Review Article

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Electrocardiography and Drug Intoxication

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Abstract

Intoxication is the deterioration of body functions due to different toxic substances. Poisoning by drugs constitutes an important part of all poisonings. Symptoms such as altered consciousness, tachycardia/bradycardia, or hypertension/hypotension may be seen because the cardiovascular system is affected. Changes in clinical findings and ECG may be revealed according to the degree of heart involvement. Rapid recognition and effective intervention by the emergency physician are of great importance. This review considers the use of ECG in the management of poisoned patients. Systematic evaluation of the ECG in a patient followed up with poisoning is essential for details that may be overlooked. Velocity, rhythm, intervals, and segments, QRS, wave morphologies, durations, ischemic changes should be followed carefully.

When performing rhythm analysis, clues to drug cardiotoxicity should be sought in unstable patients. Are there ectopic beats on the ECG? The answer to this question may carry important clues. Automaticity caused by sympathomimetics may underlie ectopic beats. This may be the first sign of a problem caused by acute coronary syndrome or electrolyte disturbances. Is the rhythm supraventricular? or ventricular? Is bradycardia with AV block? Or without AV block? Is tachycardia narrow complex? Or is it a large complex? Answers to questions such as: For life-threatening rhythms, ventricular tachycardia, ventricular fibrillation, and complete AV-block, the guidelines developed should be followed, and first intervention should be made. Agents that can cause tachycardia; are sympathomimetics (methamphetamine), anticholinergics (antidepressants, antipsychotics), class 1A and 1C antidysrhythmics, and TCA. Agents that can cause bradycardia; calcium channel / beta blockers / digoxin (AV block), opioids / ethanol, organophosphates, lithium. Prolonging the PR interval may indicate beta-adrenergic antagonism, calcium channel antagonism, or digoxin poisoning. Typical ECG of TCA poisoning shows sinus tachycardia with first-degree AV block, wide QRS complexes, and positive R' wave in aVR. The ECG should be taken and evaluated in patients presenting with poisoning within the first 10 minutes. Suppose the poisoning agent is an agent that influences the cardiovascular system. In that case, it should be kept in mind that continuous cardiac monitoring and control ECG evaluation should be performed in addition to the application of ECG.

Keywords: Intoxication, Electrocardiography, Cardiotoxic

Introduction

Substances that cause death with their chemical and physiological effects when taken in toxic doses are called toxins[1]. Intoxication is the deterioration of body functions due to different toxic substances[2]. This can affect the person's vital functions. Depending on the causes of poisoning, various symptoms can be seen in the person. Poisonings: In terms of the way it occurs, it can be environmental, industrial, home accidents, occupational, suicidal, murder accidental, and because of an attack. The annual incidence of poisoning in our country is between 0.8-5%3. When the applications made are examined, poisoning cases are mostly seen in the 0-6 age group among children and 17-29 years old among adults4. The mortality and morbidity of poisonings are high. This rate ranges from 0.3% to 27%[5]. Poisoning by drugs constitutes an important part of all poisonings. Causes such as wrong drug use, wrong dose, drug-drug interactions, drug side effects, abused over-the-counter drugs, and exposure to chemical and biological agents constitute an important part of poisoning. The severity of poisoning may vary depending on the type, amount, and personal characteristics of the toxic substance. Organ involvements such as gastrointestinal, central nervous system, respiratory system, cardiovascular, eye, skin, and mucous membranes are seen[6]. For example, symptoms such as altered consciousness, tachycardia/bradycardia, or hypertension/hypotension may be seen because the cardiovascular system is being affected. Changes in clinical findings and ECG may be revealed according to the degree of heart involvement. It has a wide spectrum that progresses from a completely asymptomatic condition to death. Rapid recognition and effective intervention by the emergency physician are of great importance.

This review considers the use of ECG in the management of poisoned patients.

Cardiovascular system involvement

Intoxications, which are accepted as "reversible causes" in cardiac arrest patients, have an important place in advanced cardiac life support[7]. One of the most common causes of death from poisoning is the clinical picture that occurs because the cardiovascular system is affected. The mortality rate in acute

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poisoning with cardiotoxic drugs is approximately 12%[8]. The cause of death is cardiovascular dysfunction, arrhythmias, and collapses. Emergency physicians may encounter many unforeseen situations when dealing with patients with a drug overdose. Multiple organ toxicity findings may progress to result in a cardiovascular collapse. Therefore, identification of a possible 'toxidrome' is invaluable in the management of poisoned patients. Thus, instead of focusing on the toxins, we will be able to intervene appropriately for the poisoned patient. Meanwhile, an easily taken electrocardiogram of the patient can provide us with valuable information.

Electrocardiography

Electrocardiography is conduction recordings obtained by recording the electrical activity occurring in the heart to examine the state of the heart muscle and conduction network[9]. It is frequently used in emergency conditions and rapid evaluations, especially because it is fast, easily accessible, inexpensive, and non-invasive. With ECG, it can easily evaluate ischemic and structural heart diseases, cardiac involvement of systemic diseases, lung diseases, and electrolyte disorders, and give us an idea about drug side effects and some poisonings. Electrocardiography can be more helpful in poisoning when evaluated together with examination findings, tests, and films. ECG has an important place in the management of poisonings; It is used for imaging, diagnosis, prognosis prediction, and patient monitoring. In poisonings, cardiotoxicity should be well illuminated to make an accurate ECG interpretation. Special needs to know about the mechanisms of cardiotoxicity: sodium channel blockade (Phase 0 prolongation, wide QRS, +R wave in aVR, right axis deviation, ventricular tachycardia and fibrillation, Brugada-like shape). K + channel blockade (prolongation in phases 2 and 3, long QT, Torsades de pointes) (Figure 1).

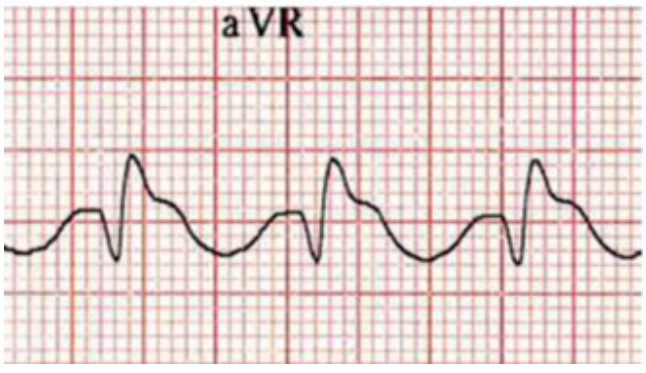

Figure 1: R-wave AVR

Beta-adrenergic receptor blockade (Sinus bradycardia, AV blocks, ventricular bradycardia). Calcium channel blockade (Sinus Bradycardia, 2nd, and 3rd-degree block, asystole)[10]. It is important to have experience in ECG interpretation, first, it is necessary to have an accurate evaluation experience in patients with chest pain, electrolyte disturbance, and shortness of breath. Because an intoxicated person may show ECG changes, which are common causes of coronary artery disease, electrolyte abnormalities, or dyspnea. ECG findings suggest electrolyte disorders such as hypokalemia, hyperkalemia, hypomagnesemia, and hypocalcemia may occur because of poisoning. Therefore, in poisoned patients, it may be useful to check whether there is an old ECG belonging to the patient and to take a serial ECG to the patient. In this way, the effects of delayed-release drugs or late-onset side effects on the heart can be evaluated. One of the most well-known pathophysiological mechanisms is the task of potassium flow from the myocardial membrane through cardiac repolarization. It occurs by blocking the outflow of potassium from the cell in Phase 3, which is the repolarization phase[11]. A possible potassium channel blockade presents as a prolonged QT interval. Also, blocking potassium channels can cause T wave abnormalities or the appearance of U waves. A long QT interval can cause torsades de pointes[12]. Antifungals (fluconazole, itraconazole, ketoconazole), diphenhydramine, amantadine, amiodarone, macrolides, etc. ECG findings include prolongation of the QT interval, sinus tachycardia, torsades de pointes (polymorphic ventricular tachycardia), and ventricular fibrillation[13]. Digoxin is the most used cardiac-positive inotropic agent. It shows its effects by inhibiting the Na-K ATPase pump in the myocardial cell membrane. Digoxin intoxications are frequently encountered due to the narrow therapeutic and toxic dose range of the drug. Ingestion of high doses of digoxin, either by accident or by suicide, can lead to acute poisoning. As the blood digoxin level rises, there is an increase in automaticity in the Purkinje fibers[14]. As a result, ectopic foci become active and ventricular ectopic beats occur. Therefore, it can cause multiple dysrhythmias. These emerging ectopic beats are the first indications that the digoxin concentration has reached the toxic level. Increased automaticity is seen because of increased intracellular calcium. As a result of increased vagal effects in the AV node, suppression of AV conduction is observed. Classic digoxin toxic dysrhythmia: Supraventricular tachycardia (increased automaticity) and slow ventricular response (suppressed AV conduction). Other arrhythmias include frequent premature ventricular complexes, including ventricular bigemia and trigeminal, sinus bradycardia or slow AF, and any type of AV block15. An effective and timely intervention in rhythm disorders, which can be seen in acute digoxin intoxications and can be fatal, can give good results. Downward ST depression inverted or biphasic T waves, and a shortened QT interval are typical with the characteristic "sagging" image. This appearance on the ECG is called the Salvador Dali mustache (Figure 2).

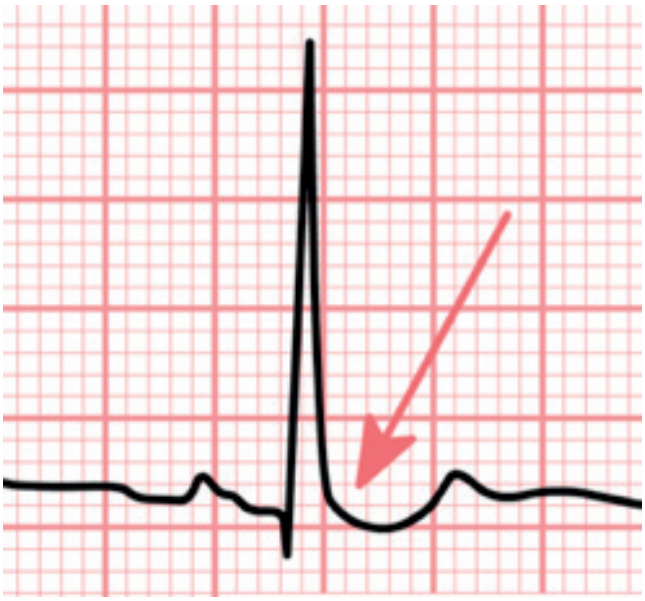

Figure 2: Digoxin intoxications

Beta-adrenergic receptor antagonists are a group of drugs commonly used in the treatment of hypertension and cardiac arrhythmia. Especially propranolol poisonings are more common than others[16]. For rapid recognition of beta-blocker poisoning treatment, we need to know the mechanism of action. With intracellular activation of beta receptors, cyclic adenosine monophosphate increases, protein kinase is activated, and intracellular calcium entry increases. In the blockade of this receptor, the contraction rate of the heart muscle and the AV node conduction rate decrease. Bradycardia and hypotension are the most common findings in beta-blocker poisoning. In overdose, cardiogenic shock may develop due to deep myocardial depression. ECG findings of poisoning include sinus bradycardia and decreased AV nodal conduction (1st to 3rd-degree heart blocks). Special consideration should be given to Propranolol (Na channel block effect) and Sotalol (K+ channel block effect). Propanolol: Acts as a TCA, blocks Na channels so that the QRS widens and a +R wave is seen in aVR. Sotalol: Blocks K channels, thereby prolonging the QT. Torsades de Pointes may develop[17].

Intoxications with tricyclic antidepressants (TCA) mediate their cardiotoxic effects through blockade of myocardial fast sodium channels (QRS prolongation, long R wave in aVR), inhibition of potassium channels (QTc prolongation), and direct myocardial depression[18]. Other toxic effects are produced by the blockade of muscarinic (M1), histamine (H1), and alpha1 adrenergic receptors. The two main side effects of poisoning with a sodium channel blocker are seizures and ventricular rhythm disturbances. Typical ECG of TCA poisoning shows: sinus tachycardia with first-degree AV block (P waves hidden in T waves, best seen in V1-2), wide QRS complexes, and positive R' wave in aVR. Significant QRS broadening, producing a sine wave image resembling hyperkalemia, indicates worsening TCA toxicity. There are situations that may be like ECG findings in TCA poisoning. Because. Poisonings whose mechanism of action is sodium channel blocker are quite common. Tricyclic antidepressants, Type Ia antiarrhythmics (quinidine, procainamide), Type Ic antiarrhythmics (flecainide, encainide), Local anesthetics (bupivacaine, ropivacaine), Antimalarials (chloroquine, hydroxychloroquine), Dextropropoxyphene, Propranolol, Kini[19]. Agents that antagonize calcium channels cause myocardial depression by reducing calcium entry into cells. Bradycardia develops because of calcium channel antagonism in the SA and AV nodes. If peripheral hypotensive effects prevail, reflex tachycardia may occur. Calcium channel blockers such as dihydropyridine often cause sinus bradycardia, and AV nodal conduction blocks (1st to 3rd-degree heart blocks).

Discussion

Evaluation of electrocardiography

Systematic evaluation of the ECG in a patient followed up with poisoning is essential for details that may be overlooked. Velocity, rhythm, intervals, and segments, QRS, wave morphologies, durations, and ischemic changes should be followed carefully[20]. In unstable patients, clues to drug cardiotoxicity should be sought when performing rhythm analysis. Are there ectopic beats on the ECG? The answer to this question may carry important clues. Automaticity caused by sympathomimetics may underlie ectopic beats. This may be the first sign of a problem caused by acute coronary syndrome or electrolyte disturbances. Is the rhythm supraventricular? or ventricular? Is bradycardia with AV block? or without AV block? Is tachycardia narrow complex? Or is it a large complex? Answers to questions such as: For life-threatening rhythms, ventricular tachycardia, ventricular fibrillation, and complete AV-block, the guidelines developed should be followed and first intervention should be made[21].

Agents that can cause tachycardia; are sympathomimetics (methamphetamine), anticholinergics (antidepressants, antipsychotics), class 1A and 1C antidysrhythmics, and TCA[22]. Agents that can cause bradycardia; calcium channel / beta blockers / digoxin (AV block), opioids / ethanol, organophosphates, lithium. Prolonging the PR interval may indicate beta-adrenergic antagonism, calcium channel antagonism, or digoxin poisoning[23]. Also, opioids via sympathomimetics and vagal tone. Clonidine or sedative hypnotics may be responsible for this effect. Examination of the PR interval is vitally important for the evaluation of AV blocks. A prolonged QRS suggests sodium channel blockade. TCAs, Class 1A antidysrhythmics, carbamazepine, right branch primarily blocked, obvious R wave – aVR. It should be noted that there is a list of drugs that prolong the QRS duration. The right-sided intraventricular conduction system is more sensitive to the toxic effects of some sodium channel blockers than the left bundle. Delayed depolarization of the

right ventricle causes changes in the morphology of the QRS complex in aVR. Therefore, there are prominent R waves in the AVR. In addition, it should not be forgotten that the Brugada pattern is among the other signs of right ventricular depolarization delay. J wave or Osborn wave in patients with hypothermia[24]. Visible. It is possible to occur due to syncope and prolonged exposure to cold after an overdose of medication. A hypothermic patient has bradycardia on the ECG strip and a positive deviation at the QRS/ST junction known as an Osborn or J wave (marked with an arrow). ST changes are closely associated with ischemia. Cardiac evaluation and follow-up are very important in reducing mortality in CO poisonings[25]. Although myocardial ischemia is an expected clinical condition in carbon monoxide poisoning, ST segment elevation can be seen in the ECG. Coronary anatomy may appear completely normal in the angiograms of these patients. If drug overdose, such as cocaine, has triggered a vasoconstriction, it may produce ST segment depressions or elevations suggestive of ischemia. Cyanide poisoning, which causes severe ischemia in tissues, and hypotension caused by calcium channel blockers may also present with ST changes. Brugada pattern can be described as a kind of ST segment elevation. Again, ST segment changes may be caused by digoxin poisoning. The QT interval may be prolonged in overdose of drugs with cardiotoxicity. In addition, although due to potassium channel blockade, prolonged QRS due to sodium or calcium channel antagonism may also increase the QT interval. Just like the list of drugs that affect the QRS duration, there is a long list of drugs that prolong the QT duration. In toxicology, absolute QT is a better predictor of Torsades risk than corrected QT (QTc). Therefore, the QT nomogram is best for risk estimation. Formulated QT corrected for QT duration, which can vary with heart rate. In general, a QTc greater than 450 ms in men and 470 ms in women is considered prolonged. Poisoned patients should be evaluated in a lead with good T waves (Figure 3).

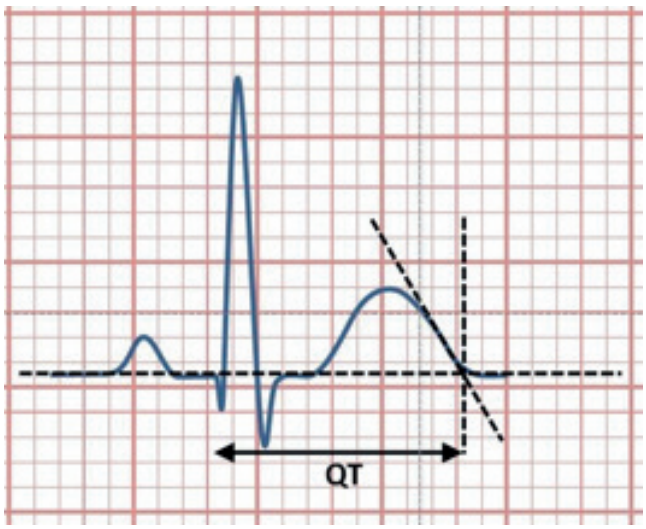

Figure 3: QT interval

It should be noted that QTc prolongation is associated with cardiac death[26]. Mad honey poisoning occurs by consuming honey obtained from plants belonging to the Rhododendron Ponticum and Luteum family, which are often grown in the Eastern Black Sea region in our country[27]. Electrocardiography has a critical importance in the diagnosis. Complication rates can be easily reduced with early diagnosis and effective treatment. In cases of poisoning caused by sodium channel blockade; Changes were observed in QRS duration, QT interval length, and atrial-ventricular depolarization-repolarization parameters[28]. ECG changes seen with symptoms and physical findings in cases of overdose are called "ECG toxidromes". ECG findings that should especially be sought in poisoned patients presenting with sinus rhythm; Signs of AV block, long QTc, or sodium channel blockade (R in aVR). In poisoned patients presenting with bradycardia, attention should be paid to blood glucose monitoring, AV blocks, and prolonged QT. Bradycardia and long QT opioids, bradycardia and nystagmus lithium, bradycardia and AV block may suggest calcium channel blocker poisoning and hyperglycemia, and bradycardia and cholinergic symptoms may suggest organophosphate poisoning. Tachycardia is a common presentation rhythm in poisoned patients. ECG of tachycardic patients suggests wide QRS complexes and sodium channel blockade (R wave in aVR). Wide QRS with tachycardia may suggest TCA, diphenhydramine, phenothiazine, bupropion, and cocaine overdoses[29]. A narrow QRS suggests antidepressants and antipsychotics, hypovolemia, acetaminophen, and carbon monoxide poisoning. In case of poisoning and its approach to ECG; rate and rhythm assessment, PR interval – looking for any degree of heart block, and II. Evaluating the QRS duration in the lead is the most important part[30].

Conclusion

In patients presenting with poisoning, the ECG should be taken and evaluated within the first 10 minutes. If the poisoning agent is an agent that influences the cardiovascular system, it should be kept in mind that continuous cardiac monitoring and control ECG evaluation should be performed in addition to the application of ECG. While evaluating the ECG, the duration of the QRS in DII should be specially checked.

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