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Analgesics

OP01 [Mar96] With regards to pethidine's physical properties:

A. It has an octanol coefficient of 10

B. It has a pKa of 8.4

C. ?

D. ?

E. ?

OP02 [Mar96] Which factor does NOT predispose to bradycardia with fentanyl in doses of 50 mcg/kg?

A. Calcium channel antagonist

B. Beta-blocker

C. Benzodiazepines

D. ?

E. Slow injection of drug

Factors predisposing to bradycardia/asystole during opioid induction

- presence of beta and/or calcium channel blockade
- premedication or concomitant use of benzodiazepines
- rapid administration
- muscle relaxants with little or no vagolytic properties
- vagotonic muscle relaxants (e.g. suxamethonium)
- added vagal stimuli (e.g. laryngoscopy)

OP03 [Mar96] [Mar99] [Jul99] [Feb00] [Apr01] Naloxone:

A. Is not an antagonist of agonist-antagonist drugs naloxone as a competitive antagonist should antagonise partial agonists (agonist/antagonists) at a high enough dose as long as they are not irreversible

B. Is not an antagonist at ?mu & sigma receptors "Naloxone is a pure opioid antagonist and will reverse opioid effects at mu, kappa and delta receptors" (Peck, Hill and Williams p. 135); as for sigma receptors, "they are not reversed by naloxone" and are no longer considered opioid receptors.

C. Causes pulmonary oedema

D. Can cause hypotension in experimental shock animal models

E. May cause an abrupt increase in sympathetic tone

OP03b [Mar97] Naloxone:

A. Is effective at antagonising a full agonist but not a partial agonist

B. Causes pulmonary oedema

C. ?

D. ?

OP04 [Mar96] [Jul99] {Diagram of numbered structure of morphine}

Which substitutions correct?

A. N17 substitution gives antagonist activity A. N17 substitution does give anatagonist activity. E.g. naloxone has CH2CHCH2 (as opposed to the CH3 in morphine. Naloxone is an oxymorphone derivative.

B. C6 methylation produces codeine B. C3 O-methylation produces codeine.

C. Glucuronidation occurs at C2 Glucuronidation occurs at C3 and C6 (hence Morphine-3-glucuronide is the major metabolite, M6G the minor metabolite)

D. Diacetylation decreases lipid solubility Diacetylation (as in C3 and C6 for diacetylmorphine = heroin) increases lipid solubility.

Also remembered as:

Morphine base structure with questions about substitutions

A. C3 and C6 increase lipid solubility

B. Acetyl group on ?C3 gives heroine

C. N- substitution gives antagonist

D. C5 glucuronidation site

E. C3 methyl gives codeine

OP05 [Mar96] [Jul98] [Jul00] Pethidine in doses of 2 to 2.5 mg/kg causes all of the following EXCEPT:

A. Bradycardia - anticholinergic properties ie tachy

B. Decreased systemic vascular resistance morphine-like opioids in therapeutic doses produce vasodilation, decreased peripheral resistance, and inhibition of baroreceptor reflexes (therefore orthostatic hypotension can occur)

C. ?Normal arterial BP / ?decreased BP

D. Increased cardiac output

OP06 [Mar96] Regarding the clearance of morphine:

A. Affected by cirrhosis

B. Affected by hepatic blood flow

C. Shows low hepatic extraction ratio

D. ?

E. ?

OP07 [Jul97] [Mar99] [Jul99] [Jul00] [Feb04] [Jul04] Fentanyl:

A. With pKa 8.4 is 90% ionised at physiological pH

B. Has an octanol coefficient of 10

C. Is 1,000 times more potent than morphine 100

D. Has first-pass lung uptake reduced to 20% by propranolol

E. Has up to 50% uptake in the lung. 75%

F. Elimination half-life < 2 hour 3-6hrs

G. Carried on albumin mostly - mostly acidic drugs

H. Carried on alpha-1 acid glycoprotein mostly

I. Can cause hypertension with MAOI - pethidine

J. Alfentanil acts faster as it has a higher unionised, unbound fraction. is higher unionised but is lower unbound

OP08 [Jul97] An opioid which can not be used for TIVA:

A. Morphine

B. Pethidine - accumulation of norpethidine

C. Fentanyl

D. Sufentanil

E. Alfentanil

OP10 [Mar98] Pethidine

A. 100mg is equal to 10mg morphine in effect 75-100mg IM = 10mg IM morphine

B. Increases heart rate

C. No effect on cardiac output

D. Is preferred to morphine for analgesia

E. ?

OP10b [Mar98] Pethidine produces:

A. Miosis - can do but antimuscarinic effects may cause mydriasis

B. More severe hypotension with comparable dose of morphine - maybe

C. More biliary spasm than morphine less

D. ?

OP11 [Mar98] TIVA with morphine causes the following EXCEPT:

A. Mydriasis

B. Muscle rigidity

C. Respiratory depression

D. ?

OP12 [Mar98] [Jul98] [Jul02] [Mar03] Codeine:

A. Substitution at C6 position of morphine. Substitution of a methyl group for the hydroxyl group on C3 of morphine.

B. 10% of codeine is metabolised to diacetyl morphine (heroin - so no. but is otherwise correct)

C. IM 100mg is equivalent to 10 mg morphine. 120mg = 10mg morphine

D. Methyl substitution at the ?C5/?C6 position of morphine

E. Can be safely given IV because causes no histamine release

F. Has higher first pass effect than morphine. limited 1st pass metab due to methyl gp on C3

OP13 [Jul98] Morphine metabolism:

A. Principally metabolised to morphine-6-glucuronide 10%

B. Metabolites have shorter half-life. longer ie days

C. Found in extrahepatic sites - renal metab makes a significant contribution

D. Metabolites freely cross the blood-brain barrier - limited

E. ?All have analgesic effect / ? Are 30% renally excreted

F. In neonates, predominantly by sulphation ??? Sulfation is an important pathway for the elimination of acetaminophen and of morphine in neonates."

G. In adults, mostly to morphine-3-glucuronide

Opioid	Plasma Half Life
Heroin	0.5 hours
Morphine	2 hours
Hydromorphone	2-3 hours
Oxymorphone	2-3 hours
Codeine	2-4 hours
Fentanyl	3-4 hours
Pethidine	3-4 hours
Methadone	15-40 hours

OP14 [Jul98] Buprenorphine:

A. Effective orally

B. ?

C. ?

- Not effective orally as high hepatic first pass metabolism
- Oral bioavailability <6%
- Is given by SC, IM, IV, sublingual or transdermal but NOT oral.

OP15 [Mar99] [Feb00] [Jul02] Sufentanil:

A. 30 times as potent as fentanyl x5-10

B. < 7% excreted unchanged in urine <1%

C. Greater protein binding than fentanyl 93% vs 84% fentanyl

D. Half-life of elimination between fentanyl & alfentanil sufentanil 2-4hrs. alfen = 1.5, fent 3-6hrs

E. Predominantly bound by ?albumin/ ? alpha1-acid glycoprotein

OP16 [Mar99] [Jul00] Pethidine is the traditionally favoured opioid in obstetrics because:

A. Norpethidine does not cross the placenta

B. Does not undergo ion trapping

C. Causes less neonatal depression

D. It does not cross the placenta

E. It is thought to cause less respiratory depression in the neonate.

OP17 [Mar99] Pethidine:

A. Better bioavailability than codeine

B. ?

C. ?

D. ?

petnidine 50%, codeine 60-70%

OP18 [Jul99] Pethidine:

A. Norpethidine metabolite

B. Pethidine 6-glucuronide - morphine

C. ?

OP19 [Jul00] Alfentanil is more lipid soluble than fentanyl because:

A. Has a pKa of 8.4 (6.5) & is 90% unionized at physiological pH

B. ?"n-Octanol coefficient is [some five digit num] [Jul96] [Mar98] [Jul04]."

C. ?

D. ?

fentanyl (813) is more lipid soluble than alfentanil (145)

OP19b [Jul01] [Jul04] Alfentanil works faster than fentanyl because:

A. More lipid soluble

B. Higher concentration unbound, unionised at physiological pH

C. Decreased protein binding

D. Larger volume of distribution

E. ?

OP20 [Jul00] [Apr01] Methadone:

A. Phenanthrene derivative morphine, hydromorphone, oxy, codeine

B. ?metabolism

C. Peak plasma levels at 3 hours. oral 2-4hrs

D. Used in chronic cancer pain due to non addictive potential

E. ?d & l isomers - l isomer opioid activity, d isomer weak agonist & NMDA antagonist

OP21 [Apr01] Tramadol:

A. Has beta blocking properties

B. Blocks noradrenaline reuptake

C. Has greater opioid activity than morphine (OR: As potent a mu agonist as morphine)

D. Is directly inhibited by yohimbine = a2 blocker & 5HT blocker

E. Only the +ve enantiomer is active

OP22 [Jul01] The most unlikely thing to occur with morphine administered in recovery is:

A. Constipation

B. Respiratory depression

C. Sedation

D. Nausea and vomiting

E. Physical dependance

F. Pruritis

OP23 -Deleted

OP24 [Jul01] Extrahepatic de-esterfication of Remifentanil

A Occurs in RBC

B By Plasma Cholinesterase

C NOT in incubated blood

D Has (?mean) clearance less than 1L/min 40-60ml/kg/min ie >2.8Lmin for 70kg

E Has an active metabolite

Alt options:

C. Hydrolysis does not occur in vitro in incubated blood

E. The drug is hydrolysed to an active metabolite which undergoes further hydrolysis

(Q75 Jul01)

OP25 [Jul01] The following are metabolites of morphine except:

A. Morphine-6-glucuronide

B. Morphine-3-glucuronide

C. Normorphone - 5%

D. Codeine - small amount

E. Hydromorphine

OP26 [Jul01] Fentanyl given at dose of 50-150 mcg/kg:

A. Causes potent cardiac depression

B. Does not cause muscle rigidity

C. Has an elimination half-time of more than 3 hours

D. Not enough to relieve the stress response to surgery

E. Preserve cardiac output - no direct effect but will ↓SNS output ⟹ veno & vasoD

OP27 [Jul04] Prolonged duration of action of morphine in renal failure is due to

A. Morphine 3-glucuronide

B. Morphine 6-glucuronide M6G is 20-40 times more potent than morphine. M6G excretion by the kidney is directly related to calculated creatinine clearance. In patients with impaired renal function, M6G may accumulate in blood and CSF,

C. Metabolism of morphine. renal metab does contribute

D. ?

E. ?

OP28 [Jul-06] Which is NOT a side effect of morphine:

A. Seizures

B. Mydriasis

C. Respiratory depression

D. Histamine release

E. ?