

This station will explore the pharmacology of opioid drugs. An elderly man has been admitted after an emergency laparotomy. He is on an infusion of morphine at 5 mg/hr. His serum creatinine has doubled overnight and he is oliguric. What are the pharmacological effects of morphine in this patient and how are they brought about? Similarly in this viva, candidates struggled with an applied knowledge of basic pharmacological principles relating to commonly used drugs. Mechanisms of action of opioids was also an area of weakness.

**“What are the pharmacological effects of morphine in this patient and how are they brought about?”**

Large range of differentials to rule out, aspiration, sepsis, hypovolaemia, nephrotoxins etc  
In normovolaemic patients high doses of morphine are unlikely to cause myocardial depression or hypotension.

In hypovolaemic patients however the associated histamine release with morphine may result in systemic hypotension.

Morphine is metabolised in both the kidney and the liver via glucuronidation.

Elimination of glucuronide metabolites may be impaired in patients with renal failure.

Oliguria is a described side effect of morphine, possibly facilitated by increased ADH release.

**“What is the mechanism of action of opiates?”**

act on opioid receptors which are a family of GPCR ( $G_{i\alpha}$  and  $G_{o\alpha}$ )

there are three major classes, delta ( $\delta$ ), kappa ( $\kappa$ ), and mu ( $\mu$ )

in general they are inhibitory via adenylyl cyclase reduction, also K channels ( $\delta$  and  $\mu$ ) Ca Channels ( $\kappa$ )

most clinically used opioids are selective for mu receptors which have three sub types

delta receptors have two subtypes with similar actions to mu, but there are no selective drugs currently

kappa receptors have three subtypes, significant side effects; dysphoria, psychotomimetic, diuretic

**“Please list the side effects of opioids”**

Nervous system - euphoria and dysphoria, reduced LOC, confusion and psychosis

Respiratory system - decreases ventilation via direct resp centre depression and indirectly via confusion  
also suppresses the cough reflex

CVS - peripheral vasodilation, reduced peripheral resistance, inhibition of baroreceptor reflexes

Musculoskeletal - muscle rigidity

Skin - may cause cutaneous vessel dilatation via histamine, pruritis

GIT - decreased gut motility, sphincter of oddi spasm, n + v

Other - miosis due to excitatory action on the parasympathetic nerve, urinary retention