ANALGESICS – OPIOIDS

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Pharmacological control of pain

Analgesics – opioids

Analgesics – NSAIDs

Local anaesthetics

General anaesthetics

Adjuvant therapy (antidepressants, antiepileptics - anticonvulsants, antimigrenics, corticoids, caffein…)

Analgesics

Analgesics – decrease pain sensation (increase of pain perception treshold) selective without influencing other sensations

Analgesics – opioids

Non-opioid analgesics

Analgesics - opioids

Block pain signal transduction between neurons in CNS (brain, cord),
the same as endogenous opioids:

Opiates

Opioids

Opioid receptors - μ κ δ (σ)

metabotropic G protein coupled, inh. of adenylate cyclase, facilitation of K^+ channels opening postsynaptically, inhibit presynaptic Ca^{2+} channels opening

- μ
- κ
- δ
- (σ)

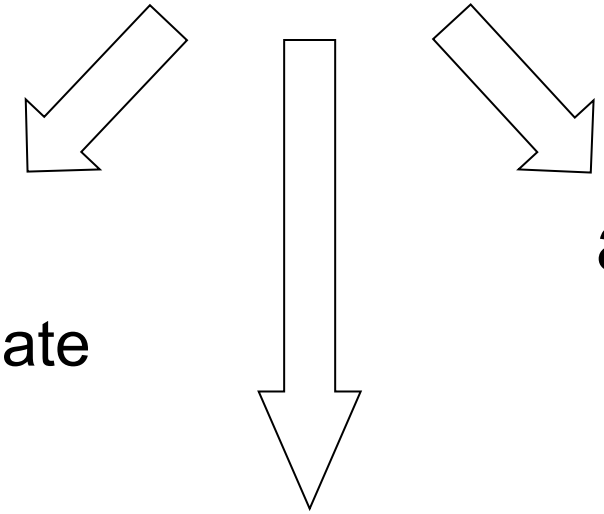
Opioidní receptory - μ κ δ (σ)

PRO ANALGÉZII JE DŮLEŽITÁ PŘEDEVŠÍM AKTIVACE RECEPTORŮ:

μ - supraspinální analgesie

κ – spinální + periferní analgezie

Opioid receptors pharmacology



agonists
(strong/intermediate
/weak.)

antagonists

partial agonists – dualists
mixed agonists - antagonists

Atypical opioids

Pharmacological effects of opioids

Central:

Pharmacological effects of opioids

Peripheral:

Pharmacological effects of opioids

TOLERANCE !!!

ADDICTION !!!

Pharmacological effects of opioids

ABSORPTION

DISTRIBUTION

Analgesics – opioids
Pharmacokinetics

BIOTRANSFORMATION

EXCRETION

Opioids

selective μ agonists

morphine app 10 % of opium content together with codein, thebain and other phenathren alkaloids

strong affinity to μ receptors

Opioid agonists

morphine

- p.o. (slow release too),
  parent. (i.v., i.m., s.c., epidural, intrathek.),
- rectal administration
- **<u>indications:</u>**

Other strong opioids

pethidine

methadon

piritramide

fentanyl, sufentanil, remifentanil,...

(heroin – diacetylmorphine)

Intermediate and weak agonists

codeine

dihydrocodeine

Partial agonists + agonists - antagonists

lower affinity to **μ** receptors, strong affinity to **κ** rcp.

lower addiction potential

lower analgesic efficacy, better safety profile

Partial agonists,

agonists-antagonists

Partial agonists + agonists - antagonists

Ex.: buprenorphine

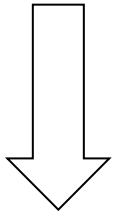
Partial agonists,

agonists-antagonists

Partial agonists + agonists - antagonists

Other drugs (used as analgesics):

mixed agonist-antagonist



nalbuphine, butorphanol, pentazocine

Partial agonists,

agonists-antagonists

Atypical opioids

tramadol

Opioid analgesics antagonists

naloxone, naltrexone

Use:

Opioids unwanted effects

- respiratory depression
- nausea and vomiting
- sedation, decreased cognition
- constipation
- seizures, spasms
- addiction

Intoxication with opioid agonists

nausea, flush, tinnitus

apathy, sedation, somnolence, miosis

superficial breathing

cyanotic, cold skin, tachycardia

asphyxia

COMA, RESPIRATORY DEPRESSION, MIOSIS

Therapy

naloxone 2-3 min. intervals/ infusions

ventilation, vital functions,

uncosciousness – fluids parenterally

Pain treatment

WHO analgesics 3 grade ladder

Pain → NSAID + adjuvant therapy

↓

persists/graduating → weak opioids + NSAID + adjuvant therapy

↓

persist/graduating → strong opioids + NSAID + adjuvant therapy