L5-Opioids & Sedatives Toxicity

هذه المذكرة شاملة كل محتوى سلايدات الدكتور!

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Objectives:

Editing File

What are Opioids?

- are substances that act on opioid receptors to produce morphine-like effects.
- Source : Exudate of the opium poppy (Papaver somniferum).
- What is the different between opioid ,opiate. Narcotic
- 1-opiod: its the synthetic form that give the mentioned effect .
- 2-Opiate : it's the natural form (MORPHINE).
- 3-Narcotic : any drug make you sleepy and you should not take.

Examples of opioid:

- **Morphine**: natural opioids (opiate) causes histamine release > vasodilation > hypotension
- **Fentanyl:** synthetic derivative (so opioid) has a cardiovascular stable effect (no hypotension)
- **Heroin**
- **Codeine**
- **Meperidine : (pethadine):** week analgesic strong euphoric
- **Methadone.**

Receptors of opioids :

are a group of inhibitory G protein-coupled receptors with opioids as ligands

receptor	Effect
MU μ	• Located at supraspinal and spinal sites • Analgesia and respiratory depression • Mioisis, euphoria, reduced GI motility
Kappa (K)	• Dorsal horn of spinal cord and brain stem • Analgesia, miosis, sedation
Delta (δ)	• Binding sites for endogenous peptides • Analgesia, dysphonia, delusions, hallucinations

Opioid toixdrome :

toxidrome: a group of signs and symptoms constituting the basis for a diagnosis of poisoning :

- Major effects:
- CNS depression.
- Respiratory depression: Decrease in respiratory rate to 6-8 (respiratory acidosis)
- Miosis.
- Other opioids effects:
- Sensorineural hearing loss.
- Mild hypotension (Histamine release as in morphine) and Bradycardia.
- Nausea & Vomiting (watch out for ileus).
- Urinary Retention. (can be very sever)
- Pruritus/ Urticarial and Flushing. because of histamine release

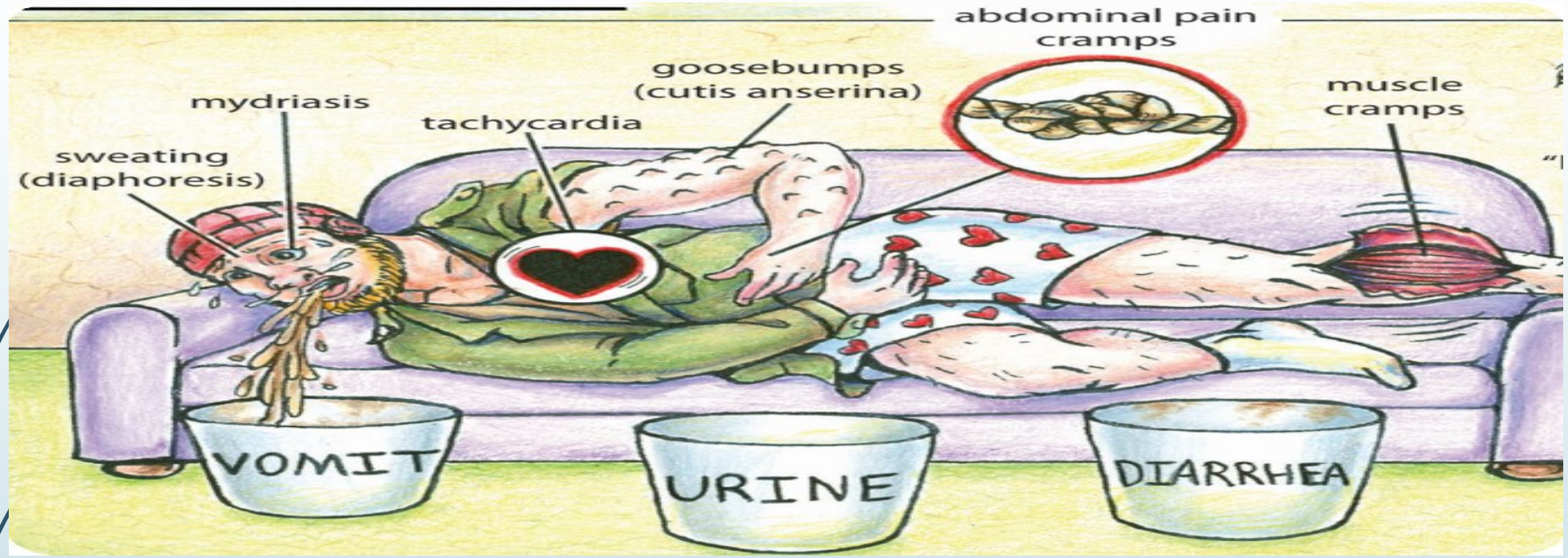
Management

- ABC's
- Supportive therapy
- **Antidote**: •
- Naloxone
- Pure Opioid antagonist.
- Routes IV, IM or subcutaneous route (Never oral)
- Competitively bind opioid receptors and reverses all opioid mediated action
- Dose: standard is (.4mg) , but we start with(.1mg) and see the response if it didn't work we increase gradually till we reach .4mg

Half Life and its important?

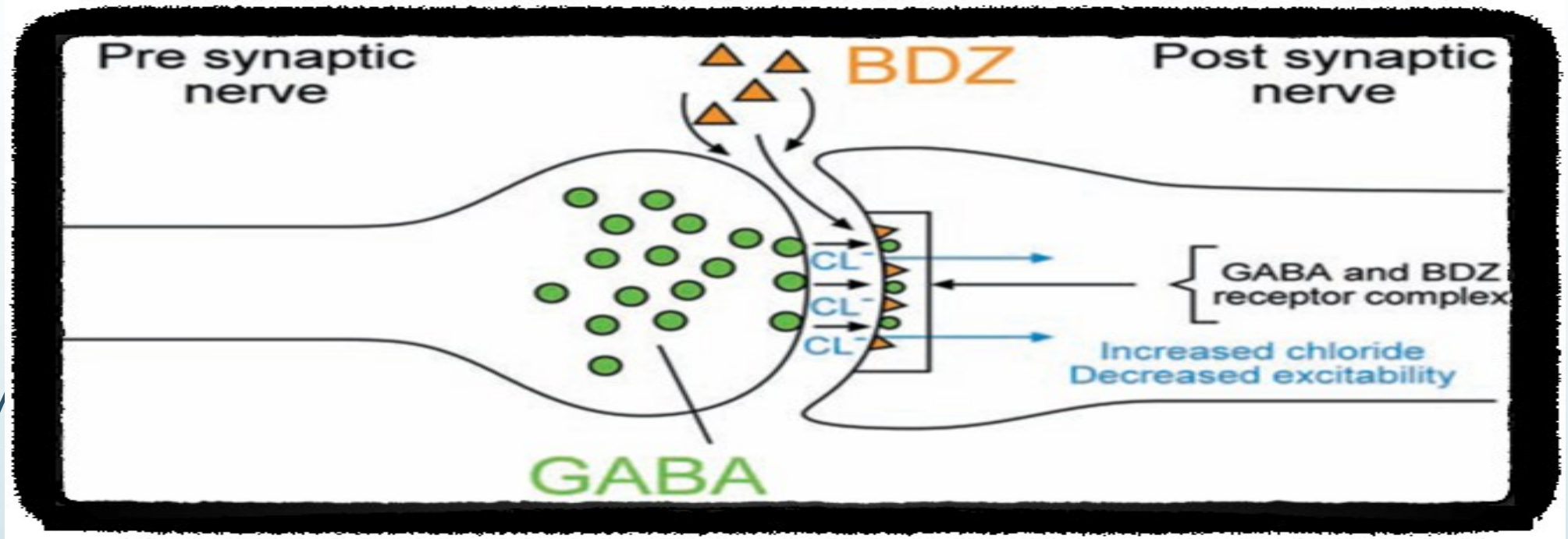
- Naloxone 1/2 life is 1 -2 hours
- Morphine 1/2 life approx. 2 hours
- So if the patient were under opioid overdose and were rescued with naloxone He should be observed for recurrence of opioid toxicity after the effect of naloxone has resolved. give again

Opioid Withdrawal (not life threating)



How to manage withdraw symptoms?
METHADONNE
Week opioid has long duration of action 24h
Require daily dose

Benzodiazepine Toxicity



MOA:
BDZ: bind to its receptor >> release of GABA>> binds to post synaptic R >>opening CL channel >> CL influx lead to hyperpolarization of neuron which inhabit its excitability

clinical effects of BDZ :

Sedative, Hypnotic,

Anxiolytic , Anticonvulsant

Clinical effects of Benzo Poisoning:

CNS depression(spectrum).

Resp. depression(non central).

Hypotension (uncommon).

Potential complications:

Aspiration and Pressure sores

High AG metabolic ACIDOSIS: can occur in patients on BDZ specially if they have hepatic-renal insufficiency

Why?

Propylene glycol: substance which is given with the benzo to facilitate the infusion, its negatively charged and buffering mechanism will occur by reducing HCO3 . (HAGMA)

How to diagnose BDZ toxicity :

How to diagnose :

- Any patient with altered mental status should have a blood glucose level rapidly determined.
- Qualitative immunoassays for benzodiazepines in urine are available but do not aid management decisions.
- Most of these tests detect only benzodiazepines that are metabolized to oxazepam glucuronide; therefore, clonazepam, lorazepam, midazolam, and alprazolam are not detected on many urine drug screens.
- Serum drug concentrations are not routinely available and do not correlate with clinical severity.

differential DDX

- Benzodiazepine overdose is usually suspected or diagnosed because of the clinical presentation.
- Many patients are arousable and can provide supporting information.
- Atypical or focal findings suggest the presence of other conditions.
- Profound coma or cardiopulmonary instability is rare with pure benzodiazepine overdose and should prompt the search for a coingestant.
- Nontoxicologic causes of CNS depression should also be considered.

Management

- Supportive
- Antidote:
- **Flumazenil**
- Nonspecific competitive antagonist of the benzo receptor. Reverse benzodiazepine-induced sedation after GA, PSA, & confirmed benzodiazepine overdose.
- Not recommended for the routine reversal of sedative overdose in the ED
- Complications:
- Seizures.
- Dysrhythmia.
- Reported mortalities.
- Precipitate withdrawal.

Indications and contraindications of Flumazenil

- Flumazenil is for Acute overdose not chronic
- It could cause seizures, so not used for seizures

Indications
Isolated benzodiazepine overdose in nonhabituated user (e.g., accidental pediatric exposure)
Reversal of conscious sedation

Absolute Contraindications
Suspected coingestant that lowers seizure threshold (e.g., tricyclic antidepressants, cocaine, lithium, methylxanthines, isoniazid, propoxyphene, monoamine oxidase inhibitors, bupropion, diphenhydramine, carbamazepine, cyclosporine, chloral hydrate)
Patient taking benzodiazepine for control of a potentially life-threatening condition (e.g., seizures)
Concurrent sedative-hypnotic withdrawal
Seizure activity or myoclonus
Hypersensitivity to flumazenil or benzodiazepines
Patient with neuromuscular blockade

Relative Contraindications
Chronic benzodiazepine use, not taken for control of life-threatening condition
Known seizure disorder not treated with benzodiazepines
Head injury
Panic attacks
Chronic alcoholism

Withdrawal of benzos

Nonspecific
Anxiety, depression, insomnia, tremor, tachycardia, sweating

Severe (rare)
Visual hallucinations, delirium, seizures

Summery

- General note :
- Routs of opioids:
- IV , IM o Sublingual , Oral . Inhaled
- Managment of opiodid toxcity Naloxone , don't forget 1/2life issue .
- management of opioid withdraw symptoms : METHADONNE .
- Management of BDZ toxicity : Flumazenil .

MCQS:

- Q1)WHICH ONE OF THE FOLLOWING OPIOID RECEPTOR WILL PRODUCE dysphonia, delusions, hallucinations WHEN STIMULATED ?
- A) (μ) B) K C) (δ) D) all of them
- Q2) which one of the following consider as cardiovascular stable effect ?
- A) MOROHIN B) Fentanyl C) HEROIN D) NON OF THEM
- Q3) BDZ , opioid can cause which one the following acid base disturbance respectively?
- A) metabolic acidosis -respiratory alkalosis
- B) metabolic acidosis - respiratory acidosis
- C) respiratory acidosis – metabolic alkalosis
- D) respiratory acidosis – metabolic acidosis

- ANS : 1) c 2) B 3) B