# Poorly Answered Pharmacological Questions

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| Applied clinical pharmacology | | | |
|---|---|---|---|
| *Competence* | *Description* | *Assessment methods* | *GMP* |
| ***Demonstrates knowledge of:*** | | | |
| PR_IK_01 | Analgesia: principles of analgesia including infusions, patient controlled analgesia; medications for chronic pain including antidepressants, anticonvulsants, antiarrhythmics; routes of administration including oral; sublingual; subcutaneous, IM; IV; inhalational analgesia, patient controlled analgesia, epidural; agents used for regional techniques and local blocks | A,C,E | 1,2 |
| PR_IK_02 | Management of acute poisoning: including aspirin; paracetamol; opioids; aminophylline; digoxin; ecstasy and other social drugs; antidepressants; alcohol | A,C,E | 1,2 |
| PR_IK_03 | Drug toxicity, causes and avoidance. Management of malignant hyperthermia. Potential risks of drug additives | A,C,E | 1 |
| PR_IK_04 | Pharmacokinetics. Including target controlled infusions and effects of renal and/or hepatic impairment on drug disposition and elimination of; influence of renal replacement therapies of commonly used drugs | A,C,E | 1,2 |
| PR_IK_05 | Cardiovascular System: principles and use of inotropes and vasodilators, including pulmonary vasodilators; pharmacological problems in cardiopulmonary bypass, cardioplegia; Management of arrhythmias | A,C,E | 1,2 |
| PR_IK_06 | Use of drugs in the management of cardiogenic shock and cardiac failure | A,C,E | 1 |
| PR_IK_07 | Management of hypertension before anaesthesia, including acute management and phaeochromocytoma. Manipulation of blood pressure to assist surgery | A,C,E | 1 |
| PR_IK_08 | Antibiotics: principles of action; choice of drug. Antibiotic prophylaxis against surgical infection including subacute bacterial endocarditis. Therapy of bacterial, fungal and viral infections | A,C,E | 1 |
| PR_IK_09 | Anticoagulant and thrombolytic prophylaxis and therapy, including management of pulmonary embolus | A,C,E | 1 |
| PR_IK_10 | The Respiratory System: management of severe asthma; use of gases: helium and nitric oxide | A,C,E | 1,2 |



Applied clinical pharmacology

| *Competence* | *Description* | *Assessment methods* | *GMP* |
|---|---|---|---|
| ***Demonstrates knowledge of:*** | | | |
| PR_IK_11 | The Gastrointestinal System: acid aspiration prophylaxis; anti-emetics | A,C,E | 1,2 |
| PR_IK_12 | CNS: general vs regional anaesthesia in all areas of anaesthesia; action of drugs on the eye; control of convulsions | A,C,E | 1,2 |
| PR_IK_13 | The Musculoskeletal System: muscle relaxants and reversal agents; anaesthetic implications of myasthenia gravis and other neuromuscular disorders | A,C,E | 1,2 |
| PR_IK_14 | Resuscitation: including management of allergy and anaphylaxis | A,C,E | 1,2 |
| PR_IK_15 | Principles of parenteral and enteral nutritional formulas in intensive care | A,C,E | 1,2 |
| PR_IK_16 | Therapeutics in pathologic states: problems associated with organ transplantation; anaesthetic relevance of drugs used in malignancy; therapy in acute and chronic respiratory diseases | A,C,E | 1,2 |
| PR_IK_17 | Problems of drug dependency and addiction | A,C,E | 1 |
| PR_IK_18 | Environmental effects of anaesthetic agents | A,C,E | 1 |
| PR_IK_19 | Influence of age on drug pharmacokinetics and pharmacodynamics | A,C,E | 1 |
| PR_IK_20 | Assessment of cognitive dysfunction issues such as delirium, POCD and dementia, and implications | A,C,E | 1 |

# Final FRCA

MCQs/SBAs

Constructed response questions/SAQs

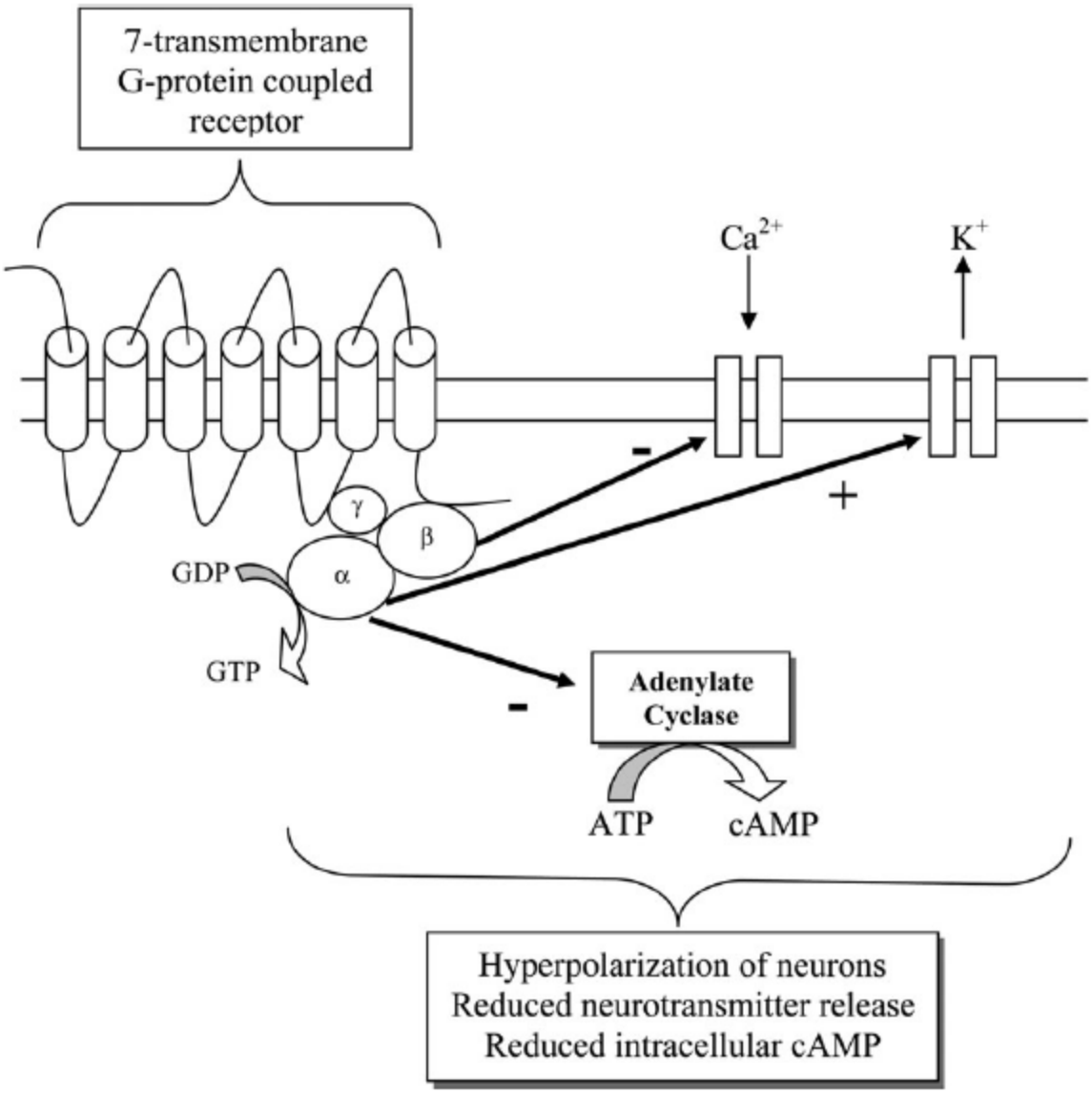
VIVA-1 pharmacological question

# QUESTION 1; March 2016

a) What are the site of action and the intra and extracellular mechanisms of analgesic effect within the spinal cord following the administration of intrathecal (IT) opioids? (6 marks)

b) List the principal side effects of IT opioids. (7 marks)

c) What factors may increase the risk of postoperative respiratory depression following administration of IT opioids? (7 marks)


7-transmembrane
G-protein coupled
receptor
$Ca^{2+}$
$K^{+}$
-
+
γ
β
α
GDP
GTP
-
Adenylate
Cyclase
ATP
cAMP
Hyperpolarization of neurons
Reduced neurotransmitter release
Reduced intracellular cAMP

# Cellular mechanism of action

(i) Closing of voltage-sensitive calcium channels

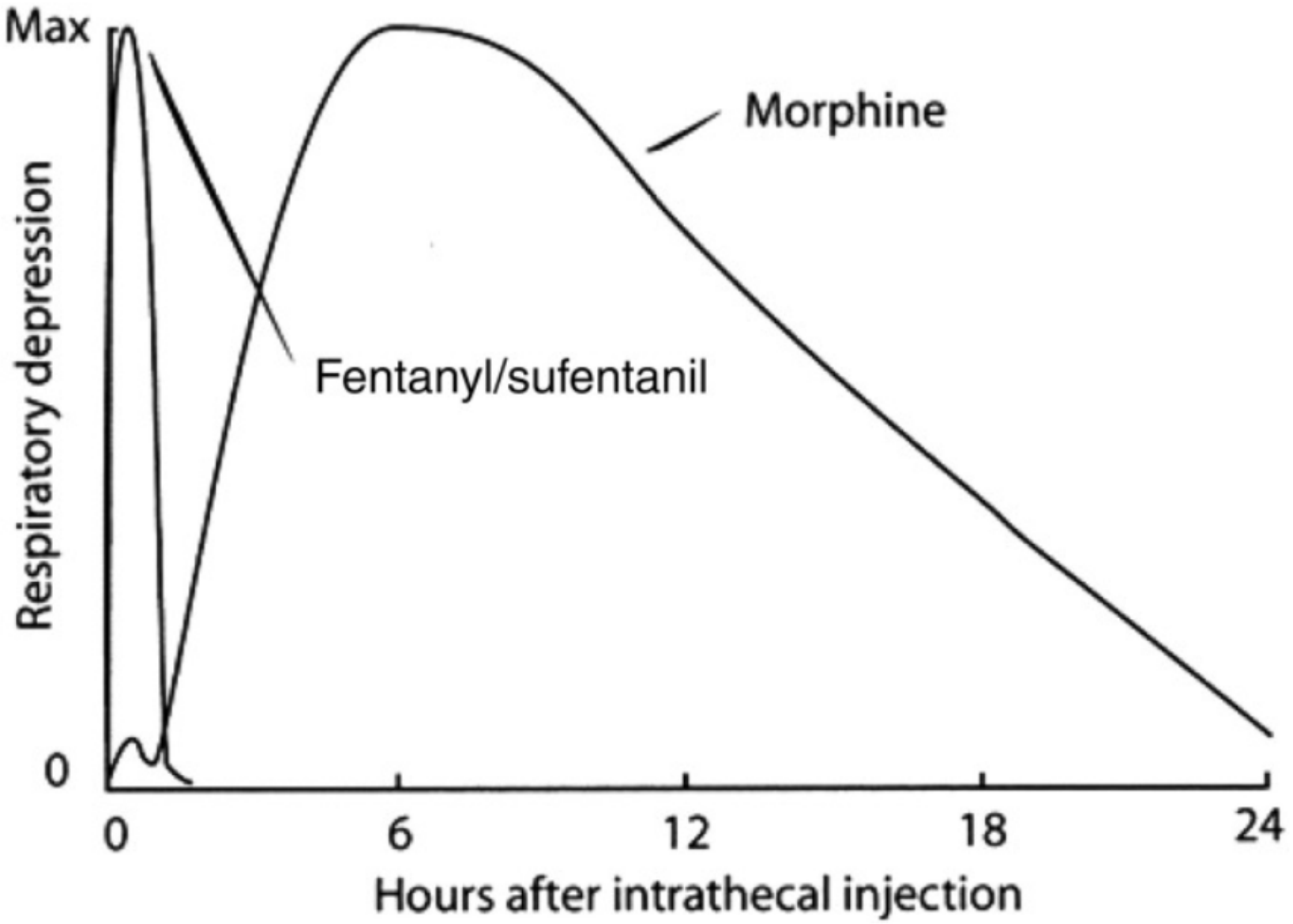
(ii) Stimulation of potassium efflux leading to hyperpolarization,

(iii) reduced cyclic adenosine monophosphate (cAMP) production via inhibition of adenylyl cyclase

Overall reduced synthesis of excitatory neurotransmitters.

# Side effects

- **Respiratory depression or arrest**
- **Nausea and/or vomiting**
- **Urinary retention**
- **Pruritis**
- Hypotension
- Bradycardia
- Dependency
- Miosis
- A headache
- Seizures


Max
Respiratory depression
0
Morphine
Fentanyl/sufentanil
0
6
12
18
24
Hours after intrathecal injection

# Risk factors for respiratory depression

- Increasing age
- Concomitant use of long-acting sedatives
- Positive pressure ventilation
- Co-existing respiratory disease
- Dose dependent
- Hydrophilic opioids

Ref;

1. Opioid receptors; CEACCP 2015

2. https://doi.org/10.1093/bjaceaccp/mkn016

# Chairman report; *Pass rate 31.7%*

It was anticipated that candidates would find this question difficult, and this proved to be the case. Intrathecal opioids are used widely in anaesthetic practice but candidates' knowledge of their use was poor. Advanced sciences are part of the intermediate curriculum so knowledge of applied pharmacology is expected. Some candidates failed to read part (b) of the question and gave the side effects of intravenous opioids or intrathecal local anaesthetic in their answer.

# Question 2

September 2009

a) List the potential clinical advantages for the use of nitrous oxide as part of a general anaesthetic. (25%)

b) List the potential clinical disadvantages of the use of nitrous oxide. (50%)

c) State the currently accepted safe occupational exposure limit for nitrous oxide. What measures are taken to achieve this within the operating theatre when nitrous oxide is used? (15%)

# Answer; a

-Induction-Second gas effect

-MAC additive-less hemodynamic disturbances

-Associated with low risk of awareness

-Anxiolytic and analgesic in obstetric population

-Potential use in chronic pain

-Procedural sedation-Adult/Paediatrics

-Major depression

# Disadvantages

-Diffusion hypoxia

-Diffusion into air filled spaces

-Absorption atelectasis

-Pneumonia

-Neurotoxicity

-Teratogenicity

-Megaloblastic anaemia

-PONV

-Green house gas effects

-Misuse

# c. Safe exposure

- Explicit occupation exposure limit; 25-50ppm
- Effective scavenging systems
- Low flow anaesthesia

Ref;


1. https://bjanaesthesia.org/article/S0007-0912(19)30063-7/fulltext
2. 2. Nitrous oxide in modern anaesthetic practice; BJA Education, 16 (3): 87–91 (2016)

# Question 3- March 2015

a) Outline the mechanisms of spontaneous recovery from neuromuscular blockade following the administration of rocuronium.

(2 marks)

b) Which classes of drugs can be used to antagonise the action of rocuronium (2 marks) and how do they work? (5 marks)

c) What are the advantages and disadvantages of these antagonist drugs? (11 marks)

# Rocuronium

a)

REDISTRIBUTION and ELIMINATION
Long elimination half life (1-2h) so depends more on redistribution for termination of effects

METABOLISM
Excreted unchanged by hepatobiliary excretion and in the urine

# Rocuronium

ANTICHOLINESTERASES

-AChE hydrolyses ACh terminating its effects

-Anticholinesterases antagonise AChE and so more ACh is available at the NMJ

-Anticholinesterases are also hydrolysed by AChE but the process is much slower and so AChE is unable to work for longer

-Increase in synaptic ACh displaces Rocuronium from nicotinic AChR restoring transmission

# Continued..

CYCLODEXTRINS (e.g. Sugammadex)

-Sugammadex encapsulates free plasma rocuronium molecules
-Ratio 1:1
-Free concentration of rocuronium in the plasma decreases
-Dissociation from NMJ increases down a concentration gradient
-Normal muscle tone is restored

# ANTICHOLINESTERASES

ADVANTAGES:
-Cheap
-Readily available preparation with glycopyrrolate
-Reliable, predictable reversal
DISADVANTAGES:
-Unable to recover patients from deep NMJ blockade
-Reversal only occurs if spontaneous recovery has commenced
-Concerns about side effects;

- -Bradycardia
- -Precipitate a bronchospasm in asthmatics
- -Increases salivation
- -Intestinal motility leads to abdominal cramps

# CYCLODEXTRINS

ADVANTAGES:

-Effective in reversing rocuronium from profound levels of NMJ blockade and quickly

-Minimal reported side effects

DISADVANTAGES:

-Expensive

-Isolated cases of hypersensitivity

-Possible QT prolongation

-May encapsulate other drugs (e.g. OCP)

-Rocuronium may be displaced from Sugammadex by flucloxacillin and fuscidic acid, potentiating the block

# Chairman report; *Pass Rate 52.7%, 10.9% of candidates received a poor fail*

The pass rate is disappointing as these agents are “meat and drink” to the profession. The mechanisms by which the action of rocuronium spontaneously degrades were poorly understood. Sugammadex may not be readily available in some Trusts but it is reasonable to expect specialist trainee anaesthetists to understand its pharmacology and clinical usage.

# Question 4-September 2014

a) What is Propofol-Related Infusion Syndrome (PRIS) and what are its clinical effects? (7 marks)

b) List the risk factors for PRIS. (5 marks)

c) What specific laboratory findings might be expected in a case of PRIS? (3 marks)

d) How may PRIS be prevented (3 marks) and managed? (2 marks)

# Propofol infusion syndrome

Acute refractory bradycardia leading to asystole in the presence of one or more of the following:

-Metabolic acidosis ( BE; -10 mmol/litre)

-Rhabdomyolysis or myoglobinuria

-Lipaemic plasma

-Enlarged liver or fatty liver

Safest dose of propofol infusion-1-4mg/kg/hr

# PRIS

Clinical effects

- New onset metabolic acidosis
- Cardiac dysfunction
- Rhabdomyolysis
- Renal failure
- Hypertriglyceridaemia

# Risks factors

- severe head injuries
- Sepsis
- High exogenous or endogenous catecholamine and glucocorticoid levels
- Low carbohydrate to high lipid intake
- inborn errors of fatty acid oxidation.

# Prevention and Management

Prevention;

- Should not exceed 4 mg/kg/hr
- Routine monitoring of CK and triglycerides

Management;

- Stop propofol infusion
- Alternative sedatives; Midazolam, Alfentanyl
- Cardiovascular support; Inotropes, Vasoconstrictors
- Renal Replacement Therapy

https://doi.org/10.1093/bjaceaccp/mkt007

# Chairman report; Pass Rate 35.8%

This question was felt to be hard to answer and was assigned a low pass mark after the Angoff process. It proved to be another very strong discriminator between candidates and was answered poorly in the main. Weak candidates had no real knowledge of the subject and did not appreciate that the cardiovascular consequences of the syndrome predominate. Many referred incorrectly to the precipitation of liver failure. Trainees undertaking a block of intensive care medicine will use propofol sedation for some patients so it is important that they understand any potential complications.

# Question 6

- March 2013

  a) What are the indications for anti-platelet drugs in clinical practice? (25%)

  b) List the agents currently in clinical use and their underlying mechanisms of action. (50%)

  c) How may active bleeding be managed following administration of one of these agents? (25%)

# Question 1-September 2015

a) How should you manage the perioperative opioid requirements of a patient who is having elective surgery and who takes regular opioids for non-malignant pain? (8 marks)

b) Give the conversion factors for oral tramadol, codeine and oxycodone to the equianalgesic oral morphine dose. (3 marks)

c) What are the perioperative implications of an existing spinal cord stimulator? (6 marks)

d) What additional perioperative precautions should be taken if the patient has an intrathecal drug delivery system fitted? (3 marks)

# Question 1

*Chairman report; Pass rate 25.0%*

- It was anticipated that candidates would find this question difficult and this proved to be the case. Some candidates lost marks because they wrote exclusively about the drugs they would use to manage opioid requirements for this patient but did not mention more general measures such as involvement of the pain team. Very few candidates gave any information about management of transdermal pain patches in the peri-operative period. There are differing opinions as to whether patches should be continued, particularly in the case of buprenorphine, but candidates were able to gain marks for either opinion provided they showed that they were aware of the potential problems of altered absorption and partial antagonism