RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 3 | March 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

47 yr Old Woman Presenting Vomiting & Confusion state with chronic atrial fibrillation- Case Report .

KEYWORDS: ST depression , Digoxin toxicity, Digibind .

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ABSTRACT *A 47-year-old Woman was admitted with Presenting complaint of confusion for the past two weeks with chronic atrial fibrillation. She was diagnosed as digitalis toxicity. In acute digoxin toxicity, patients or family members may provide the history of exposure or suicidality. Acute digoxin toxicity is characterised by patients being asymptomatic for minutes to hours after an exposure to digoxin, followed by a rapid deterioration. The symptoms usually include nausea, vomiting, anorexia, diarrhoea, and/or abdominal pain (less common), and may include palpitations, syncope and dyspnoea. Chronic digoxin toxicity is more common in elderly patients. It represent as : nausea, anorexia, abdominal pain, weakness, fatigue, palpitations, syncope, dyspnoea, disturbances of colour vision with a tendency to yellow halos (xanthopsia), blurred vision, and diplopia. Patients most often present with GI signs (anorexia and vomiting) and generalised non-specific complaints (generalised weakness and malaise), but could also present with CNS depression.*

Introduction-

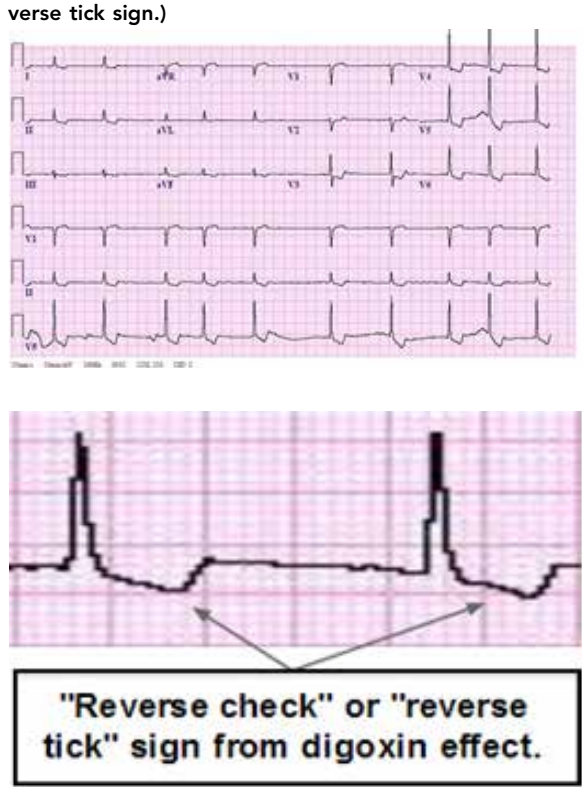
Digoxin toxicity is a life-threatening condition. The most common symptoms are gastrointestinal and include nausea, vomiting,confusion,syncope, abdominal pain and diarrhea. The cardiac manifestations are the most concerning and can be fatal.Digoxin toxicity can induce literally every arrhythmia except for rapidly conducted atrial arrhythmias (atrial fibrillation and atrial flutter). The classic arrhythmias seen during digoxin toxicity include atrial tachycardia with a 2:1 conduction, bidirectional ventricular tachycardia and atrial fibrillation with a slow ventricular response. The classic digoxin effect or the"reverse checkmark" or "reverse tick" sign on the ECG is not considered an indication of toxicity.

History , Examination & Investigation-

Patient , a 47-year-old Woman, was admitted to the coronary care unit via accident and emergency. Presenting complaint she had been suffering from confusion for the past two weeks. she had been feeling nauseous and had been vomiting, and was not eating or drinking properly. She was not in pain or short of breath but felt dizzy and sleepy. Previous medical history- her medical history included type 2 diabetes mellitus, hypertension, aortic valve stenosis and chronic obstructive pulmonary disease. she had permanent atrial fibrillation (AF). Her heart rate control had been variable in the past and an ambulatory electrocardiogram (24-hour tape) taken two years ago showed AF with rates varying from an average of 55 to 125 beats per minute). Drug history-she was taking: Rosuvastatin 10mg ,Bumetanide 2mg , Bisoprolol 7.5mg , Warfarin (variable dose) for stroke prevention , Digoxin 250µg.

On examination she was found to be in AF with a pulse rate of 45 to 65 beats per minute. Her ECG showed widespread ST depression (reverse tick sign.) suggestive of digoxin toxicity(Figure-1) . Other results were:Blood pressure 170/98 mmHg ,Respiratory rate 16 breaths per minute,Raised WBC counts, serum creatinine , urea (initially revealed) and digoxin level(later picked up); WBC counts -15540 cells/mcL (3,500 to 10,500 cells/mcL) Creatinine 2.7 mg/dl (0.6-1.5 mg/dl), Urea 59 mg/dl (9–22 mg/dl), Potassium 5.5mmol/L (3.5–5 mmol/L), Other electrolytes normal, including magnesium . HbA1c 7.9 [4–5.9], Hb 13gm/dL [13–18], No fever, normal lactate and arterial blood gases , INR 1.5 [2–3] and Digoxin 9nmol/L (0.9–2.56 nmol/L) or 7ng/ml [0.8–2ng/ml].

Figure-1(Digoxin toxicity showed ST depression –reverse tick sign.)



Diagnosis & Treatment-

It was initially suspected that her confusion may have been caused by sepsis. However, the test results showed no fever but a very high digoxin level. It was thought that her slow AF may be secondary to a combination of bisoprolol use and digoxin toxicity, in the presence of deteriorating

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renal function.The decision was made to stop the digoxin immediately and administer digoxin-specific antibody fragments (Digibind) to counteract the toxicity. The pharmacist was contacted to discuss digoxin toxicity and the use of Digibind, and another blood level was taken just before starting Digibind (see discussion below). The bisoprolol dose was reduced to 5mg om because of her low heart rate and deteriorating renal function. Since she was dizzy and therefore at risk of falls, warfarin was stopped (due to the risk of bleeding) and she was started on enoxaparin 1.5mg/kg daily. Intravenous normal saline was administered (1L over 8 hours and repeated), after which she was encouraged to eat and drink.

Discussion-

Several mechanisms can contribute to digoxin toxicity. These include:Renal function impairment (digoxin is excreted mainly by the kidneys) , a reduction in the volume of distribution of digoxin, due to advanced age, renal impairment or congestive cardiac failure Electrolyte imbalance; particularly hypokalaemia, hypomagnesaemia and hypercalcaemia, which can potentiate toxicity Concomitant drugs (such as amiodarone, calcium antagonists, quinine, diuretics, indometacin or propafenone) which may interfere with the plasma protein binding of digoxin. Certain diseases such as hypothyroidism or chronic lung disease which may increase sensitivity to digoxin.It is important to consider all of these factors in a patient presenting with digoxin toxicity. In her case, her renal function was deteriorating (as observed by the increase in urea and creatinine) and she has heart failure and COPD. Since these factors can all contribute to digoxin toxicity, therapeutic drug monitoring was essential in her case.

The clinical features of digoxin toxicity can be divided into cardiac and non-cardiac effects. Cardiac effects may occur with increasing toxicity and may include heart block, bradycardia and tachyarrhythmias. These can be life-threatening. Regular and frequent ECG monitoring is essential in patients showing cardiac symptoms of digoxin toxicity. Non-cardiac effects may include nausea, vomiting, dizziness, drowsiness, lethargy, headache, confusion and visual disturbances. She presented with both cardiac and non-cardiac effects of digoxin toxicity.

Hyperkalaemia is a major concern in digoxin toxicity because it can lead to atrioventricular (AV) block, increasing the risk of death, particularly at levels greater than 5mmol/L as was the case with her. Digoxin levels has a narrow therapeutic index and, as a general rule,the therapeutic level is 0.8–2ng/ml (0.9–2.56nmol/L). The concentrations below 0.8ng/ml (1nmol/L) are considered to be subtherapeutic and levels greater than 2ng/ml (2.56nmol/L) are considered to be toxic. However, there is significant variation between patients. For example, one patient may exhibit signs of toxicity at a digoxin plasma level of only 0.8ngml, while another may be symptom-free at 3ng/ml. Plasma concentration measurements may therefore be of limited clinical value, although they are useful to confirm clinical signs of toxicity or to establish whether a patient is still benefiting from a therapeutic effect at a reduced dose. Digoxin levels may also be useful to monitor concordance and to help make dose adjustments in the presence of concomitant drugs that raise or lower digoxin levels. Digoxin levels should not be measured within 6 hours of taking or administering a dose. The drug takes 6 to 8 hours to distribute into the tissues, so taking a sample too early is likely to result in a false positive result. In this case she was asked what time he had taken his last digoxin tablet, but he could not remember due to her confusion. Her husband said that she would probably have taken it in the morning. Because of this uncertainty, another blood sample was taken to measure the plasma digoxin concentration immediately before Digibind was started.

Management with Digibind Patients at risk of severe outcomes from digoxin toxicity are given digoxin-specific antibody fragments (Digibind). This binds with free digoxin in both the intravascular and interstitial spaces. Digoxin in the tissues starts to move out of the cells, where it is bound by Digibind. The Digibind/digoxin complex is excreted via the kidneys.Dosing of Digibind is dependent on the history of digoxin ingestion (acute overdose or chronic dosing), the patient's weight and plasma digoxin concentration. The following equation can be used to calculate the estimated adult dose of Digibind (in number of vials) from steady state digoxin concentration in chronic dosing:Dose (number of vials) = (plasma digoxin concentration in ng/ml xweight in kg) divided by 100. The above calculation should not be used in cases of acute digoxin ingestion or for children.In her case his dose was based on a chronic dosing schedule and his digoxin plasma concentration (7ng/ml), using the dosing table available in the drug monograph. Five vials of Digibind were administered to Mrs over 30 minutes. Following the administration of Digibind, digoxin plasma concentrations will be distorted for up to one week, since the Digibind will have pulled the digoxin out of the tissues and into the bloodstream for excretion.

her AF had been persistent for many years, with variable rates (slow and fast AF). AF is the most common significant arrhythmia associated with the risk of stroke and subsequent cardiovascular morbidity and mortality. The objective of treatment for AF is controlling the ventricular rate or maintaining sinus rhythm and preventing embolic complications.

Independent risk factors for AF include age, valvular heart disease, hypertension, diabetes and myocardial infarction. She hadmost of these risk factors. she had been prescribed amiodarone in the past but had been takenoff this because of intolerable side effects, and started on digoxin instead. However her AF remained a problem. she was discharged free of digoxin toxicity, on bisoprolol 5mg om. she was given an ambulatory 24-hour ECG monitor to identify the pattern of AF and an outpatient appointment was scheduled to decide whether digoxin should be restarted at a lower dose. Should digoxin be restarted, the patient must be educated about the signs and symptoms of digoxin toxicity. It would also be essential to routinely monitor urea, electrolytes and renal function in this patient. her potassium levels returned to normal the day after Digibind administration. Had the level been over 5.5, hyperkalaemia would have been treated with a glucose/insulin drip or sodium bicarbonate. Intravenous calcium is usually avoided in these cases because it may precipitate ventricular fibrillation or cardiac arrest.

Conclusion-

Physicians should ensure that patients taking digoxin are aware of the symptoms of digitalis toxicity. In addition, patients should be educated about drug interactions and about maintaining adequate hydration. Parents of pediatric patients should be educated about effective home childproofing and preventive measures

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