CHAPTER 15

RECURRENT INTRACTABLE ILIOFEMORAL DVTS IN YOUNG INDIVIDUALS; THE PHENOMENON TO KEEP IN MIND 'IVC AGENESIS'

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The embryonic development of inferior vena cava (IVC) is a complex process and there are wide variety of anomalous developmental forms of IVC and its tributaries. IVC agenesis (IVCA) is is one of the less prevelant malformations of IVC (**1).** Pathophysiological mechanism is controversial. Defective development of the embryonic veins and also intrauterine/perinatal IVC thrombosis are both suggested as a possible underlying mechanism. Although this can be an incidental finding in some cases due to well developped collateral venous circulation, serious complications may also be the clinical presentation. Recurrent and unproveked DVTs in multipl locations particularly in lower extremities and especially proximal parts in young individuals are the most common of these presentations. Due to the recurrence and proximal DVTs, postthrombotic syndrome (PTS) is an important concern in these patients. PTS refers to chronic venous insufficiency that follow extensive deep vein thrombosis (DVT) of the lims (1,2**).** The underlying pathophysiologic background is thought to be the valvular incompetence and resulted venous hypertention.The venous valves are permanently damaged due to an inflammatory response taking place to recanalize the thrombus in the presence of thrombotic obstruction of the deep veins. As a result of valvular incompetence reflux with stasis and chronic venous hypertention develops **(3,4).** The clinical signs and symptoms of patientsmay include limb pain and swelling, venous dilatations with formation of varicose veins, , discolouration and pigmentation, and venous ulcers. This complication of recurrent DVT is much more common in cases with proximal iliofemoral or iliocaval DVT.

ANATOMICAL AND RADIOLOGICAL POINT OF VIEW:

In the normal anatomy, the IVC is formed by the unition of two common iliac veins (CIVs) at the level of L5 vertebra. It is located on the right side of the aorta.

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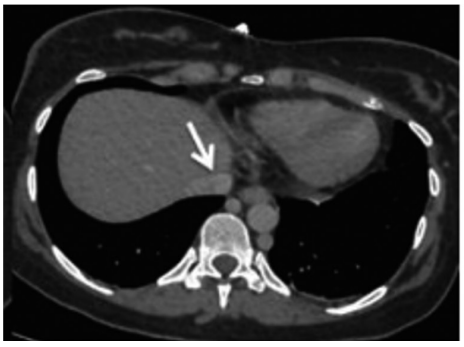
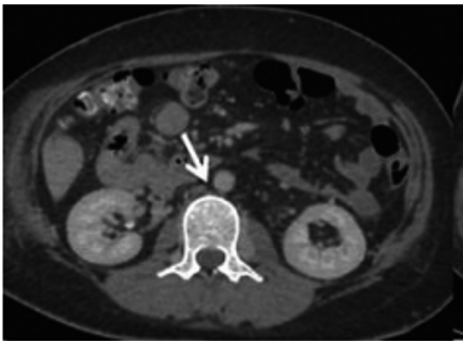
It drains venous blood from the abdominopelvic part of the body and the lower extremities to the right atrium. The inferior phrenic veins, the lumbar veins, right gonadal vein, renal veins, right suprarenal vein, and hepatic veins drain into the IVC which then passes the diaphragm at T8 level and drain into the right atrium. On the left side, the gonadal and suprarenal veins drain into the left renal vein. The azygous/hemiazygous venous system connect the superior and inferior caval systems.

There are two forms of IVCA **(2).**

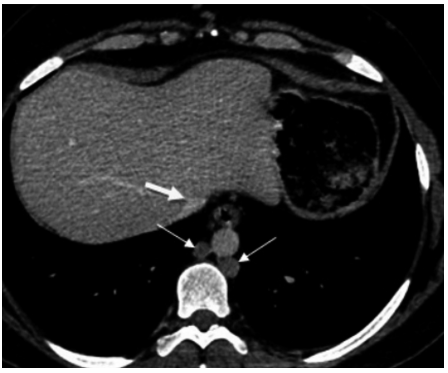
-'the interuption of infrarenal segment with preservation of the suprarenal IVC (type 1)





In CT venography images show thw absence of infrarenal IVC segments with preservation of suprarenal segments.

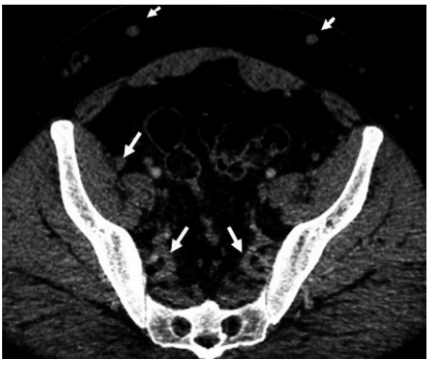
-'the interuption of the infrahepatic segment with azygous/hemiazygous continuation (type 2)



In CT venography images show the absence of infrarenal IVC segments. The

suprarenal segment is seen as hypoplasic (thick arrow). The azgous/hemiazygous continuation is marked with thin arrows.

In the radiological evaluation of the IVC, ultrasonography (US) and Doppler US has a limited role due to the superimposed bowel gas in the abdomen particularly in the evaluation of the infrahepatic IVC in adults. US and Doppler US is used in the establisment of the presence of DVTs progressing through the iliofemoral veins. This makes the abdominopelvic radiological evaluation necessary to visualize the continuation of the proximal iliofemoral DVTs. As provide a clue for more proximal involvement spectral analysis on the common femoral vein (CFV) of the contralateral asymptomatic side can be performed in cases with a proximal iliofemoral DVT. Although the presence of phasic flow and good augmentation cannot exclude proximal obstruction, nonphasic or asymmetrical pattern of flow in the CFV during respiration suggests an involvement of a more proximal vein **(5).** On the other hand, for the direct evaluation of IVC the gold standard imaging is conventional venography, which is an invasive technique. Intravenous (IV) contrast enhanced abdominopelvic computed tomography (CT) scan, that is CT venography is the method of choice as a noninvasive technique. The delayed venous phase images demonstrate the venous structures very well. In cases with IVCA the absent or obviously hypoplasic/fibrotic segments of IVC is easily seen. In addition, various dilated collateral veins draining into the azygos and hemiazygos system. This alternate pathways of venous return can be so dilated that they can be mistaken as mass lesions or even rupture resulting in retroperitoneal hematoma. In cases with contrindications for IV contrast agent, magnetic resonance imaging may be used to show flow voids or flow-associated enhancement in order to differentiate the anomalous collateral venous structures from retroperitoneal masses or adenopathy



In CT venography image, pelvic collateral veins and also the dilated venous collaterals involving the abdominal walls are marked.

Management

In recurrent DVTs particularly when unprovoked in young individuals and particularly involving proximal iliofemoral veins, IVCA should be kept in mind and appropriate radiological imaging modalities should be used in diagnosis. Timely treatment of acute DVTs in addition to prevention of recurrent DVTs with thromboprophylaxis in order to prevent PTS is critical in these patientsl. Long-term anticoagulation, compression stockings are among the prevention strategies. On the other hand as we previously reported, in the management of acute DVTs in these patients compression stockings may have a worse effect when acute DVT is associated with IVCA **(6).**Weight loss, and smoking cessation is recommended.

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CHAPTER 16

TREATMENT OF TOXICOLOGICAL CASES IN EMERGENCY DEPARTMENT

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INTRODUCTION

Medical toxicology is one of the most critical and dynamic areas in medicine, because physicians face with the management of poisoning, adverse drug effects and overdose intake. Determination of the prevalence and incidence of human poisoning is not easy. The American Association of Poison Control Centers declared that more than 2 million toxication cases occurred in the USA in 2018 alone, causing 1,300 deaths (Lee et al., 2021). The in-hospital mortality rate of intoxicated people is around 0.5% (Gunnel, Ho & Murray, 2004). However, death from poisoning is underreported, accounting for only 5% of the actual figure (Kim et al., 2019).

Determination of the substance that caused toxication and time to reach the hospital are associated with prognosis of the patient. Antidotes or decontamination therapy can be effective for certain substances. Even if a substance does not influence treatment, it can help physicians determine the treatment direction for patients with uncleasr diagnosis (Roberts, 2019). Intoxicated patients often hesitate to provide details on the substance they have ingested. Therefore, these patients may not receive appropriate treatment, spend a longer time in emergency department (ED) than needed and cause a significant burden and workload on healthcare staff working in EDs that are already overwhekmed with surge of necessary and unbecessary presentations. Treatment of toxicological cases in ED is challenging, mainly due to the differences in establishing the correct diagnosis. Signs and symptoms in toxicological cases afre similar to many disease and thus, they can easily confused with other causes. Establishing a toxicology lab in a hospital is not fisible because of time, manpower and costs, making the diagnosis

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further difficult (Monte et al., 2015). Moreover, most of the intoxication cases require urgent intervention and as in most other conditions, emergency physicians are in a race for not to loss golden times. This chapter addresses several aspects of the ED treatment of intoxicated patients poisoned by the most commonly encountered toxic substances.

GENERAL MANAGEMENT OF INTOXICATION CASES IN EMERGENCY MEDICINE

A systematic approach is used to poisoned patients in ED, include resuscitation, history taking, physical exam, and management. First, life-threatening conditionsare stabilized, including vitals, electrocardiogram (ECG), pulse oximeter, conscious level and pupil size. Continuous cardiac monitoring should be performed in hemodynamically unstable intoxicated. IV cannulation should be established and glucose level must be controlled without wasting time (Aki & Alessai, 2019).

Resuscitation

Top priorities for a toxicological case presented to ED are stabilization of the airway and breathing and providing control of the circulation. in poisoned patients whose mental status is depressed, intubation and ventilation must be carried out immediately.

First line treatment of hypoyension is i.v. fluid bolus at a dose of 10-20 mL/Kg. If the patient does not response, vasopressors such as norepinephrine should be added. Hypertension is treated with sedatives such as benzodiazepines, if there is no response, calcium-channel blockers are administered (Little, 2009).

Sodium bicarbonate is the first line treatment in ventricular tachycardia resulted from tricyclic antidepressant toxicity. Using antiarrhythmic agents may be potentially dangerous. Atropine and/or temporary pacing is administered in the case of bradyarrhythmias. Hyperthermia cases due to drug toxicity must be managed aggressively with sedation and active cooling in order to avoid complications. Patients presenting with opioid overdose must be give naloxone as soon as possible (Erickson, Thompson & Lu, 2007).

History

Medical history should be directly received from alert and conscious patients. However, a history after an intended ingestion is frequently not reliable. This make the history taking challenging. In the case of comatose patients, history can be taken from the patient's family, relatives or emergency medical service (EMS) staff. Medical records of the patient should be reviewed to reveal a possible suicide attempt, psychiatric disorder, drug abuse etc. in the past. History must include time of the poisoning, amount intake, intentional or unintentional exposure to

the substance, missing drug boxes or bottles around an ill family member. It is also important to question the use of herbal or traditional or supplementation (Shaun, 2016).

Physical Exam

Physical exam of poisoned patients may provide information about the agent which was abused. The steps of physical exam in poisoned patients are given in Figure 1.

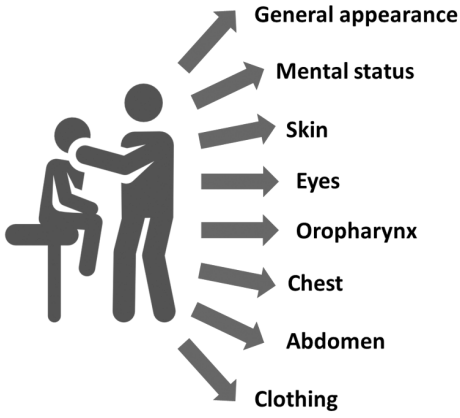

Figure 1. Evaluations during physical examination

Physical exam involves general appearance, mental status (confused or agitated), skin (for signs of IV drug), eyes (nystagmus and pupil size), odour (bitter almonds, garlic, alcohol etc. that may give clue of ingested substance), oropharynx for fryness or hypersalivation, chest for wheezing, breath sounds, heart rate, regularity of rhythm, abdomen for tenderness, rigidity and bowel sounds), limbs for tremor and patients' clothing for tracks of illegal drugs etc. (Erickson, Thompson & Lu, 2007).

DECONTAMINATION

Decontamination refers to the removal of the poisoning substance from the body of the patient or to remove the patient from the toxin through gross washing outside of the patients or gastrointestinal decontamination inside the body.

Gross Decontamination

Regardless of duration from the exposure, intoxicated patient is undressed and washed thoroughly with water. This process should be performed in an isolated setting. Gross decontamination is performed in the case of irradiation, biologi-

cal, and chemical exposure. Health care personne should use personal protective equipment during gross decontamination (Bailey, 2008).

Ocular Decontamination

First a local anesthetic is administered and irrigation with a crystalloid solution is carried out. Normal saline is preferred for use in the eyes. The eyes should be irrigated with copious amount of water for at leasy 30 minutes. Local ophthalmic anaesthetics may be instilled to obtain patient compliance for the prolonged irrigation (Jaga & Dharmani, 2006).

Gastrointestinal (GI) Decontamination

Several methods are used for GI decontamination:

- Emesis
- Gastric lavage
- Activated charcoal
- Whole-bowel irrigation

Each method has contraindications andn complications, and the method to be used should be selected according to the intoxication characteristics and general status of the patient (Manoguerra and Cobaugh, 2005).

Activated Charcoal

One of the commonly used agents in toxicity, activated charcoil is a super heating carbon material. Activated charcoil excerts its action by decreasing the absorbation of ingested substance in the gastrointestinal lumen, although is of limited effectiveness in metal, lithium, alcohols and corrosives. The optimum result can be obtained when activated coal is administered within gthe first hour of toxication. Activated charcoal can be administered using a nasıgastric or orogastric tube in in intubated patients (Olson, 2010).

Irrigation of Whole Bowel

Irrigation of whole bowel is cleaning of the entire gastrointestinal tract to decrease the apsorption of toxins. This can be permormed using polyethylene glycol solution. In awake and cooperative patients, polyethylene glycol can be administered via the oral route. Raising the patient's head up to 30°C decreases the risk of aspiration. Absence of foreign body on imaging considered the endpoint of the procedure (Aki & Alessai, 2019).

Enhanced Elimination

This is a technique used to increase the elimination of toxins from the body in order to decrease severity duration and severity of clinical toxicity. This method can not be routinely applied in all intocicated patients (Shaun, 2016). The common, but not limited indications for enhanced elimination include poor outcomes with supportive care and/or antidotes, slow endogenous rate of elimination and severe toxicity cases.

Extracorporeal Membrane Oxygenation (ECMO)

ECMO is a supportive technique used to treat severely poisoned patients. It is used in critically ill patients and those who can not provide a sufficient amount of perfusion and gas exchange. This method may be utilized especially in intoxication by cardiotoxic drugs overdoses (Rona et al., 2011).

Inhalation of gases, fumes, dust or aerosols may irritate the lungs and lead to cardiogenic shock and acute respiratory distress syndrome (ARDS) and (Gorguner & Akgun, 2010). Cardiac arrest and cardiogenic shock resulting from acute toxic inhalation are related with significant morbimortality (de Lange, Sikma & Meulenbelt, 2013). Antidotes used to control the damage resulted from several toxins may not be effective in all cases. ECMO has been proven to be effectively used in cases of ARDS (Meltzer & Fins , 2012). However, there is still lack of studies investigating the use of ECMO in the cases of toxication (Yu et al., 2021).

Antidotes

Supportive care is the mainstay of treatment patients with intoxication in ED, although in some cases administration of specific antidotes can be potentially life-saving. Antidotes are substances that can prevent further intoxication from specific agents (Aki & Alessai, 2019).

TREATMENT OF INTOXICATED PATIENTS WITH SPECIFIC SUBSTANCES IN EMERGENCY DEPARTMENT

Acetaminofen Poisoning

Acetaminofen has been clinically used for the first time in 1950 and has become the most commonlu used analgesic drug. Acetaminofen is the most common cause of acute liver failure in the USA (Bunchorntavakul & Reddy, 2013). In large overdoses, the pharmacokinetic pathways become overwhelmed and the nontoxic pathways are saturated.

Clinical features: Symptoms are absent or non-specific at early stage of toxication. Clinical presentation of acetaminofen poisoning is classified into four stages:

1. (first 24 hours): nausea, vomiting, malaise, anorexia, or asymptomatic.
2. (2-3 days): abdominal pain at the right upper quadrant, nausea/vomiting, hepatotoxicity. The levels of AST and ALT highly elevate.
3. (3-4 days): jaundice, renal failure, coagulopathy, encephalopathy, maximum hepatotoxicity, coma, ARDS and cerebral edema
4. (7-8 days): recovery or poor prognosis with multi-organ failure and mortality (Fontana, 2008).

Treatment: First airway is stabilized, circulation and breathing are provided. GI discontamination with active charcoal should be considered. Studies have reported that if N-acetylcysteine (NAC) is administered within the first 8 hours of ingestion, it can completely prevent hepatotoxicity. NAC should only be give to patients who are at risk for hepatotoxicity. NAC dose can be adjusted as i.v. 150 mg/kg loading dose administered as 50 mg/kg for 4 h 100 mg/kg for 16 h (Naraki et al., 2021).

Cyclic Antidepressants (CA) Poisoning

CAs have been used to treat depression in the past, although more safer agents have reduced their use. In 2013, CA were the most common cause of death from overdose drug ingestion (Mowry et al., 2013). Overdose features vary according to the particular cyclic antidepressant ingested and its pharmacological properties.

Mechanism of action: CA has multiplr pharmacological features including antihistamine effects, antimuscarinic effects, Inhibition of α-adrenergic receptors, amine reuptake, sodium channel block and potassium channel block.

Clinical features: symptoms of CA intoxication are seen within 2 hours in a wide range from mild symptoms to severe cardiotoxicity. Intoxicated patients may present with drowsiness, confusion, speech disorder, urinary retention, hyperreflexia, sinus tachycardia and ataxia. In the case of serious toxicity that occurs within the first six 6 hours of ingestion, patients present with hypotension, cardiac conduction delays, supraventricular tachycardia, and seizures and coma (White, Litovitz & Clancy, 2008).

Treatment: Treatment in CA poisoning is initiated with supportive care and securing airway. GI decontamination is performed with active charcoal within 1 hour of toxication. Vasopressors are added in the case of refractory hypotension. Blood pH is kept between 7.50-7.55. Seizures are treated with benzodiazepines. Some drugs are contraindicated in CA toxicity including lidocaine, phenytoin, flecainide, amiodarone and sotalol (LoVecchio, 2016).

Salicylate (Aspirin) Poisoning

Aspirin is the most commonly used over-the – counter drug in the treatment of cardiovascular and cerebrovascular disease. Widespread use of aspirin may lead to intentional or accidental toxicity (Herres, Ryan & Salzman, 2009). Poisoning by aspirin is is under-represented in poison center data, because it is often not recognized (Gerald & O'Malley, 2007).

Mechanism of action: Aspirin causes gastric mucosal injury and platelet dysfunction. Salicylate that stimulates the chemoreceptor trigger region, resulting in nausea/vomiting. In addition, it causes hyperventilation and respiratory alkalosis (O'Malley, 2007).

Clinical features: Acute aspirin poisoning manifests with GI, CNS and metabolic effects. Patients may present with gastrşic irritation, nausea and vomiting at early stages of ingestion. With the progression of toxicity, the effects on the CNS may progress to agitation, hallucinations, delirium, lethargy and seizures. Chronic poisoning is seen when patients take more drugs than that they can tolerate. Acute poisoning has a slower onset with lesser severity.

Treatment: First steps in the treatment of aspirin toxicity include stabilization of the airway, and taking circulation abd breathing under control. Intubation should be avoided as much as possible, because it increases severity of toxicity. IV fluid treatment is started in the case of acidosis and volume depletion. GI decontamination with active charcoil may be helpful in early ingestion. In case of massive ingestion, whole bowel irrigation can be attempted. Patients with aspirin intoxication may need hemodialysis in case of severe acid-base disturbance clinical deterioration, acute lung injury and altered mental status and (Thanacoody, 2015; Juurlink, 2015).

Opioids Poisoning

Opioid abuse is an important public health problem worldwide. The number of opioid misuses and mortality due to opioids has been considerably raised within the last decade. Opioids are defined as all agents derived from opium. Opioids have analgesic and sedative impacts (Boyer, 2012). Opioid analgesic overdose is potentially fatal condition that results from prescribing practices, errors in drug administration, inadequate understanding on the patient's part of the risks of medication misuse, and pharmaceutical abuse (Okie 2010).

Clinical features: Signs and symptoms of opioid poisoning include decreased respiratory rate, constricted pupils, altered mental status, urinary retention, decreased bowel sounds, and urticaria.

Treatment: First important steps in the treatment include securing airway and provide adequate ventilation and oxygenation though a bag-valve mask. Serum glucose level should be studied. Patients with minimally depressed respiration are administered naloxone 0.4 mg IV. If the patient is opioid-dependent, since large doses may induce withdrawal symptoms smaller doses of naloxone (e.g. 0.1 mg i.v.) are given.

Sympathomimetic Poisoning

Cocaine was first used in the field of medicine as a local anesthetic in 1884. Cocaine is among the most common causes of acute drug-related presentations to EDs.

Clinical features: Patients with acute cocaine poisoning present with life-threatening symptoms involving several organ systems (Heard, Palmer & Zahniser, 2008). Cocain toxicity can cause vasoconstrictive and sympathomimetic effects on CNS, cardiovascular system etc. Patients with cocaine poisoning present with tachycardia, high blood pressure, coronary artery dissection, AF and SVT, and cardiomyopathy. In addition, agitation, seizures and coma state are seen in these patients.

Treatment: First, airway is secured and adequate breathing is provided. CNS symptoms are treated by applying sedation with benzodiazepines. Hyperthermic patients should be cooled immediately. The infusion of phentolamine or sodium nitroprusside should be performed in patients with severe hypertension unresponsive to sedation. Whereas, aspirin is used to treat acute coronary syndrom related to cocaine poisoning (Prosser & Perrone, 2016).

Digitalis Glycosides Poisoning

Cardiac glycosides have been used for a long time in case of the failed treatment. Digoxin is the most commonly used digitalis drug for treatment of congestive heart failure and atrial fibrillation (Bauman, DiDomenico & Galanter, 2006).

Clinical features: Acute digoxin toxicity is usually in the form of intentional or accidental ingestion. Patients present dizziness, headache, abdominai pain and nausea/ vomiting. Severe toxication may lead to seizures and come. Alterations in color vision is the most common findings at physical exam.

Chronic digoxin poisoning is often seen in elderly patients mainly due to interaction with other drugs. CNS symptoms are more markedly encountered in chronic toxicity. Ventricular dysrhythmias common in chronic toxicity (Bauman, DiDomenico & Galanter, 2006).

Treatment: Securing airway and adequate ventilation as well as bolus IV fluid are the first steps in treatment of digoxin toxicity in ED. Activated charcoal is helpful at early stage of ingestion. Atropine can be used in symptomatic patients with bradycardia. Sodium bicarbonate, insulin and dextrose can be used to treat hyperkalemia (Roberts & Buckley, 2006). However, there are no evidence-based guidelines for the management of mild to moderate toxicity so there is a wide variation in treatment (Kirrane et al. 2009).

Beta-Blockers Intoxication

These agents have been used in treatment of different neurological cardiovascular, and ophthalmological diseases for a long time (Mowry et al. 2013). Although safe for most patients when taken as prescribed, beta blocker toxicity is associated with significant morbidity and mortality (Bronstein et al., 2006).

Clinical features: Beta blockers toxicity most commonly affect the cardiovascular system in patients present with hypotension and bradycardia. Beta blockers also affect CNS and pulmonary system. Neurologic symptoms of beta-blocker toxicity include delirium, seizures and coma. In addition, bronchospasm and hypoglycaemia may also be observed in beta-blocker poisoning (Kerns, 2007).

Treatment: GI contamination with active charcoal can be performed within 1 hour of ingestion. Securing airway is the mainstay of the treatment of beta-blocker toxicity with focus on restoration of perfusion to critical organ systems. Vasopressors (epinephrine), high dose insulin-glucose (1 unit/kg IV bolus) and glucagon (3–10 mg) can be used for this purpose. In the refractory cases; hemodialysis, hemoperfusion, cardiac pacing, intra-aortic balloon pumps can be used (Jang et al., 2014).

CONCLUSION

Approach to intoxicated patients in ED is challenging because of the difficulty in receiving history, and the need of looking at signs of illegal drug abuse. Treatment of toxicological cases in emergency department should be initiated with stabilization of the airway, breathing and taking circulation under control. Especially in intentional cases such as suicide attempt taking history can be quite difficult. ED physician should try to get information from the patient's family and relatives as much as possible and carefully review previous medical redords. Physical examination should include all relevant sites including general appearance, mental status, skin, eyes, odour, oropharynx, chest, and abdomen. In most of intoxicated patients, decontamination in addition to supportive can be sufficient, although antidotes are the cornerstone of the treatment of toxicological cases in ED.

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