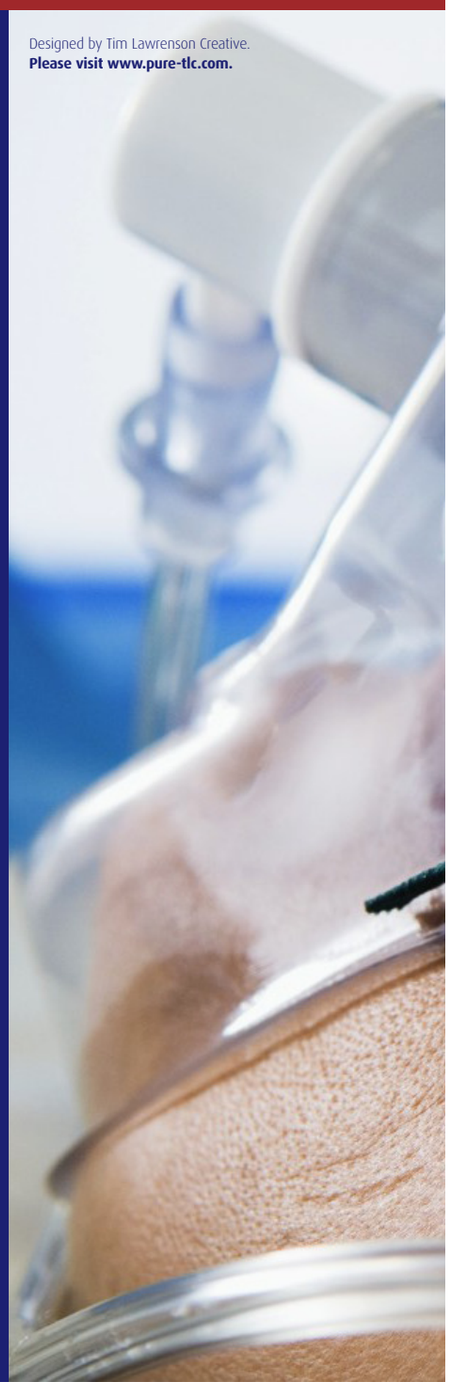

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