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Review Article

"Toxidrome" A Review

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Abstract

For many years medical community has attempted to standardize its approach to the assessment of patients. The vital signs are a valuable parameter with which to assess and monitor a patient's response to supportive treatment and antidote therapy. Vital signs play an important role in the practice of medical toxicology beyond evaluating and monitoring a patient's overall status as they are frequently valuable physiological clues to toxicology and disease gravity. In 1970's two paediatric physicians Howard C Mortenson and Joseph Greensher, coined a term "Toxidromes" which is a combination word of toxic syndromes. They have quoted "Some common combination of manifestation which we have termed toxidromes can give a clue to the drug involved" in an article "The unknown Poison". ***Aim:*** This paper aims to provide an understanding on the various vital signs and symptoms which is observed during poison treatment. ***Methodology:*** An extensive review of literature was carried out to elicit information on various vital signs and toxic syndromes. ***Results:*** The study revealed that the health care professionals on understanding various toxidromes can help them to identify the type of poison, its antidote and the can provide a better treatment. ***Conclusion:*** The healthcare professionals has to undergo training on toxidromes. Which can improve the treatment and outcome in any poisoning case.

Keywords: Toxidromes, Poisoning, Overdose, ABCDE assessment, Decontamination.

INTRODUCTION

When dealing with a poisoned patient there are four steps to go through. The most important thing to remember is to treat the patient first, not the poison.

Step-I

The assessment of poisoning with start with ABCDE [1] (Airway, breathing, circulation, disability, exposure) approach which can determine their general condition and to treat. The next step is to try to name the toxidrome.

Step-II

Toxidrome are collection of symptoms that reflect drug class effect. Toxidromes help in figuring out what type of poison the patient has ingested.

Step-III

Risk assessment has to be assessed concerning the specific drugs. To do a better assessment, the following points are mandatory.

1. What did they take?
2. How much did they take?
3. When did they take?
4. How did they ingest the drug?
5. What's their body weight?
6. Are they on other medication?
7. Do they have any liver or kidney problem?

For the above questions the patient not be able to answer or they won't answer truthfully.

Step-IV

General treatment we can easily remember by using DEAD [2] (Decontamination, Enhanced elimination, Antidotes disposition).

DECONTAMINATION

The goal of decontamination is to decrease or delay absorption If its topical like skin or the eye, then rigorous rinsing for oral ingested drugs. This includes gastric lavage, the administration of active charcoal and whole bowel irrigation [3].

Gastric lavage [4] is performed by inserting a gastric tube placing the patient on to their left -side (pylorus pointing up) and flushing the tube with 300c of

water or normal saline. There are many other methods also available.

Contraindication of gastric lavage are. If the patient has ingested corrosive material like acids or volatile substances as the gastric lavage can increase the risk of aspiration. Patient specific contraindications include a decreased level of consciousness or agitation or ABC instability.

Gastric lavage is only effective when performed within 1 hr of ingestion, and it can be considered within 4 hrs of ingestion depending upon the substance ingested.

Activated Charcoal [5] It is a binding agent to prevent absorption. It is performed by making the charcoal with water and administered. Orally either drinking or administered if oral a gastric tube after gastric lavage the typical dose is for 50 mg.

The contraindications of charcoal are absent bowel movements or ileus gastrointestinal haemorrhage and in non- cooperative patients. It could cause aspiration in patients with reduced levels of consciousness. It is effective only in certain drugs and performed early after ingestion usually within the hour. IT is ineffective for metals or alcohol.

Whole Bowel Irrigation [6] This technique is used when there are drugs involved that don't bind to activated charcoal with slow release preparations. It decreases the transit time of the ingested drug. It is performed by ingesting 3-6 litres of polyethylene glycol either the patient drinks or by nasogastric tube. The contraindications are similar like charcoal, as the volume load is a lot higher for whole bowel irrigation then if it is for activated charcoal, it should not be performed in un conscious or uncooperative patients. Consider intubating if necessary.

ENHANCED ELIMINATION [7]:

There are three common way of enhanced drug elimination.

1. Multiple Dose of Activated Charcoal

This interrupts the enterohepatic circulation. Druginclude theophylline, phenobarbital, dapsone, carbamazepine and quinine.

When multiple dose of charcoal is given when requires addition of laxative in the treatment.

2. Alkanizing the Urine

Ionized molecules are more water soluble than non- ionized molecules. Therefore, non-ionized molecules are better at crossing cell membranes. Sodium bicarbonate increase the alkalinity of urine. As this ionizes weak acids like aspirin and phenobarbital which helps in maintaining the alkalinity in the blood. The aim for urine PH is 7.5 and serum PH is between 7.45- 7.55 check for hypokalaemia.

3. Extra Corporeal Techniques

The most well know are haemodialysis and hemofiltration. Haemodialysis effectively enhances elimination of any drug that is a small molecule, has a small volume of distribution, rapid redistribution from tissues and plasma, slow endogenous elimination. Hemoperfusion is traditionally used for highly protein-bound agents, but is now rarely used due to high cost and poor availability of charcoal cartridges, systemic adverse effects, rarity of theophylline overdoses, increased effectiveness of modern haemodialysis filters. The toxins such as salicylates, theophylline, methanol, barbiturates, lithium, ethylene glycol can be eliminated using this technique.

TOXIDROMES [8]

These are a collection of symptoms frequently seen in poison patients. If we recognise the toxidromes then we can predict what drug the patient has used and how to treat the poisoning. Then we predict what drug the patient has used and how to treat the poisoning. The assessment of patients is based on symptoms seen in eye skin, body secretions, add vital signs by observing the above four signs we can predict and narrow down the differential diagnosis of substance which they are exposed.

Poisoning agent can be broadly classified into five toxidromes namely Sympathomimetic, anticholinergic, opioid and sedative toxidromes respectively.

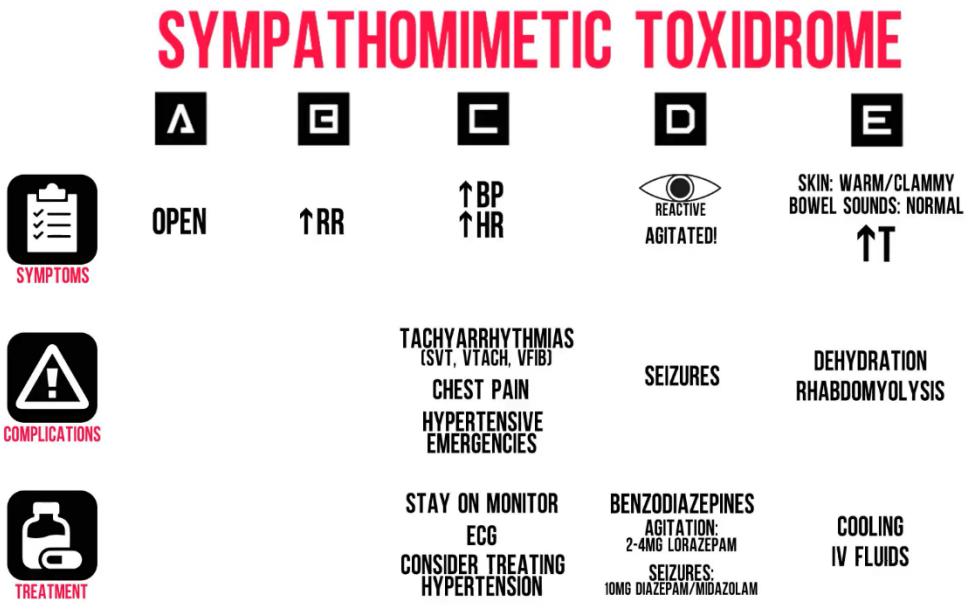
SYMPATHOMIMETIC TOXIDROME [9]**:**

Sympathomimetic nerve system which involves increase in heartrate, increase in blood pressure and dilate the pupil when activated. There are many drugs like amphetamine cocaine which minimize the effect of sympathomimetic stimulation.

- an open airway
- Breathing – increased respiratory rate, normal oxygen saturation and clear lung sounds,
- Cardiac-increased blood pressure and tachycardia usually sinus tachycardia. Their skin feels warm. The expected complications in cardiac systems are tach arrhythmias like SVT, VTACH, VFIB. The patient might experience chest pain which might be caused by hypertensive emergency or coronary spasm especially in case of cocaine use. Other hypertensive emergency like aortic dissection, cerebral haemorrhage, etc. In this condition ECG has to be checked and start with antihypertensive therapy.
- Disability: The pupil will be dilated and reactive to light. Their view will be normal without lateralization. If the patient has any previous vascular complications, then they will be extremely agile and could develop seizures. The

recommended treatment for agitation is 2-4 mg lorazepam add 10mg of diazepam /midazolam in case of seizures Decontamination is contraindicated in agitated patient.

- EXPOSURE: The skin will be warm or clammy. The bowel sounds will be normal. There will be hyperthermia due to which dehydration and rhabdomyolysis. For cooling iv fluids add cold blankets can be used.



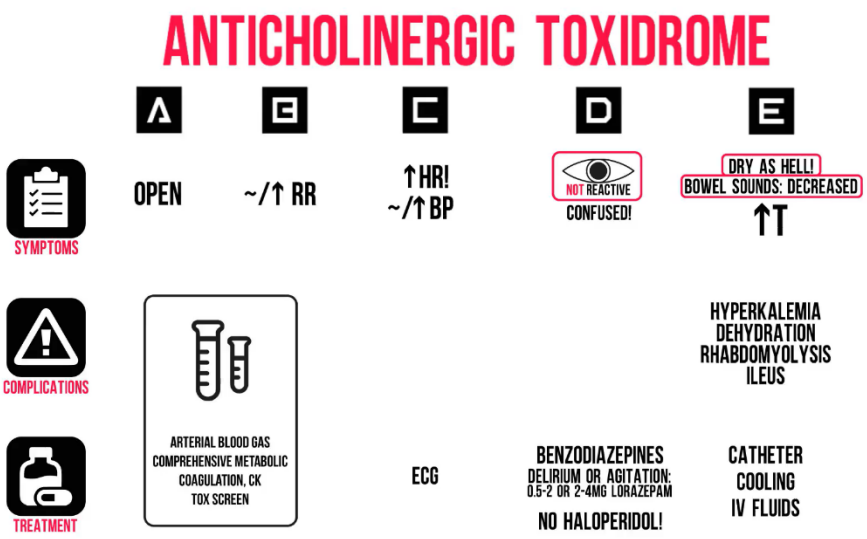
ANTICHOLINERGIC TOXIDROMES [10, 11]**:**

The anticholinergic toxidrome resembles the sympathomimetic toxidromes in many areas. Anticholinergic neurotransmitters which block the acetylcholine by which it activates the nervous system through muscarinic and nicotinic receptors, with a profound effect on the parasympathetic nervous system. So, all the drugs or toxins which because anticholinergic effects would cause sympathetic like effects.

- An open airway
- There will be increased respiratory rate but usually normal oxygen saturation and lung sound are typically normal.
- The heart rate will be increased It is fortunate that the life-threatening tachyarrhythmia's are only rarely seen. Monitoring the patient and ECG is mandatory. Blood pressure is usually normal or increased. But in several cases hypertension is seen. The hypotension is due to dehydration.
- This patient will have dilated. Pupils which are similar to sympathomimetic toxidromes This patient are non -reactive to light which helps to differentiate between anticholinergic and sympathomimetic toxidrome. Without lateralization their eye verbal and motor. sensation is normal. The patient will be conducted and hallucinating but not agitated Benzodiazepines 0.5-2 years, lorazepam 2-4 mg are the first drug for choice for agitation and hallucination. Haloperidol is contraindicated because it has anticholinergic effects by itself.
- These patients have decreased or absence of bowel movements. They are visibly dry mouth no sweating, no tears and urinary retention. The skin is dry but red and warm. The patient will experience severe hyperthermia which could lead to several metabolic changes like hyperkalaemia, dehydration and rhabdomyolysis. Treat the patient with iv fluids add cooling blankets for hyperthermia watch out for ileus.

Antidote: physostigmine – 1 mg in 10 min IV

It acts by inhibiting the breakdown of acetylcholine, the overdose of physostigmine will cause bradycardia.



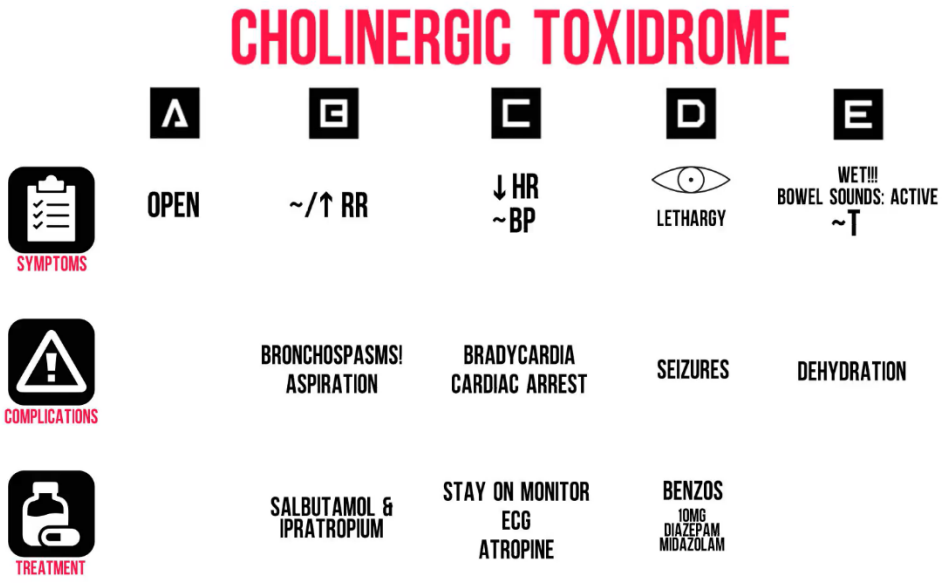
CHOLINERGIC TOXIDROMES [12]**:**

Most of the intentional poisoning will be having cholinergic effect.

- Open airway
- Usually normal to mild increased respiratory rate will be noticed in high doses bronchospasms are observed Treat salbutamol and ipratropium as nebulizer for bronchospasm. The patients are at risk for aspiration.
- Decreased heart rate bradycardia monitor the patient continuously with ECG for cardiac arrest. Keep atropine for emergency.
- The pupil size is pin point. Their mental state is usually normal but they could also be lethargic Complications are seizures which could be treated with benzodiazepines (10 mg diazepam or midazolam).
- This patient will secrete fluid from every possible pore like sweating, frothing, at the mouth running nose, diarrhoea, urinary incontinence. They have active bowel movements and their temperature is usually normal.

Antidote: ATROPINE – 1-3 MG BOLUS +0.5 - 2MG/HR

Titrate atropine until respiratory improvement. Atropine acts only by blocking the muscarinic receptors .so to block the nicotinic receptors we need to use pralidoxime is used.



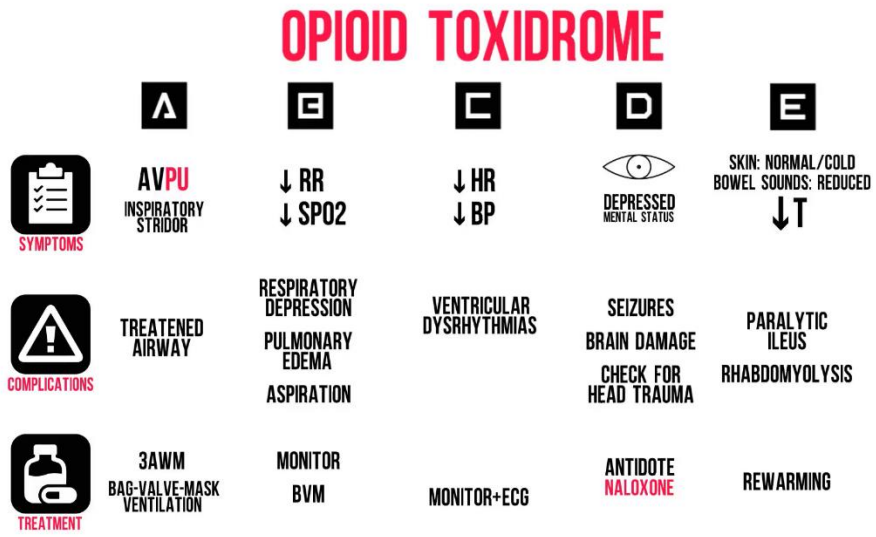
OPIOID TOXIDROME [13, 14]

In the opioid toxidrome all vitals are down regulated and respiratory depression is common.

- If your patient has reduced level of consciousness, then the airway is threatened. apply the triple airway manoeuvre. If the patient breathes insufficiently start bagging.
- The patient will experience bradypnea. In severe bradypnea the oxygen saturation will start to fall, lung sounds are usually normal, but severe opiate overdose is associated with pulmonary oedema. The patients have the risk for aspiration due to their reduced level of consciousness. Monitor the respiratory rate closely and bagging.
- There will be reduced heartrate so bradycardia and hypotension are common. hemodynamic complications are not usually seen. Risk of development ventricular dysrhythmias so monitor ECG regularly.
- Pinpoint pupils are a hallmark symptom and they have depressed mental study. They could lose their respiratory rate, so monitoring the respiratory rate is mandatory. The opioid associated overdose can cause irreversible brain damage. Other complications include seizures.
- The bowel sounds are reduced due to paralytic ileus. There is a several chance for hypothermia and rhabdomyolysis but the skin feels normal to cool. Rewarm your patient using blankets a bair hugger or warm infusion.

Antidote: NALOXONE

Dilute 0.4 mg in 10 cc of ns and titrate up patient starts breathing. 0.04mg/ml, 1 ml every 2 min. Naloxone should be only used in in respiratory depression, the [patient should be on monitor caution in chronic users which will led to withdrawal symptoms which can resemble a sympathomimetic toxidrome.



SEDATIVE TOXIDROME [15]

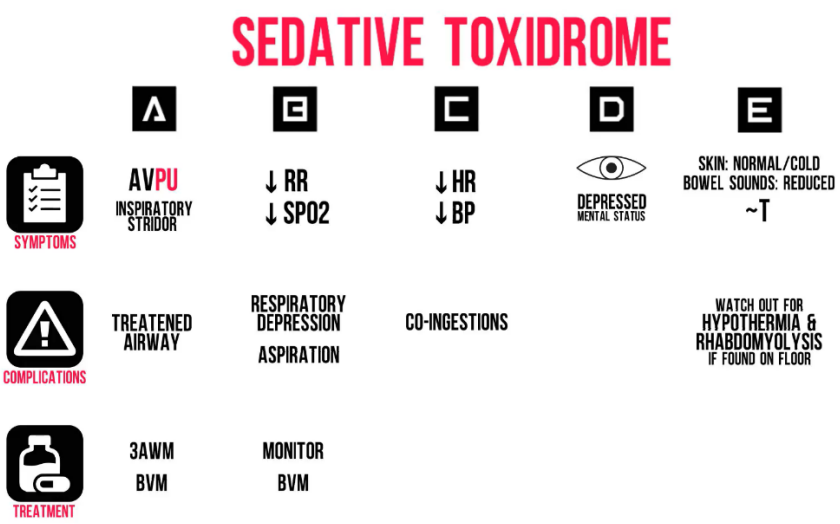
The sedative toxidromes are having similarities with opioid toxidrome and opposite of sympathomimetic toxidrome.

- If the patient has a reduced level of consciousness, then the airway is threatened. apply the triple airway manoeuvre. If the patient breathes insufficiently then start bagging.
- Patient will suffer with severe bradypnea. if it's more severe the oxygen saturation will start to fall. Monitor respiration for aspiration closely start bugging if needed.
- Bradycardia and hypotension are rarely seen complication .so co-ingested drug may cause cardiac arrthymias.
- The people size is normal they have a depressed metal status and could therefore lose their respiratory drive so monitor breathing.
- Bowel sounds are reduced but they don't items. Body temperature is normal but hypothermic and rhabdomyolysis may occur if the patient has been laying on the floor for an unknown period of time. The skin feels normal to cold.

Antidote: FLUMAZENIL

It is reversed for patients who are chronic users of the same drug and could go into withdrawal symptoms. The chances of the co ingested medications are antiphyscosis or tricyclic antidepressants which would cause seizures and cardiac arrhythmias.

Therefore, the sedative intoxication should be therefore regarded as their protection for more severe complications. The most important treatment is supportive and respiratory care with dose cardiac monitoring.



ESSENTIAL PRINCIPLES OF MANAGING POISONING [16]

- Use your knowledge of toxidromes to narrow the differential.
- Externally decontaminate your patient to protect yourself and them.
- Provide aggressive supportive care _ ABCDEs
- Recognize potential high-toxicity ingestions and get help.
- Consider GI decontamination – but avoid aspiration.

TOXICOKINETIC

When patients take an overdose of a prescription drug, there will be abnormal Pharmacokinetic reaction caused by the drug. This is because they were derived from therapeutic doses, not from toxic doses. A certain drug dose corresponds with a certain plasma level i.e. drug concentration at which a drug excretes 50% of its desired therapeutic effect is called the ED50, the concentration at which the drug excerpts 50% of its toxic effects is called the TD50. If the ED50 and the TD50 are close to one another, then it's called as narrow therapeutic indexed drug. A small increased dose can lead to over dose. Example like lithium and digoxin.

Saturable Kinetics

This is more commonly known as a nonlinear kinetics or zero order kinetics. It means that the rate of elimination is constant and does not depend on the drug concentration whereas in first-order kinetics the fraction of the drug eliminated is constant, but the amount changes with drug concentration.

Absorption

In the condition of overdose the patient have consumed excessive amount of medication, this decreases the solubility and the transporters responsible for absorption is saturated. So, time to full absorption (T max) is increased. It is similar for the metabolic enzymes that cause the first pass effect. This means the bioavailability could be higher than expected.

Distribution

Protein binding can be saturated which will lead to higher free drug concentrations, which is directly proportional to higher toxicity.

Metabolism

The conjugation phase can be saturated due to increased drug concentration, which take longer to metabolize all of the drug. This increases the half-life of the drug.

Excretion

Excretion through the kidney or bile which is governed by several transporting enzymes that can also be saturated. This slows the renal clearance and increase half-life of the drug.

CONCLUSION

Although the toxidrome concepts allow us to identify the majority of our overdose / poisoning patients quickly and accurately, this is by no means a whole concept. There are several common overdoses that do not fit perfectly in one of the toxidromes mentioned. New drugs are being constantly on the market, innovative ways to abuse old drugs are being found. The best way to keep up-to-date with emerging trends is through well-known sources. Do not worry to ask the hospital staff to ask a patient who appeared to be present in a way that seems not to be "fit." Good luck in the handling of these patients!

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