



## **Identification, Prevention and Treatment of Drug Toxicity in the Primary Care Settings**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i58A34127

### **Open Peer Review History:**

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/79756>

**Review Article**

**Received 10 October 2021**

**Accepted 14 December 2021**

**Published 15 December 2021**

## **ABSTRACT**

Studies from global countries indicate that poisoning is a common etiology for morbidities and associated mortality. Most of the cases did not require medical intervention as they were treated at home. However, around one-fourth required management at a healthcare facility. In addition to the healthcare burdens, evidence indicates that these events also have significant economic burdens on the affected patients and healthcare facilities. The present literature review provided evidence regarding the proper ways to identify patients presenting with suspected medication poisoning and

the recommended management approaches. Obtaining a complete history from the patient should be the first step that can lead to diagnostic clues. Then, a thorough examination should be provided, followed by relevant imaging and laboratory studies to confirm the diagnosis. Management might be supportive in many cases, and an antidote can enhance the treatment process. Approaches should also be conducted to achieve decontamination and enhance the elimination of the affected patients.

*Keywords: Poisoning; drug toxicity; toxicology; management; diagnosis.*

## 1. INTRODUCTION

Studies from global countries indicate that poisoning is a common etiology for morbidities and associated mortality. According to the American Association of Poison Control Centers, exposure to poisons was estimated to affect 2.4 million patients in the United States in 2006. Most of these cases did not require medical intervention as they were treated at home. However, around one-fourth required management at a healthcare facility [1]. In addition to the healthcare burdens, evidence indicates that these events also have significant economic burdens on the affected patients and healthcare facilities [2]. A variety of reasons has been reported to cause poisoning. These include different pesticides, chemicals, pharmaceuticals, and even cosmetics. However, it has been demonstrated that poisoning secondary to administration of over-the-counter medications was reported to be the leading etiology in around half of the patients [1,3]. Therefore, adequate attention was given to identifying and managing patients with drug poisoning to relieve this burden.

Evidence shows that analgesics and sedatives are the most typical drugs associated with poisoning in adults in the United States. On the other hand, analgesics and topical preparations are the most prevalent medications causing poisoning [1]. Furthermore, measuring or dispensing errors, administering extra doses, intentional overdose, and exposure through breast milk are the most common causes of drug poisoning [1]. In the present literature review, we aim to review how to identify and manage patients with drug poisoning based on data from the current literature.

## 2. LITERATURE REVIEW

### 2.1 Identification

Patients with drug toxicity usually present with an acute alteration in their mental status. Therefore,

attending physicians should always consider the diagnosis of drug toxicity in patients presenting with abnormality. Having a thorough history of the patient is the cornerstone in identifying these patients. Therefore, it is recommended that primary healthcare physicians should ask presenting patients and their relatives about any potential ingestion of abnormal amounts or types of medications [4]. Besides, a thorough examination of the patients might provide evidence regarding any existing pills or medications suggestive of the patient's clinical presentation.

Studies in the literature indicate that patients suffering from drug toxicity usually contact their primary care physicians in three settings: hospital, office, and telephone. However, it should be noted that whenever drug toxicity has been suspected, affected patients or surrounding personnel should contact the poison control center or corresponding services as early as possible. These services can significantly achieve the management of poisoned patients [5]. Besides, it has been suggested that these approaches are usually helpful for patients contacting their primary healthcare provider on the telephone. This is evident especially for asymptomatic patients, have contacted a reliable poison management center and have ingested non-hazardous amounts of the intoxicating agent. On the other hand, it should be noted that an ambulance might be needed to transfer patients to the emergency department when being symptomatic following the exposure to uncertain amounts of drugs. Furthermore, it should also be noted that hospital admission is necessary to perform decontamination of the gastrointestinal tract. Therefore, identification and management in office settings should only be conducted for patients that do not require any emergency interventions [3].

After taking a thorough history from the patient, many approaches should be conducted in the emergency settings before establishing a specific prognosis and a subsequent appropriate

management plan. For instance, it has been recommended that an electrocardiogram should be conducted for all the presenting patients. Evidence shows that it should be conducted whether the patient presents or symptoms, especially when there is evidence regarding the administration of cardiotoxic agents [6]. This approach would be helpful in these situations to assess the conduction and rate of the potentially affected myocardium [7]. Therefore, it might be used as a useful diagnostic and prognostic tool for managing the affected patients. It has been furtherly reported that attending physicians should pay adequate attention to QT and QRS intervals on ECG. For instance, sodium bicarbonate infusion should be adequately considered in cases of QRS or QT interval prolongation. Conducting radiographic studies might also be helpful in some cases. However, it should be noted that such approaches are not helpful for all patients. In addition, they might help detect radioopaque modalities. The latter have been adequately discussed in the literature. Furthermore, it has been reported that radiographic investigations can detect cases of drug-related pulmonary affection. For instance, evidence shows that conducting chest X-rays might be diagnostic in acute respiratory distress syndrome and non-cardiogenic pulmonary edema [6]. On the other hand, it should be noted that conducting ultrasonography is of limited value for patients with drug intoxication, and studies show that it has no role in these settings [8].

Conducting laboratory investigations might help with detecting the underlying etiology of drug intoxication. It has been shown that conducting blood tests should be done for the presenting patients with drug intoxication. This is important, especially for patients with intentional overdose administration. Basic laboratory investigations should be included in the initial assessment of patients. These include testing for electrolyte abnormalities, liver and kidney function tests, and complete blood pictures. Moreover, it has been indicated that for patients presenting with intentional overdosing and altered mental status, conducting acetaminophen screening is critical in these events to rule out the potential drug poisoning [9,10]. Serum osmolarity should also be evaluated in cases when there are acid-base abnormalities. For instance, it has been demonstrated that alcohol intoxication can be identified utilizing the increased osmolar gap. In cases when there is an anion gap, such cases might help physicians diagnose an underlying

metabolic acidosis, which develops secondary to multiple etiologies. Some of these include toxication by different medications, including methanol, ethylene glycol, and salicylates. It has been shown that these medications metabolic acidosis with a high anion gap. Furthermore, it should be considered that lactate, ketones, glucose, and serum creatinine should also be evaluated in these situations to determine the underlying cause of metabolic acidosis [11]. Other diagnostic tests are presented in Fig. 1.

In cases of diabetic ketoacidosis and isopropyl alcohol toxicity, it has been demonstrated that elevated serum creatinine levels and normal blood urea nitrogen might help with the diagnosis of these cases. In addition, the diagnosis of methemoglobinemia and carbon monoxide toxicity might also be achieved by co-oximetry [12,13]. In another context, evidence shows that toxicology screening is another useful tool that should be conducted in the settings of asymptomatic presentations. However, it has been reported that such screening is not adequately valuable in cases when the clinical presentation is suggestive of the typical clinical course of the drug poisoning. For instance, research shows that conducting immunoassay urine screening helps diagnose drug toxicity of phencyclidine, tetrahydrocannabinol, tricyclic antidepressants, barbiturates, cocaine metabolites, benzodiazepines, and opioids. However, it should be noted that it is advisable to conduct other investigations and evaluatory approaches to confirm the diagnosis of medication abuse in these situations. This is because negative and positive results of toxicology screening do not necessarily establish an appropriate diagnosis. Moreover, it should be noted that many limitations were reported for these screening tests and should be considered when approached by physicians in emergency settings. The first limitation is that these tests are not specific and are only designated to diagnose a single case of medication poisoning. Therefore, they do not help evaluate the toxicity of other medications. For instance, it has been shown that opioid screens cannot detect meperidine poisoning, and amphetamine screens cannot detect methylenedi oxymethampheta mine poisoning [14,15]. Moreover, a positive test does not necessarily mean a case of acute poisoning, and the diagnosis might be established after days or weeks. Cross-reactivity between multiple medications was also previously reported in the literature. For instance, tricyclic antidepressants poisoning might be positive with chlorpromazine,

Blood gas analysis	Salicylates and acid–base disturbances
Complete blood count	Methotrexate and colchicine
Liver profile	Hepatotoxins (aminita phalloides and acetaminophen)
Lactate	Metformin, seizures, cyanide, and propylene glycol
Creatinine kinase	Rhabdomyolysis
Ammonia	Valproic acid and liver failure
Acetaminophen concentration	Symptoms of overdose may appear in delayed fashion
Prothrombin time (INR)	Coumadin and superwarfarins
Ketones	Isopropanol and acetone
Urinalysis	pH can guide urinary alkalization therapy
Electrocardiogram	QRS and QT intervals and cardiac rhythm in cardiotoxic agents

**Fig. 1. A summary of the commonest diagnostic modalities to identify cases of drug poisoning [16]**

cyproheptadine, and carbamazepine screens. In the same context, diluted urine might also give false-negative results. Therefore, physicians should consider other approaches to diagnose drug intoxication cases better [3,16].

## 2.2 Treatment and Prevention

Assessment of airway, breathing, and circulation should be the first management approach of the presenting patients with drug poisoning. Estimates show that only <1% of patients with drug poisoning will eventually die. Therefore, attending physicians should be aware that not all cases of medication poisoning are fatal [17]. If the patient is asymptomatic, the treatment would most probably be conservative. However, if a specific antidote was available, it should be administered. Some non-complex approaches can even manage some cases. For instance, hypovolemic shock can be managed by fluid resuscitation and Trendelenburg's position. Hypo- or hyperthermia can also be managed by cooling or warming measures. Symptomatic management of patients should be conducted based on the clinical manifestations and signs obtained during the examination process and laboratory and imaging findings.

Treatment options should be provided for patients presenting with severe manifestations and unstable cases of drug poisoning. Maintaining adequate circulation and correcting acidosis and hypoxia should be the first approaches provided to these patients. Moreover, it should be noted that standard ventilation would not function at an acceptable efficacy for patients requiring ventilation and will not correct the underlying metabolic acidosis. Finally, it should also be noted that physicians should continuously look after patients' vital signs

and hemodynamics, although there might be favorable signs of compensating the metabolic acidosis. In the same context, standard life support guidelines might not be adequate in cases of cardiovascular collapse. For example, it has been shown that in cases of calcium channel antagonist overdose, the administration of high doses of epinephrine is vital to manage these cases and enhance the outcomes [6]. Specific antibodies are also reported as valuable options for treating cases of drug poisoning. These modalities are specific to each case of medication intoxication and have been adequately reported elsewhere in the literature [3,16]. It should be noted that some cases might require intensive care unit admission, and others might need a referral to a tertiary care hospital. Extracorporeal membrane oxygenation (ECMO) was described in the literature as a valuable treatment option, especially in cases of drug-induced cardiotoxicity. Approaches should also be conducted to achieve decontamination and enhance the elimination of the affected patients. Gross, ocular, and gastrointestinal decontamination should be conducted based on the drug responsible for poisoning and the degree. Different approaches have been proposed to achieve gastrointestinal decontamination. Some of these include the induction of emesis, gastric lavage, activated charcoal, and whole bowel irrigation [18]. In the same context, it has been reported that enhanced elimination might be a valuable step. However, it is not commonly approached in the settings of drug poisoning. It can be done by urine alkalization and multiple-dose activated charcoal, with several indications and adverse events [17-25]. Therefore, these approaches should be carefully evaluated before being conducted in emergency settings.

Treatment approaches of drug poisoning for both children and adults are similar, as reported among studies. However, evidence shows that the risk of death might be higher among children based on the administered toxic dose of the medication, which is usually lower than the toxic dose for adults [26]. This has been furtherly discussed in the literature with a better insight into managing medication poisoning in this population [27-29]. In addition, there are many different factors to consider before disposition or hospital discharge after the management of acute drug poisoning. Observing stable patients should be based on the pharmacokinetics of the administered medication, including the dose and the plasma half-life of the medication. A psychiatric evaluation might also be indicated for patients that attempted suicide, and counseling is recommended for patients with substance abuse [4,11].

#### 4. CONCLUSION

Drug poisoning is a commonly encountered issue in the emergency department and primary care settings and can be associated with significant morbidities and mortality. The present literature review provided evidence regarding the proper ways to identify patients presenting with suspected medication poisoning and the recommended management approaches. Obtaining a complete history from the patient should be the first step that can lead to diagnostic clues. Then, a thorough examination should be provided, followed by relevant imaging and laboratory studies to confirm the diagnosis. Management might be supportive in many cases, and an antidote can enhance the treatment process. Approaches should also be conducted to achieve decontamination and enhance the elimination of the affected patients.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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The peer review history for this paper can be accessed here:  
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