Case report

Reversible high degree AV block following phenytoin infusion

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Introduction:

Phenytoin intravenously is an effective and well tolerated drug in the treatment of epilepsy when given at recommended infusion rates and doses.(1) It is class IB antiarrhythmic agent that has been successfully utilized for over half a century for treatment of ventricular arrhythmias. It primarily shortens action potentials and inhibits rapid inward sodium current. Over the recent years it has been replaced by newer, more effective and less toxic antiarrhythmic agents. (2)

Slow administration of phenytoin is advised because it may cause

atrioventricular-block (AVB) (up to 2% with infusion rates of more than 50 mg/minute) or hypotension (up to 50% with infusion rates of >50 mg/minute). (3)

This case reviews a patient who developed reversible high degree AVB (second and third degree) after slow infusion 4 mg /min intravenous administration of phenytoin

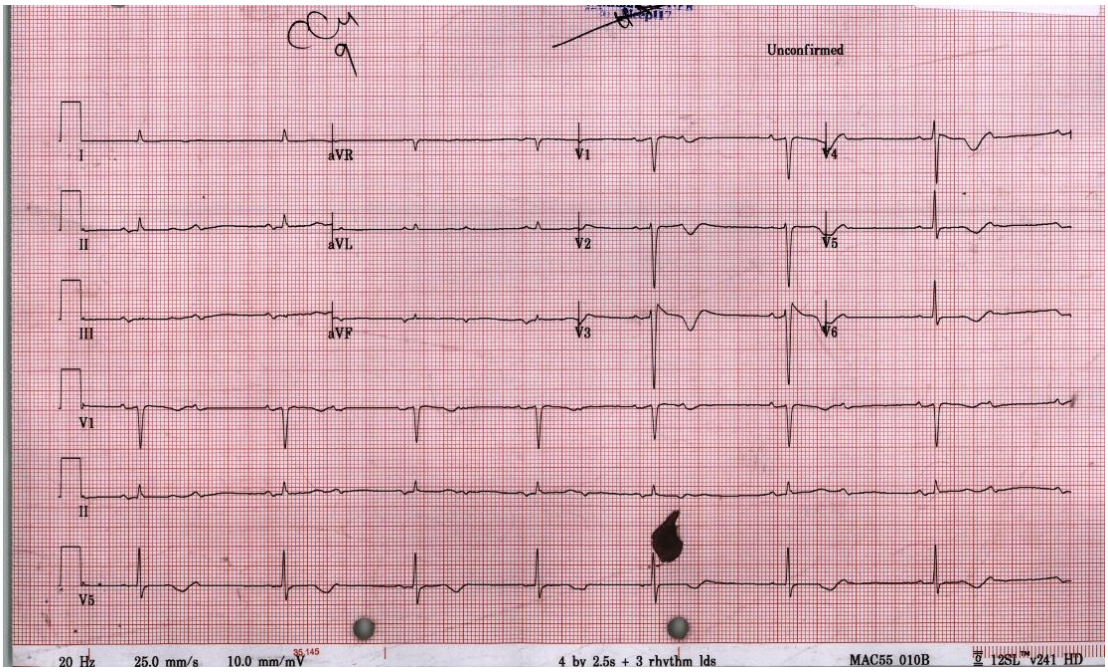
Key words: high degree AV block, phenytoin, infusion rate, case report

Interest of conflict: no conflict was declared

Case presentation:

We present an 89-year-old woman presented to the emergency room with tonic clonic seizures and decreased level of consciousness due to missing doses of leviceritam for 3 days. Past medical history includes, diabetes mellitus (DM), epilepsy, and cerebrovascular accident (CVA) with residual right hemiparesis. Home medications were: Levetiracetam 500 mg PO OD; gliclazide 30 PO OD; Atorvastatin 20 mg PO OD; Mirtazepine 30 mg PO OD; ASA 81 mg PO OD; Pantoprazol40 mg PO OD. There is no family history of coronary artery disease or sudden cardiac death. Vital signs on presentation were, a temperature of 36.5°C, blood pressure of 144/74mm/Hg, heart rate of 83 beats per minute and respiratory rate of 20 breaths per minute, and oxygen saturation was 93% on two liters of oxygen via nasal cannula. Heart exam was unremarkable. The remaining physical exam was normal apart from right sided hemiparesis. ECG was not done initially because she was convulsing at

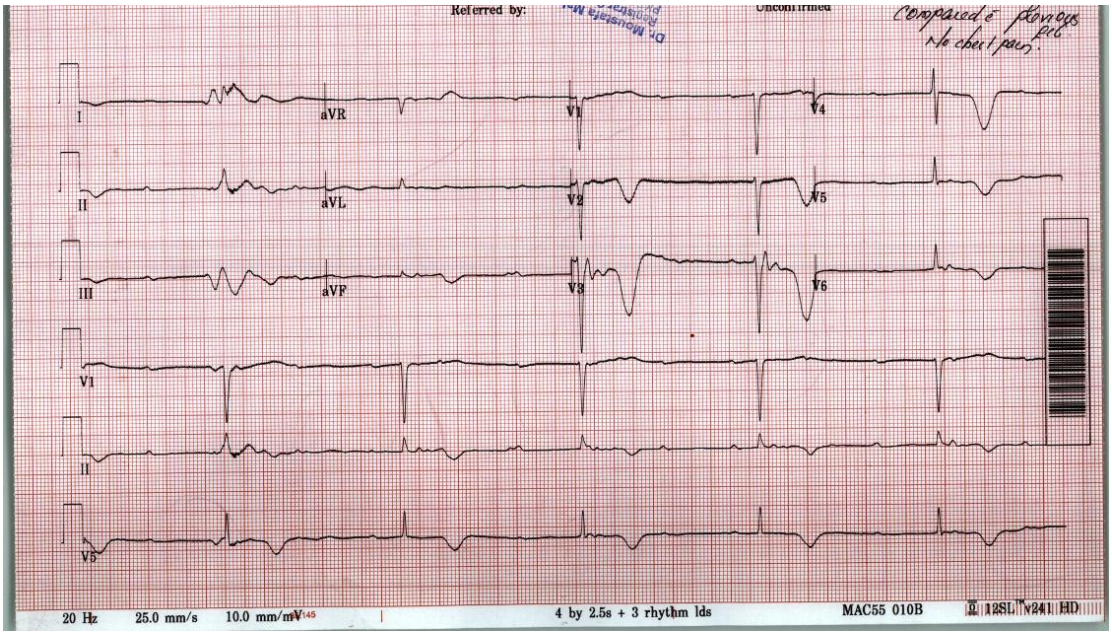
presentation. In ER initially, 5mg IV diazepam was given stat and 500 mg of IV phenytoin in 500 ml of normal saline over 2 hours (4mg /min). Laboratory findings on admission were all normal apart from mild decrease in serum potassium and, magnesium (3.4 meq/L is 0.6 mmol/L, respectively) which were corrected later , cardiac biomarkers and thyroid function test were normal as well as Transthoracic echocardiogram (TTE). CT brain showed age related global atrophic changes old ischemic left frontal parasagittal region, Chest X-ray was normal. Shortly after phenytoin infusion she developed second degree AVB (2:1 block) with HR 45 bpm (beats per minute) with some repolarization abnormality (**Figure 1**).



(Fig-1) 2:1 AV block after IV phenytoin with repolarization abnormality

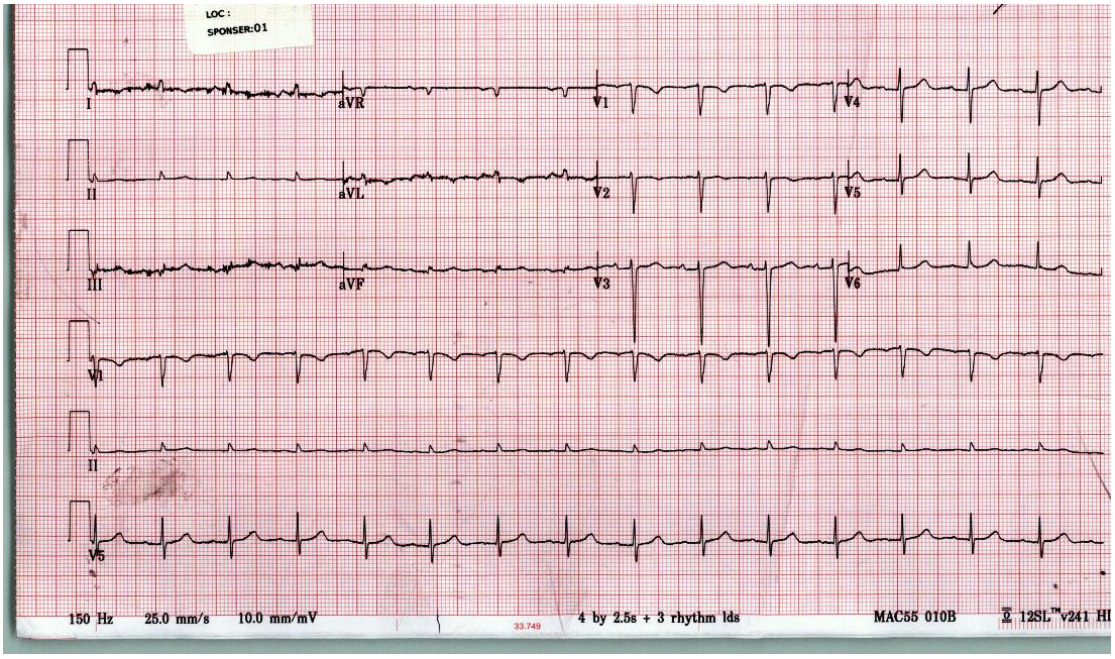
Atropine 0.5mg was given IV STAT and dopamine infusion was started and titrated to 10 mcg/kg /min according to HR response and was transferred to CCU (cardiac care unit).. The serum phenytoin level was checked and came in therapeutic range at 10.4 (therapeutic is 10– 20 microgram/dL). Next day she developed complete atrio-ventricular block

(CHB), HR of 30 bpm with QT prolongation and deeper T-Wave inversion (**Figure 2**) without symptoms or signs of hypo perfusion and temporary pacing wire was not inserted. On the 3rd day morning she resumed her normal rhythm and rate with 1:1 conduction HR 88 BPM and repolarization has normalized. (**Figure 3).**



(fig-2) complete heart block with more T wave inversion next day after IV phenytoin

She stayed at CCU for another 72 hours after dopamine holding with no episodes of bradycardia, and discharged home on her previous home medications Serum troponin were repeatedly within normal limits. No events for almost 1 month after discharge.



(fig-3) resumption of 1:1 conduction with normalization of repolarization on day 3 after IV phenytoin

Discussion:

Phenytoin is known to be a cell membrane depressant, it inhibits both automaticity and excitability of myocardial cell.(4) Unwanted effects of phenytoin on cardiovascular system which have been reported include depression of myocardial contractility, decreased peripheral vascular resistance and disturbances of rate and rhythm.(5) Clinically, the effect of phenytoin on sinus cycle length is variable (6) and sinus arrest has been reported.(7) Factors that have been reported to precipitate side effects of phenytoin are as follows; old age, severe heart failure, severe anemia, hypotension, hypoxia, and acidosis(8). In our patient all these factors were not present, other probable cardiac causes of CHB, such as ischemic heart disease, heart failure, cardiomyopathy, or infection (myocarditis, rheumatic) were all ruled out. Several other secondary causes of conduction defects such as hyperkalemia or hypokalemia, azotemia,

endocrine abnormalities (hypothyroidism) were excluded, because after correction of mild electrolytes disturbances (hypomagnesaemia and hypokalemia) her conduction abnormality didn't improve. In regards to repolarization abnormality that detected in the ECG after phenytoin infusion can be explained by the effect of phenytoin as it's NA blocking agent and it can affect both depolarization and repolarization as Naruya Ishizue and his group has reported that, some antiepileptic drugs which possess sodium blocking effect can result in repolarization abnormality (ST-T changes) when given in high doses, however little is known about ECG changes that occur at therapeutic antiepileptic doses .(12)

After excluding the common causes of CHB we came to the following conclusion that, high degree AVB (second and third degree AVB) can be induced by phenytoin administration regardless of infusion rate. Several reports of worsening AV nodal conduction have been reported with the use of intravenous phenytoin in critically ill patients (9) .However they are all attributed that to rapid infusion rate of phenytoin , underlying structural or conduction heart disease that were reported in their patients(10, 11). But in our case the patient developed conduction abnormality after slow and recommended infusion rate, (<50mg/min) , which makes us reconsider that the infusion rate is not more important factor than the advance age as well as the possibility of female gender in the occurrence of cardiovascular side effect of phenytoin despite its slow administration and normal range of therapeutic level .

Conclusion:

The advance age and may be female gender are more important risk factors that render the patient more prone and sensitive to develop the cardiovascular side effects of phenytoin mainly the conduction defects.

Slow infusion rate still shouldn’t be ignored and it's wise to follow the recommended rate. ST-T changes following phenytoin administration still needs to be more investigated.

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