

Lecture 6: Opioids & Sedatives Toxicity

Opioids

- Exudate of the opium poppy (**origin**) (Papaver somniferum).
- Known to relieve pain, diarrhea, produce euphoria.
- Addiction to opium became commonplace.

- **Opioid** : synthetic derivative (e.g: Fentanyl)
- **Opiate**: natural form (e.g: Morphine)
- **Narcotic**: anything that makes you sleep

❖ Examples of opioid:

- ✓ Morphine: **natural opiodios** causes histamine release > vasodilation > **hypotension** (cause nausea and vomiting and it has a good analgesic affect)
- ✓ Heroin
- ✓ Codeine
- ✓ Fentanyl: **synthetic derivative** has a cardiovascular stable effect (**no hypotension**)
- ✓ Meperidine (pethadine) : **it is an opioid**, very weak pain killer effect but strong euphoric effect
- ✓ Methadone.

Receptors opioids work on:

Mu (μ)

- Located at supraspinal and spinal sites.
- Analgesia and respiratory depression.
- Miosis, euphoria, reduced GI motility.

Kappa (κ)

- Dorsal horn of spinal cord and brain stem.
- Analgesia, miosis, sedation.

Delta (δ)

- Binding sites for endogenous peptides.
- Analgesia, dysphoria, delusions, hallucinations.

❖ Routs of opioids:

- IV
- IM
- Sublingual
- Oral
- Inhaled
- Chasing the dragon methods

The Opioid Toxidrome

❖ Major effects:

- CNS depression.
- Respiratory depression. **Decrease in respiratory rate to 6-8 (respiratory acidosis)**
- Miosis.

❖ Other opioids effects:

- Sensorineural hearing loss. other than opioids: gentamycin, aspirin and Lasix
- Mild hypotension (Histamine release as in morphine) and Bradycardia.
- Nausea & Vomiting (watch out for ileus).
- Urinary Retention.
- Pruritus/ Urticaria and Flushing. **because of histamine release**

Tests:

Blood toxicology: aspirin , paracetamole , alcohol (ONLY)

urine toxicology: more types of toxics BUT !!

misleading information due to toxins stay in urine for a long time .

False positive information such as pantrazole



Management

□ ABC's and Supportive therapy

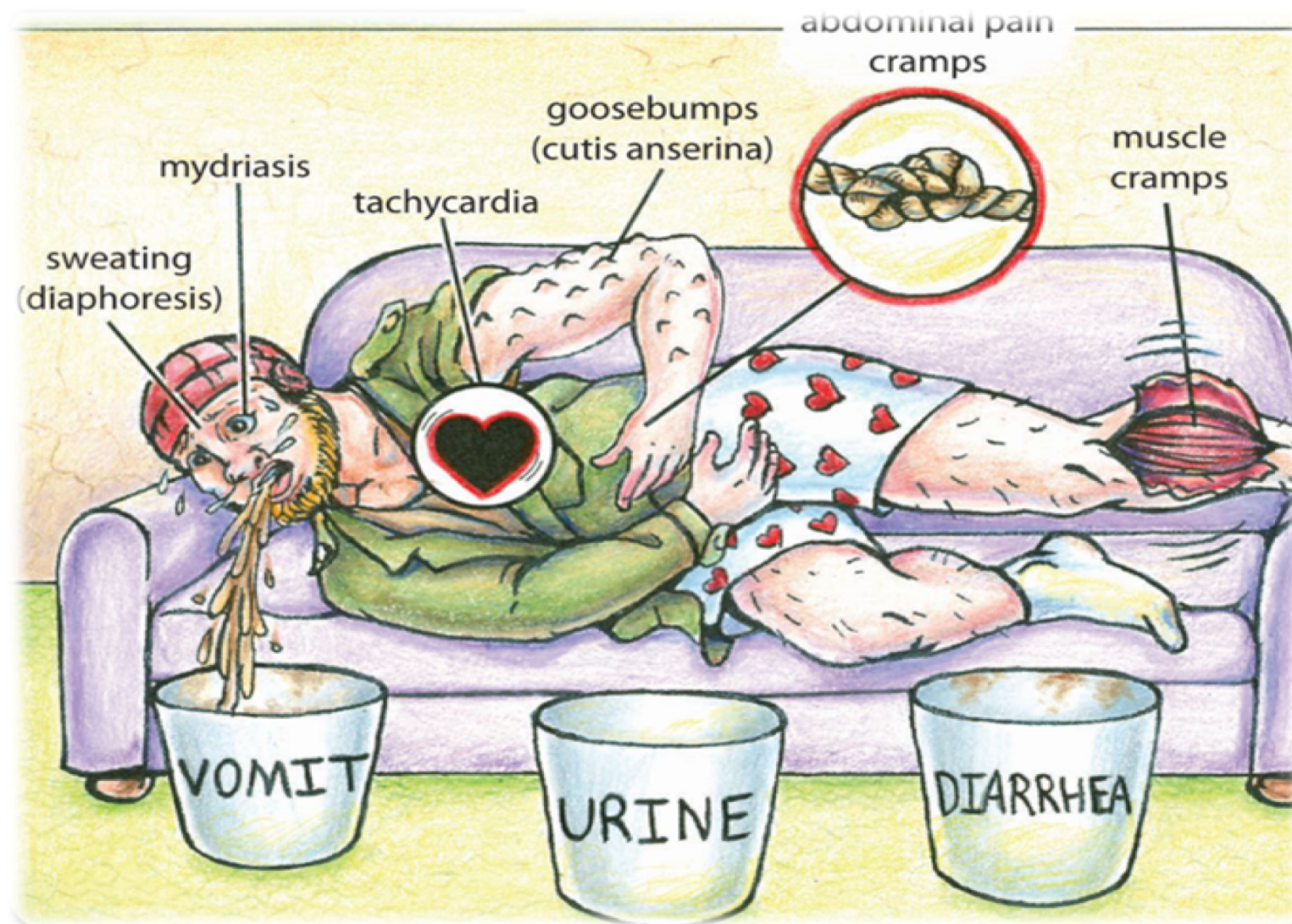
□ Antidote:

• Naloxone

- Pure Opioid antagonist.
- Routes:
 - ✓ IV, IM or subcutaneous route (**Never oral**)
- Competitively bind opioid receptors and reverses all opioid mediated action.
- Dose :
 - ✓ We give very small doses of antidotes
 - ✓ Standard: .4 mg
 - ✓ We give .04 mg .01 mg .1 and we observe ¼ of the recommended dose
 - ✓ -If it works that's good (stop)
 - ✓ Went down again we repeat the dose
- Half Life? Why is it important ??
 - ✓ The duration of action of many opioids, especially after overdose, is significantly longer than that of naloxone. **Patients responsive to naloxone should be observed for recurrence of opioid toxicity after the effect of naloxone has resolved.**
 - ✓ Opioids can have the half life of more than 2h and up to 24h
 - ✓ Naloxone 1/2 life is 1 -2 hours
 - ✓ Morphine 1/2 life approx. 2 hours



Opioid Withdrawal



Goosebumps

NOT LIFE THREATENING!

- **How to manage Opioid withdrawal?**

- **METHADONE:**

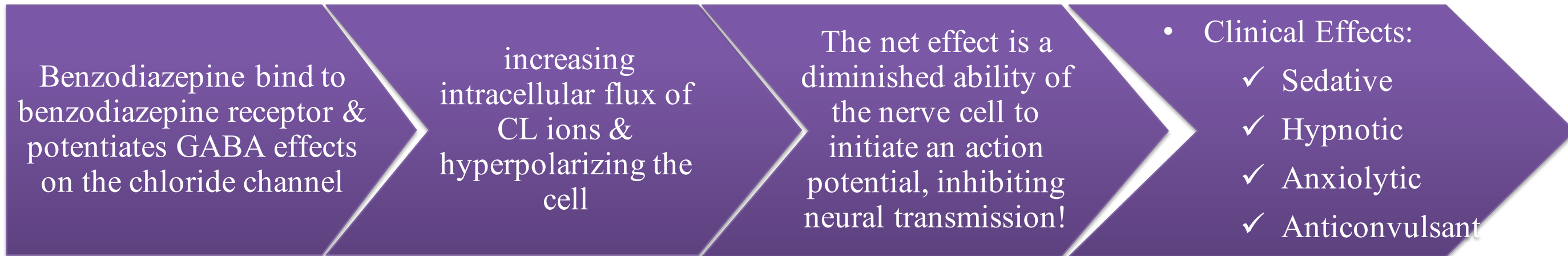
- ✓ It's an opioid used to maintain the opioid withdrawal symptoms
 - ✓ Long half life. Up to 24hrs
 - ✓ Requires a dose every 24hrs

Benzodiazepine Toxicity

For people who have panic attack , phobias

Mechanism of Action

GABA release CL which affect the action potential



NAME	USUAL DOSE	ORAL PEAK (hr)	HALF-LIFE (hr)	PARENT METABOLITE ACTIVITY
Alprazolam (Xanax)	0.25-0.5 mg	1-2	6-27	Inactive
Chlordiazepoxide(Librium)	5-25 mg	0.5-4	5-30	Active
Clonazepam (Klonopin)	0.25-0.5 mg	1-2	18-50	Inactive
Clorazepate (Tranxene)	7.5-15 mg	1-2	1-3	Active
Diazepam (Valium)	2-10 mg	0.5-1	20-50	Active
Estazolam (ProSom)	1-2 mg	2	8-28	Inactive
Flurazepam (Dalmane)	15-30 mg	0.5-1	2-3	Active
Halazepam (Paxipam)	20-40 mg	1-3	14	Active
Lorazepam (Ativan)	0.5-2 mg	2-4	10-20	Inactive
Midazolam (Versed)	0.025-0.1 mg/kg	1-2	1.5-3	Active
Oxazepam (Serax)	10-30 mg	2-4	5-20	Inactive
Quazepam (Doral)	7.5-15 mg	2	39-41	Active
Temazepam (Restoril)	7.5-30 mg	1-2	3-19	Inactive
Triazolam (Halcion)	0.125-0.25 mg	1-2	1.5-5.5	Inactive

Most important indication is : seizures

❖ Clinical effects of Benzo Poisoning:

- ✓ CNS depression (spectrum).
- ✓ Resp. depression (non central).
- ✓ Hypotension (uncommon).
- ✓ Potential complications:
 - Aspiration - Pressure sores

❖ Why do they get high anion gap metabolic acidosis ?

- **Propylene glycol:**

- ✓ It is a substance which is given with the benzo to facilitate the infusion
- ✓ It is the responsible element of high anion gap metabolic acidosis
- ✓ Patients with renal or hepatic insufficiency are at increased risk for this complication.

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

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

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

Withdrawal of benzos

Nonspecific

Anxiety, depression, insomnia, tremor, tachycardia, sweating

Severe (rare)

Visual hallucinations, delirium, seizures

Questions

1- which one is a natural opioid?

A- Fentanyl B- Morphine C- Meperidine

2-what of the followings is an opioid toxicity symptom?

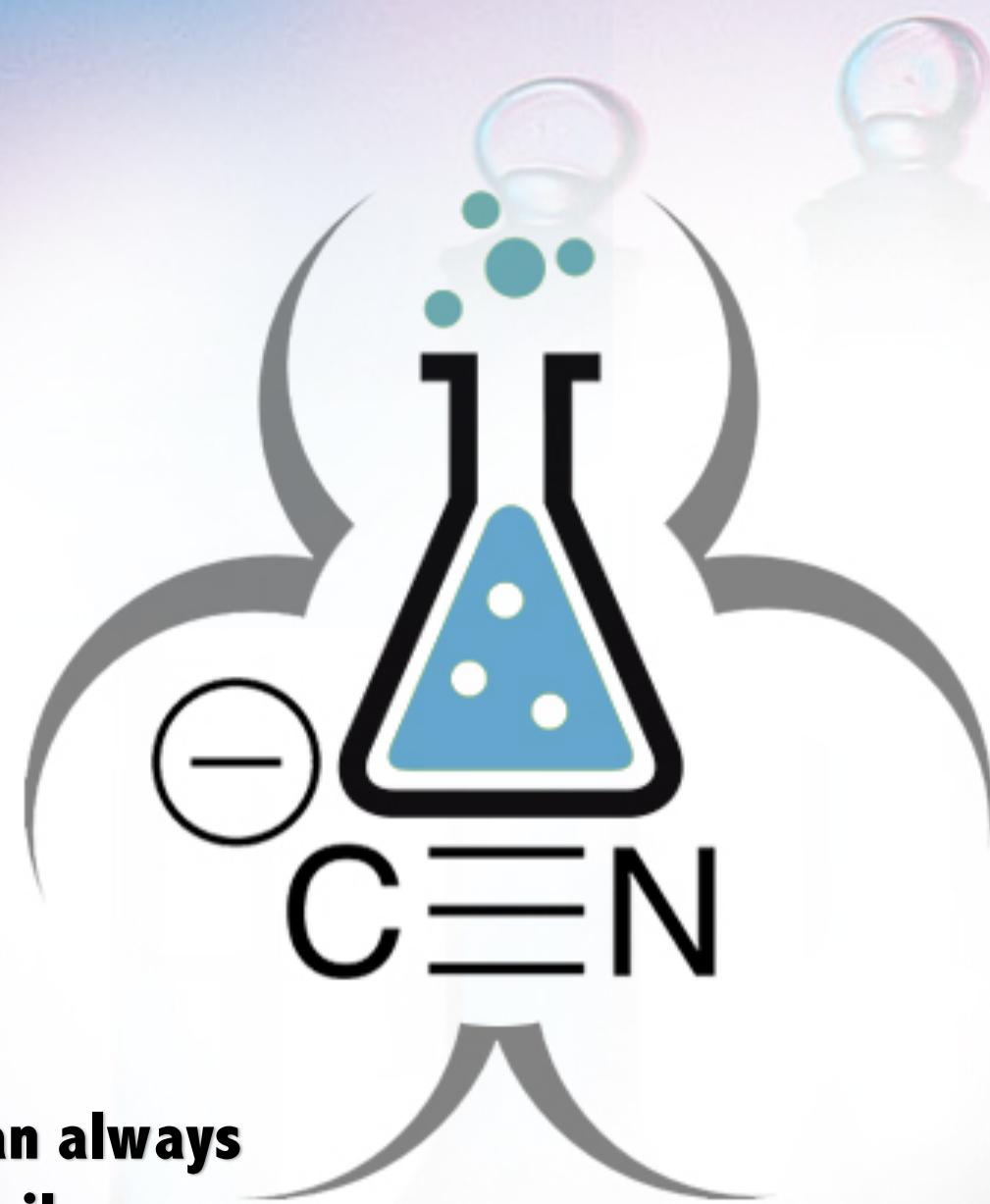
A- respiratory acidosis B- respiratory alkalosis C- metabolic acidosis

3- What is the medication which maintains opioids withdrawal symptoms?

A- Morphine B- Naloxone C- Methadone

4-patient known to have seizures attaches had an overdosed from Xanax what is the antidote that we should avoid?

A- Morphine B- Naloxone C- Flumazenil



**If you have any questions You can always
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